word is widely distrusted by politicians precisely because they are experts. Xenophon stalks among us again. The proponents of regulation, and those who support and encourage them, are all too often convinced that experts are venal and devoid of public spirit (just as the free citizens of ancient Greece regarded their bonded craftsmen). When the mining specialists plead public interest, the fact that the plea comes from them at once invalidates it. But the inevitable consequence is that the same judgment is being applied to the regulators themselves: they have by now as great an interest vested in the increase of regulations as the protesters have in their abatement. Not only that: those miners, MSEs, and may others to whom by implication Xenophon's cold dictum is attached, conclude that their honesty is disbelieved by some of the most powerful in the land, and when a professional's integrity is systematically impugned, he is driven at last towards political extremes; at the least he will come to distrust the regulators' own honesty of purpose. The prospect is not enticing, and the American crisis of regulations should give us in Britain pause. □

Aetiology of natural scrapie

from H. B. Parry

THE crux of the problem raised by Kimberlin recently in News and Views[1] is the principal means by which natural scrapie of sheep is disseminated. My report[2], which stimulated him, was confined to providing new evidence for a heriditary factor and to demonstrating a new practical means of genetic control under current agricultural practice. Kimberlin's account[1], summarising the published laboratory studies of his colleagues[3], widens the issue of aetiology without considering relevant evidence from the epidemiology of the natural disease or from the possible pathogenesis of the characteristic sequential localised neuronal decay.

There are two main aetiological factors. First, a neurotoxic agent is present in the tissues of animals with the pathological lesions of scrapie and is transmissible artificially[4]. This is commonly called a 'slow virus', or more accurately a transmissible spongiform encephalopathic agent (TSEPA) from the pathological nature of the special neurotoxic damage developing in inoculated animals. In the absence of any reliable means of detecting the TSEPA in the living animal, we have no data on the occurrence of the agent in any sheep population. Second, there is a hereditary factor, probably a single autosomal recessive gene, with an 'all-or-none' effect on the development of the primary neuronal decay, for which no simple peripheral 'marker' reaction is known. However, indirect inferences of the gene's likely presence can be made on the basis of the results of test-mating procedures and meticulous breeding records[1].

Without such data, assessments of recessive allele frequencies are notoriously hazardous when based solely on the statements of individual flockowners and shepherds[5-7]. In my view the term 'scrapie-free' should mean free of the scrapie-allele, at least to a probability of less than 1 in 100; such sheep are available.

Spread of scrapie

The inferences of natural spread among experimental flocks, quoted by Kimberlin, are contrary to my field experience within breeding groups. Using recording methods designed to reveal such spread, I detected none, which is in accord with the evidence of many reliable observers since 1750[5-7] and with the results of other less well controlled current field observations. No spread has followed the introduction since 1950 of British sheep, which developed the disease, into certain countries that are free of the disease and have not operated any quarantine or slaughter policy. One therefore seeks possible explanations for the anomalous conclusions quoted by Kimberlin. There are four main considerations.

First, the data he quotes relate to four British sheep breeds, all of which have had substantial scrapie attack-rates at some period since 1900 and three very seriously in some sectors of their breeds since 1950 until the present time. In these circumstances the designation 'scrapie-free' applied to a sheep, a flock or a breed without meticulously supervised and relevant records, covering at least one decade before and continuously during the experimental period, lacks any precise scientific meaning. This is because the TSEPA cannot be detected and the recessive scrapie allele is likely to be widespread but clinically 'silent' in these breeds and may at any time without prior evidence reach frequencies leading to clinical manifestation[2]. Thus the group designated 'scrapie-free' is likely to consist of mixed populations of the three genotypes. The authors quoted by Kimberlin provide no indication that the proper safeguards against these possibilities have been enforced. The meaningful interpretation of results from such populations on the present evidence is thus not possible.

The second consideration is that the results quoted are commonly presented as totals of all matings between so-called 'scrapie-free' and 'scrapie-affected' groups without any attempt to assess presumptive recessive genotype frequencies in each group. Third, the aggregation of the results of different sire-progeny groups as accumulated totals masks information relevant to their proper evaluation, for example, the possible proportions of the three recessive genotypes and allele frequencies in different sectors of the breeding population, the degree of in-breeding, occurrences of associated sub-normal health and reproductive efficiency, which may affect the totals manifesting scrapie and their ratios. Fourth, the American experience, quoted by Kimberlin, kindly made available by Dr. J. L. Hourrigan, when analysed, as far as the data allow, on a provisional genotype basis, are approximately compatible with my own. I therefore have serious reservations of the validity of the conclusions derived from the experimental flocks quoted as evidence for the normal dissemination of natural scrapie by the spread of a communicable agent.

Artificial scrapie and genetic control

The artificially induced form of scrapie disease is probably not identical to the natural form and the precise transferring of the results of the one to the other is questionable. In most of the studies quoted by Kimberlin the source of inocula of scrapie TSEPA material designated SSPB/1 was derived from 40 affected sheep brains. After 20 years this is now very much more toxic than any TSEPA we have been able to demonstrate in the natural disease on first transfer.

These reservations do not preclude extrinsic factors operating in natural scrapie, merely that their possible occurrence requires more precise definition. Any aetiological hypothesis must also provide an acceptable explanation of the specific characteristics of the neuronal degeneration in the natural disease[8]. □

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H. B. Parry works at the Nuffield Institute for Medical Research, University of Oxford, UK.

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