Veterinary research at the Central Veterinary Laboratory, Weybridge, with special reference to scrapie and bovine spongiform encephalopathy

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Mr R. Bradley is an independent consultant who is now retired from the staff of the Central Veterinary Laboratory. The views presented in this paper are those of the author alone.

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Summary
A Veterinary Laboratory Service was commissioned by the Ministry of Agriculture, Fisheries and Food of the United Kingdom in 1894 and the Service commenced veterinary research in 1905. The Central Veterinary Laboratory (CVL) was opened in 1917 and has become known world-wide under the name 'Weybridge'. In 1922, a network of Veterinary Investigation Centres was established in England and Wales and these continue to make an important contribution to surveillance for animal diseases. Problems recognised at these centres provide an important stimulus for research at the CVL, a good example being the case of bovine spongiform encephalopathy (BSE). Research into many non-infectious and infectious diseases is conducted, and research into scrapie was already in progress when BSE was discovered in 1986. A research programme was commenced to investigate the clinical signs, diagnostic methods, pathology, pathogenesis and epidemiology of BSE and the transmission characteristics of the BSE agent in farm animals. Some of the results of these studies and prospects for the future are discussed.

Keywords
Bovine spongiform encephalopathy – Cattle diseases – Central Veterinary Laboratory – Prion diseases – Scrapie – Sheep diseases – Veterinary Laboratories Agency – Veterinary research.

Introduction
The Veterinary Laboratory Service of the Ministry of Agriculture, Fisheries and Food (MAFF) in the United Kingdom (UK) was commissioned in 1894 to provide support for animal disease eradication schemes and particularly to deal with an epidemic of classical swine fever. The Service commenced veterinary research in 1905 under the direction of the Chief Veterinary Officer, Sir Stewart Stockman. However, only in 1917 was the Central Veterinary Laboratory (CVL) opened on the present site, now known world-wide as 'Weybridge'. The CVL was one of the first purpose-built State veterinary laboratories in the world.

The CVL is situated in the Borough of Runnymede (historically well-known because of the Magna Carta) and was originally in the postal district of Weybridge (now Addlestone), hence the name. In 1937, a satellite laboratory was established in Lasswade, Edinburgh, to monitor animal health in Scotland. The main campus now occupies
approximately 12 ha, with 78 ha of associated grassland. A further 46 ha are situated on a separate site, in addition to animal facilities at other sites now privatised. All of these are used to support the various research and service projects concerned with animal and public health.

From 1922, a network of Veterinary Investigation Centres (VIC) was established in Great Britain, managed separately as the Veterinary Investigation Service (VIS) in England and Wales (controlled by central Government) and the Scottish VIS in Scotland (controlled by the appropriate departments of the Scottish Colleges of Agriculture [SAC] and the Central Office of the SAC). One of the major functions of the VIC is to conduct surveillance for livestock diseases in their locality, drawing the attention of the CVL to deviations from the norm. An equivalent system operates in Northern Ireland, through the Northern Ireland Department of Agriculture. These centres work closely with, and provide a laboratory service for, veterinary surgeons in private practice for the benefit of livestock farmers. The expert knowledge of veterinarians at the centres, in terms of local conditions and problems, makes a vital contribution to the overall awareness of the health status of livestock in the country. Importantly, the strong connections between VIC and the central laboratories provide the essential stimulus for research to commence rapidly following initial detection of a disease. The VIC also provide the pathological or serological samples necessary to initiate investigation.

In 1990, the CVL became an Executive Agency of MAFF, assuming responsibility for the management of affairs and balancing income and expenditure within the Agency. Much of the work of the CVL is contracted with MAFF to support and develop policy in regard to animal health and welfare, public health and food safety. However, the agency now has an increased ability to provide services to the private sector. In 1995, the CVL and the VIS were merged under the CVL Chief Executive, to form the Veterinary Laboratories Agency (VLA). The new organisation thrives on the strength of these constituent parts and enables further rationalisation of services to provide even higher standards that benefit all customers. The VLA remains at the heart of new developments in animal disease recognition, diagnosis, surveillance and monitoring, enabling MAFF to develop control policies with a sound scientific basis. This is in line with the aims of the European Commission (EC), the Office International des Epizooties (OIE) and the World Health Organization (WHO), whose collective purpose is to promote public health, animal health and welfare, and food safety. The OIE provides the guidelines for trade in live animals and animal products for the World Trade Association, to allow movement between countries with negligible risk of introducing disease. Nowhere is this more evident than in the field of bovine and other spongiform encephalopathies of animals, subjects that currently occupy a significant proportion of the service and research facilities of the VLA.

General research activities

Flexibility of operation has always been one of the hallmarks of research at the CVL. For example, research into foot and mouth disease was initiated in 1924, but was transferred to the high security disease laboratories of the Animal Virus Research Institute at Pirbright in 1939. Such flexibility has always been an essential part of research at the CVL. The Agriculture Act of 1937, which demanded greater resources for diagnosis, prevention and eradication of livestock diseases, resulted in the expansion of facilities to discharge the additional responsibilities. Tuberculin has been manufactured and standardised at the CVL since 1939. Production of vaccines against anthrax, brucellosis caused by Brucella abortus (strain 19 vaccine) and classical swine fever (crystal violet vaccine) followed. Each of these has contributed to the eradication of the diseases.

At one time, thirteen departments existed at the CVL, some aetiological, others specialist, some on site, others remote. The identity of these departments is now less evident, as the departmental structures have been altered to accommodate new requirements. Other notable CVL successes in infectious disease investigation have included research into Newcastle disease and avian influenza (the CVL is an EC, OIE and Food and Agriculture Organization [FAO] Reference Laboratory for both of these diseases), brucellosis, rabies and international standards (for each of which CVL is a WHO Collaborating Centre) and a range of bovine, caprine, equine, ovine, porcine and avian diseases (for which the CVL is an OIE Reference Laboratory). The work of the CVL is truly international in this respect.

Infectious diseases, such as tuberculosis, Johne's disease, salmonellosis, bovine mastitis, respiratory and enteric viral and parasitic diseases caused by conventional organisms, have historically been the principal areas of research. However, since the 1960s, pathology, and more recently, epidemiology, have been dominant disciplines in elucidating the morphological nature of diseases, the causes and the associated factors. The design of surveys, analysis of risk, the effect of different risk management strategies on disease outcome, and the prediction of future incidence for budgeting and other purposes are also important responsibilities.

The opposite end of the spectrum to epidemiology is molecular biology, which is also used to elucidate disease mechanisms and develop diagnostic tests. This is particularly evident in scrapie and BSE research which is discussed in greater detail below. The advent of the monoclonal antibody, the development and application of the polymerase chain reaction and immunocytochemistry have all been applied to these and other diseases and have aided the production of more sensitive and specific tests for particular agents and disease confirmation. These recent developments are reminiscent of the work performed in the early 1940s by
R.A. Coombs, a John Lucas Walker student working with an Agricultural Research Council grant in the CVL Pathology Department under N.H. Hole (at that time Head of Department). Coombs and Hole published a series of papers on the conglutination phenomenon (17) which had a considerable relevance to the detection of haemolytic disease of the new-born, to forensic medicine and to bacterial serology. Coombs moved to the University of Cambridge in 1945 and subsequently became a member of the Royal Society. The anti-globulin test he also developed, known world-wide as the Coombs' test, is still used in the serology. Coombs' test for Johne's disease and up to 15,000 tests were performed annually for diagnostic, sale and export purposes. However, this was insignificant when compared to the annual three million automated Rose Bengal tests for bovine brucellosis, which were conducted collectively in the Diseases of Breeding Department, CVL Lasswade, and the VIC at Worcester, at the height of the B. abortus eradication programme in cattle. The disease is now eradicated.

Morphological pathology gained prominence through the elucidation of a range of ill-defined nervous diseases of poultry, such as epidemic tremor and encephalomalacia. Concurrently, Hole had developed the complement fixation test for Johnes's disease and up to 15,000 tests were performed annually for diagnostic, sale and export purposes. However, this was insignificant when compared to the annual three million automated Rose Bengal tests for bovine brucellosis, which were conducted collectively in the Diseases of Breeding Department, CVL Lasswade, and the VIC at Worcester, at the height of the B. abortus eradication programme in cattle. The disease is now eradicated.

The subject of neuropathology became the dominant work of the Pathology Department during the 1960s. Many hitherto unrecognised diseases were discovered and morphologically defined at the histological level. Neuropathology became an important tool in regard to the diagnosis, control and eventual eradication of classical swine fever and resulted in vast numbers of porcine brains being processed for microscopical examination. During this productive period, eosinophilic meningoencephalitis, Talfan disease, cerebrospinal angiopathy and various types of porcine congenital tremor were investigated and described. In ruminants, cerebrocortical necrosis (polioencephalomalacia) of cattle and sheep, border disease and pulmonary adenomatosis (jaagsiekte) of sheep were investigated and fundamental reports were published.

In the 1970s, the expertise in neuropathology was further developed using specialised techniques including electron microscopy. Studies of reproductive pathology and a wide range of muscle diseases were added to the repertoire. Amongst the latter was bovine and ovine myodegeneration (white muscle disease), a complex multifactorial disease associated with dietary deficiencies of selenium and vitamin E and other environmental factors. This was investigated by a team comprising pathologists, biochemists and epidemiologists in the laboratory, and VIC staff, practitioners and farmers in the field. This enabled advice to be given, particularly in regard to nutrition, to prevent the occurrence of this often fatal disease. The Epidemiology Department (which begun life earlier as a small sub-Section of the Pathology Department) was developing rapidly and becoming a major discipline.

Reproductive pathology was developed in both pigs and ruminants. Notably, expertise at the international level was developed in embryo transfer methodology, to enable advice to be given to MAFF of any aspect of risk from infectious disease, in regard to international trade in embryos. All of these events prepared the CVL for the crisis that commenced in November 1986, namely, the advent of bovine spongiform encephalopathy (BSE). All the major disciplines necessary to investigate the new phenomenon were in place. The Pathology Department received from the VIC the first brains for microscopic examination from cattle with a novel neurological disease. The Department already had internationally recognised expertise in neuropathology (the method used internationally to confirm the disease). The CVL also had internationally recognised expertise in epidemiology. This enabled the cause to be identified, the risks to be analysed and predictions made about the future course of the epidemic. Exemplary expertise in embryo transfer enabled the largest project of this kind to be initiated. The objectives were to determine whether or not bovine embryos derived from BSE-affected cattle were infective for recipient dams and progeny if collected and transferred according to the protocols of the International Embryo Transfer Society. For this purpose, 350 BSE-free heifers were imported from New Zealand by air. To date, no evidence has been found to suggest that bovine embryos transmit BSE. Some of these aspects will be discussed in more detail below.

**Bovine spongiform encephalopathy**

Bovine spongiform encephalopathy is a member of the group of diseases previously known as sub-acute transmissible spongiform encephalopathies, or prion diseases (28). This group includes Creutzfeldt-Jakob disease (CJD) and kuru of humans, and scrapie of sheep and goats. All are fatal, experimentally transmissible and exhibit the fundamental neuropathological triad of spongiform change, neuronal cell loss and astrocytosis in the brain. Another unique feature is the presence of the disease-specific form (PrPSc) of the normal membrane protein, PrP (31). This protein can be recognised directly in tissue sections of fixed material using immunohistochemical methods and in unfixed brain tissue by immunoblotting (Western blotting and variations, e.g. dot blot, enzyme-linked immunosorbent assay [ELISA] and sandwich immunoassay) or by electron microscopic examination of proteinase K-treated, electron densely-stained, detergent extracts of brain. In the latter examination, the investigator searches for disease-specific fibrils, termed scrapie-associated fibrils (S AF) (21). In some brains affected with some forms of transmissible spongiform encephalopathy...
(TSE), amyloid plaques are observed in tissue sections, even with simple morphological stains, although these plaques also stain positively for both amyloid and for prion protein (PrP).

At the outset, in November 1986, it was recognised that if BSE (as the new disease was later to be called [48]) was indeed a transmissible spongiform encephalopathy or prion disease, and was to occur on a significant scale, serious repercussions for international trade in cattle and cattle products were likely. This was clear because of existing trading restrictions on live sheep exports from countries with scrapie. In addition, concerns were raised that BSE may have a different pathogenicity for humans than scrapie, which is regarded solely as an animal pathogen.

A research programme was developed to investigate the clinical signs, pathology and epidemiology of BSE and subsequently to research diagnostic methods, pathogenesis and transmission characteristics of the agent that causes the disease.

Clinical-pathology

The neurological signs of BSE are insidious in onset and progressive leading to recumbency and death. The duration of signs is from seven days to fourteen months, but is typically one to two months. Signs manifest as changes in mental status exhibited as apprehension, frenzy and nervousness of doorways, changes in sensation, notably hyperaesthesia to touch and sound (48), and abnormalities of posture and movement, particularly low head carriage, hind limb ataxia, tremors and falling. Of these signs, the most frequently recorded are apprehension, hyperaesthesia and ataxia (57). General signs include loss of condition and milk yield. Rumination is reduced (2). Latent signs can be precipitated by stress such as that caused by transportation.

Lesions are restricted to the central nervous system and generally resemble those observed in scrapie. The lesions consist of microcystic cavitation of the grey matter neuropil, i.e. spongiosis or spongiform change, solitary or multiple vacuolation of neuronal perikarya (56), astrocyte hypertrophy, neuronal cell loss, particularly in the vestibular complex (19), and the presence of PrPSc.

The clinical signs are sufficiently clear to permit identification of suspect cases for further investigation. However, a number of clinically similar conditions exist, with which BSE can be confused. Microscopic examination of the brain is a precise means for confirming the disease with a high degree of accuracy, providing the fixation quality is adequate. If the brain is autolysed, supplementary methods, such as detection of SAF (40) or PrPSc by immunoblotting (23) can confirm the clinical diagnosis. In the UK, approximately 85% of clinically suspect cases of BSE are confirmed, although the percentage of confirmations made by brain examination of suspect cases is currently declining, as would be expected as the disease approaches elimination. Eventually, when elimination is achieved, clinically suspect cases may still be reported but none will be confirmed, as is now the case in BSE-free countries conducting effective surveillance for the disease. This is because the cause of the neurological signs in these animals is distinct from BSE. Methods for post-mortem confirmation are given in the OIE Manual of Standards for Diagnostic Tests and Vaccines (24).

Epidemiology

Epidemiological studies (34) have revealed that BSE is a new disease of adult cattle with a peak age at onset of four to five years and a mean incubation period of sixty months (32). All breeds appear to be susceptible and, unlike sheep scrapie, no major genetic component contributes to disease occurrence. The disease is caused by an unconventional transmissible agent or prion, the precise origin of which remains to be determined. The vehicle of infection is meat-and-bone meal (MBM) that was incorporated into concentrate feedstuffs or feed supplements. The feeding of ruminant or mammalian protein to ruminant animals is now prohibited in many countries of the world, regardless of whether the country has experienced BSE. In the UK, the ban is even more extensive (see below). The majority of cases of BSE in the UK have resulted from the recycling of rendered, infected cattle offal, through MBM (55).

Ruminant feed bans have reduced the risk of new exposure, and thus reduced cases of clinical disease in recent years, but have not been found to be completely effective in preventing new exposure. Such is the case in ten countries of western Europe that have experienced BSE in native-born cattle. Cross-contamination of ruminant feedstuffs with ruminant protein during production, transportation and use is the cause (52, 53). To prevent this problem in the UK, since March 1996, mamalian MBM has been prohibited for feeding to any species of food-producing animal, including horses and fish. From 1 August 1996 (the date by which all feed mills and on-farm feed stores were cleaned and decontaminated), no further exposure from feed should have been possible. These measures, in addition to the introduction of a specified bovine offal ban in the UK in 1989 and 1990 and subsequently extended as a ban on specified risk materials (SRM) have resulted in a massive decline in the BSE epidemic. The epidemic in the UK is predicted to be close to extinction by 2001 (1) and this may be accelerated by the operation of the 'Over Thirty Months Scheme' (60). This scheme removes from the food chain, cattle over the age of thirty months in the UK. However, one case of BSE has occurred in an animal born in the UK after 1 August 1996. Furthermore, analyses of more recent data from the epidemic in the UK suggest that a few cases may be reported after 2001, although none of these should enter the human or animal food chains.

The within-herd incidence of confirmed BSE has always been below 3% and has declined with the epidemic. This supports other epidemiological data that horizontal transmission does not occur, or is a very rare event. The concept of a low random
has been confirmed in the Republic of Ireland and two contrast with the UK, which had reported nearly 177,000 definite cases and one possible case reported in France. In seven probable cases that are still alive. In addition, one case probable cases of vCJD have been reported in the UK and cattle before the specified bovine offal ban was in place in UK, initially reported in 1996 (59), is of concern because the consumption of infected central nervous tissues from infected are not, the origin. If cattle products are responsible, then however, to date, no proof exists that cattle products are, or indistinguishable from the agent that causes BSE (9). The agent isolated from humans with vCJD was biologically related to exposure through feed or as true maternal transmission is unresolved. If maternal transmission does occur, this will not significantly prolong the epidemic or transmission can be achieved. The risk of BSE occurrence in the offspring of BSE-affected cattle may be slightly greater than average (58). However, whether this can be interpreted as an undefined genetic effect related to exposure through feed or as true maternal transmission is unresolved. If maternal transmission does occur, this will not significantly prolong the epidemic or prevent eradication.

The occurrence of a new variant form of CJD (vCJD) in the UK, initially reported in 1996 (59), is of concern because the agent isolated from humans with vCJD was biologically indistinguishable from the agent that causes BSE (9). However, to date, no proof exists that cattle products are, or are not, the origin. If cattle products are responsible, then exposure is most likely to have occurred through consumption of infected central nervous tissues from infected cattle before the specified bovine offal ban was in place in 1989. To date (August 2000), a total of sixty-eight definite or probable cases of vCJD have been reported in the UK and seven probable cases that are still alive. In addition, one case has been confirmed in the Republic of Ireland and two definite cases and one possible case reported in France. In contrast with the UK, which had reported nearly 177,000 cases of BSE by May 2000, the Republic of Ireland had reported less than 500 cases and France less than 100 cases in native-born cattle, by the same date. All these features and the consequences for industries producing animal feed, human food, medicines, devices or cosmetics using bovine materials, have caused world-wide concern. All raw materials used in these industries should be obtained from safe sources. Despite all these unwelcome incidents, the CVL has responded to the challenge of BSE and led the world in supplying the scientific information upon which control and eventually eradication can be achieved.

Transmission studies

Concurrent with the epidemic of BSE in cattle, new TSEs of several other species of Bovidae and Felidae were reported (3). Excluding cases in domestic cats (30), all have been in captive wild animals in Great Britain or in animals that have been exported from Great Britain. The origin in Bovidae is infected MBM. In captive wild cats, consumption of uncooked BSE-infected central nervous tissue is more likely to be responsible. The origin in domestic cats is less clear, but is likely to have been feed. The incidence in all these species has declined as a result of the various control measures implemented during the period from 1988 to 1990. A BSE-like agent has been isolated from three domestic cats, a nyala and a greater kudu, suggesting a bovine origin (7, 8).

Experimentally, BSE has been transmitted to cattle, sheep, goats, pigs, mink, mice and four species of non-human primate (4, 14, 33; C.J. Gibbs Jr, personal communication). Pigs have resisted high dose experimental oral infection (G.A.H. Wells, personal communication). Direct transmission to either chickens or hamsters following high dose experimental challenge with brain from affected cattle has not been successful.

In clinically affected cattle which have been naturally infected with BSE, infectivity has been detected only in the central nervous system, namely the brain, spinal cord and retina. No infectivity was detected in a wide range of other tissues, including skeletal muscle, mammary gland (6, 15, 22; H. Fraser, personal communication) and milk (44). Bovine milk and semen are amongst a range of commodities that can be traded without restriction, even from countries with a high incidence of BSE, because these products are recognised to be safe in regard to BSE (26).

Following high dose oral challenge (100 g of untreated brain from cattle naturally-infected with BSE, infectivity has been found in the distal ileum six to eighteen months after dosing (49), and again after the onset of clinical disease at thirty-five months post challenge. Infectivity is believed, but not proven, to be associated with the occurrence of lymphoreticular tissue in the form of Peyer's patches, which abound at this site. From thirty-two months post challenge (three months before the onset of clinical signs), infectivity was detected consistently in brain, spinal cord and cerebral and dorsal root ganglia (50).
No infectivity was detected in any of a range of other tissues other than in a single instance in the bone marrow collected during the clinical phase of disease. However, some doubts have been voiced about the integrity of this particular result (51).

In an incomplete comparative bioassay using mice and cattle, the latter species was demonstrated to be approximately 1,000 times more sensitive for detection of infectivity in the brain. No infectivity has been detected in spleen or lymph nodes by mice and so far, based on clinical evidence at over eighty months post challenge, the result in cattle is the same (S.A.C. Hawkins, personal communication).

**Scrapie**

Scrapie has been well known in England and the rest of Europe since at least the 18th Century. The characteristic lesion of scrapie (neuronal vacuolation) was reported in the spinal cord of sheep in France following pathological studies in the 1890s (3). During the period from 1910 to 1926, Sir Stewart Stockman, as Director and Chief Veterinary Officer at the CVL, studied scrapie of sheep and published articles on this enigmatic disease, including the results following treatment (42, 43). Some of the clinical cases of natural scrapie that were brought to Weybridge subsequently recovered (43), an occurrence which still remains to be explained. Subsequently in France, Cuillé and Chelle from the Toulouse Veterinary School had succeeded in transmitting infected spinal cord tissue (11).

The CVL continued involvement in scrapie through the pathological diagnostic service developed in the 1960s. However, little formal research was performed other than to establish an alternative, practical means of diagnosis of scrapie by electron microscopic examination for SAF (41). During this period, important discoveries were made at the Institute for Animal Health (IAH), first at Compton by Chandler, Pattison, Kimberlin, G. Hunter and others, and subsequently by Dickinson, Kimberlin, Fraser, Bruce, Hope, N. Hunter and others at the Neuropathogenesis Unit (NPU) in Edinburgh. These included the establishment of the mouse and hamster as experimental models for studying scrapie pathogenesis, the nature of the scrapie agent and transmission characteristics, and most importantly, the role of host genes in the control of the incubation period (13). Polymorphism in the ovine PrP gene at codons 136, 154 and 171 influence the clinical occurrence of experimental scrapie in Cheviot sheep. The latter study initiated by N. Hunter and Goldmann has progressed by investigation of the PrP genotypes of sheep in flocks with and without natural scrapie (18). For clinical disease to result, infection appears to be required, in addition to the occurrence of particular allelic combinations. Thus, scrapie does not appear to be purely a hereditary disease, as was once believed. Furthermore, different breeds carry different combinations of alleles. These findings have been applied at the CVL and other laboratories (12) to rid flocks of scrapie-susceptible sheep over a period, by changing the frequency of alleles associated with the occurrence of clinical scrapie. This is achieved by introducing long incubation period alleles, so-called 'resistance' alleles, through the ram. However, many questions remain unanswered, for example whether or not 'scrapie resistant' sheep could be carriers of infection and whether all of the scrapie strains that occur in nature interact in a similar way with the PrP gene.

Although epidemiological investigations of scrapie have been conducted in the past, interpretations have been hampered by the long incubation period, the absence of knowledge regarding the genetic influence on disease occurrence, and the absence of a test to detect infected sheep. These problems are now close to being solved by genetic testing and by applying the recently developed tests for PrPSc to biopsies of tonsil (36, 39), nictitating membrane (third eyelid) (27) and blood (34). Thus, the outlook for improved epidemiological interpretation and eventual control and perhaps eradication of scrapie from flocks has never been more optimistic. The research that has led to this improved situation has been conducted by dedicated professionals with a long-term interest in scrapie, mainly in Great Britain, the United States of America (USA) and the Netherlands. These countries have scrapie in the native stock, but other researchers in Europe and Japan have also contributed to the pool of knowledge. What is now needed is a rapid and inexpensive test to distinguish, for example, between the BSE agent and scrapie agents. Such a test, based on cleavage sites and the glycosylation pattern of PrPSc, is being developed in various laboratories (10).

The discovery of BSE, and particularly the advent of vCJD, has stimulated a very large TSE research programme involving both BSE and scrapie. Of current interest is the possible role of MBM in the transmission of scrapie and the possible infection of sheep with the BSE agent by this route. No evidence has been found to suggest that this has happened or that an unexplained epidemic of TSE is occurring in sheep in any country. However, the true prevalence and incidence of scrapie, at least in countries of Europe, is not known with any certainty, as the disease can be concealed. The disease is not always officially reported even when incentives, such as financial compensation, are offered. In addition, whether some cases of scrapie are due to the BSE agent rather than to scrapie agents has not been established. Thus, the absence of observable or non-attributable change in the incidence of scrapie in different countries, does not permit any conclusion to be drawn as to whether the BSE agent is, or is not, responsible for any incident. Nevertheless, agent strain typing studies in a limited number of sheep in Great Britain (nine completed and over thirty others sufficiently advanced to allow preliminary judgement) have failed to reveal the singular fingerprint of the BSE agent so far. Further studies are in progress on a much larger scale at the VLA and the NPU. In
the meantime, TSE risk reduction policies have been adopted in some countries, notably Belgium, France, the Netherlands and the UK, to protect public and animal health from exposure to any TSE agent, including the theoretical presence of the BSE agent in small ruminants. The skull or head (including the brain and eye), spinal cord (in some countries limited by age) and spleen from sheep and goats are prohibited from entering any food chain. An EC Decision has recently been introduced which specifies that the skull (including the brains and eyes), the tonsils and the spinal cord of all sheep and goats over twelve months of age will be designated as SRM, as will the spleen of sheep and goats of all ages. This is due to come into effect on 1 October 2000 throughout the European Union (EU). This can be anticipated to significantly reduce any risks to consumers or animals from TSE agents in small ruminants, provided the ban is effectively enforced. The SRM will be removed in the abattoir (or cutting plant) and stained to distinguish from all other materials, before destruction. Should the BSE agent ever be isolated from a sheep or goat, more stringent measures are likely to be deemed necessary to ensure full protection of humans and animals.

Historically, scrapie has tended to become an endemic disease once introduced to a flock or country, unless stringent measures are taken. Sometimes even severe measures fail to eradicate the disease. This is because scrapie spreads not only by maternal transmission, by the placenta (29), but also by horizontal transmission (16), perhaps even from an infected environment. Thus, if BSE were ever to occur naturally in sheep, despite effective control of mammalian MBM in feed, the disease could theoretically be maintained by maternal and horizontal transmission. Research is currently in progress in the UK to investigate whether or not experimental BSE in sheep, despite effective control of mammalian MBM in feed, can be transmitted in these ways, and if so, by what mechanism. In the UK, the applied research approach at CVL complements the more fundamental studies conducted at the IAH in Compton, at the NPU in Edinburgh and in other UK laboratories, but international collaboration is vital to achieve progress in scrapie research. By such means, rules for safe trading can be established that have a scientific basis and are thus more likely to be supported by Member Countries of the OIE.

The future

The world economy relies on trade, of which trade in live animals and animal products is a vital component. Although protection of public health is paramount, the damaging effect of animal diseases on the viability of the livestock industry is also very important. According to the 1997-1998 report of the Controller and Auditor General in Great Britain, the BSE crisis had cost £2.5 billion since March 1996 and was estimated to cost £1 billion more by the year 2000. Thus, BSE has been a very costly disease to manage and eradicate. Eradication has not yet been accomplished in any country in which BSE has been found in native-born animals, although the disease is on course for extinction in the UK and is also declining in Switzerland and possibly in other countries.

Public confidence in the safety of food has played a prominent role in recent years in Europe, the USA and other developed countries, due to such problems as Salmonella Enteritidis phage type 4 in eggs, Listeria in cheese and Escherichia coli O157:H7 in meat. All individuals have a right to safe food. As veterinarians are intimately involved with the maintenance of food-animal health and with ante- and post-mortem examination of animals presented for slaughter for human consumption, they play an important role in ensuring the safety of food from animals. A vigilant veterinary profession, trained to the highest standards is therefore essential in all countries. These standards should be maintained by continuous professional development. The VLA has a central role in current programmes for maintaining and developing public and animal health in the UK.

The requirement and consumer demand for an integrated approach to food safety throughout the food chain has recently resulted in the creation of a Food Standards Agency (FSA) by the Government of the UK. This will be an ‘open’ organisation, independent of agricultural interests, thereby assuring consumers that the safety of food is the priority. A similar ‘farm to plate’ policy has been adopted by the EC and by several Member States of the EU.

In regard to the safety of animal feed, an Advisory Committee on animal feedstuffs has been established, as recommended in 1992 by the Expert Working Group on the subject. This should reduce the future risk from epidemics of feed-related illness, such as BSE, that result from unevaluated changes in feed sources, processing and compounding. The Committee will report to the FSA.

The changing requirements of the animal and public health sector, wherever they occur, must be fulfilled. In the UK, the VLA has adapted to the new situation by building on past strengths to deliver high quality veterinary surveillance, research and laboratory services on a cost effective basis. These strengths rely upon the network of communication in animal health matters from farm and practitioner, through the VIS, the Scottish VIS and the comparable centre in Northern Ireland, to the respective central laboratories, including the CVL. The most recent reorganisation, named ‘Springboard’, has the aim of enabling the staff of the VLA (i.e. the CVL and the VIC in England and Wales) to focus on the needs of the customer and to provide greater transparency and opportunity for services to be improved and rationalised and so provide better value for money. This template could be used by other veterinary laboratories world-wide to meet the needs of applied farm animal veterinary science in the 21st Century.
Rather than merely protect animals and the public by introducing barriers to trade, governments must seek advice about risks from TSEs arising from importation and indigenous sources. The latter risk is frequently ignored. All these risks can be minimised to a negligible level. In regard to BSE, this can be achieved by adopting the recommendations and guidance in the OIE International Animal Health Code chapter on BSE and the supporting document (25, 26). In regard to scrapie, guidelines are currently still under development, but the draft OIE Code chapter on scrapie gives valuable guidance.

In countries without scrapie or BSE, the establishment of basic research programmes for these complex diseases would be inappropriate. However, these countries must conduct continuous monitoring and surveillance for BSE, scrapie and CJD. Education and awareness programmes for BSE and scrapie, and a scientifically-based assessment of risk from both exogenous and endogenous sources would also be advised. Several countries have done this (including some in which BSE and scrapie are absent) and published relevant documents. Few countries are without risk, but the risks present can be managed and communicated without difficulty and at a much lower cost than that of managing an outbreak. The role of the OIE in regard to animal disease and of the WHO in regard to human disease, is paramount. Future work must elucidate the nature of the agent and develop a test for infection in the live animal before clinical signs develop. In humans, methods for disease prevention and treatment are required.

The veterinary and medical professions must be continually vigilant as the enigmatic prion, virino or unconventional virus (whatever the agent may be [35]) appears to recur unexpectedly in different guises and in different species. No legislation is likely to protect against sporadic occurrences of TSE, but vigilance is necessary for detection and investigation to ascertain whether the TSE is of importance or merely a scientific curiosity. Fortunately, researchers at the CVL did not take the latter view of BSE following the initial discovery, but rather chose to diligently investigate the disease in depth, despite the difficulties caused by the climate of veterinary research at the time.

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La recherche au Laboratoire vétérinaire central de Weybridge, en particulier sur la tremblante et l’encéphalopathie spongiforme bovine

R. Bradley

Résumé
Créé en 1894 par une décision du ministère britannique de l’Agriculture, de la Pêche et de l’Alimentation, le Service des laboratoires vétérinaires a commencé ses travaux de recherche en 1905. Le Laboratoire vétérinaire central, inauguré en 1917, est connu dans le monde entier sous le nom de « Weybridge ». Quant au réseau des Centres de recherche vétérinaire mis en service en 1922 en Angleterre et au Pays de Galles, il continue à ce jour de jouer un rôle important dans la surveillance des maladies animales. Les problèmes identifiés dans ces Centres sont à l’origine de nombreux travaux de recherche du Laboratoire vétérinaire central ; l’encéphalopathie spongiforme bovine (ESB) en est un bon exemple. Les travaux portent sur nombre de maladies infectieuses et non

Mots-clés

Investigación veterinaria en el Laboratorio Veterinario Central, Weybridge, con especial referencia al prurigo lumbar y la encefalopatía espongiforme bovina

R. Bradley

Resumen
En 1894, el Ministerio de Agricultura, Pesca y Alimentación del Reino Unido encargó la creación de un Servicio de laboratorio veterinario. En 1905, aquel Servicio iniciaba actividades de investigación veterinaria, y en 1917 se inauguraba el Laboratorio Veterinario Central, conocido en el mundo entero con el nombre de "Weybridge". En 1922 se creó una red de Centros ingleses y galeses de investigación veterinaria, que hoy en día siguen contribuyendo significativamente a la vigilancia de las enfermedades animales. La identificación de problemas en esos centros a menudo se concretiza en el Laboratorio Veterinario Central con nuevas investigaciones, como ocurrió con la encefalopatía espongiforme bovina (EEB). En el Laboratorio Veterinario Central se investiga sobre muchas enfermedades, tanto no infecciosas como infecciosas, y entre estas últimas figura el prurigo lumbar, que ya se estaba investigando en 1986, cuando se descubrió la EEB. Se dio comienzo a un programa de investigación sobre la EEB destinado a estudiar los signos clínicos y métodos de diagnóstico, la patología, patogénesis y epidemiología de la enfermedad y las propiedades de transmisión de su agente etiológico entre animales de granja. El autor examina algunos de los resultados de esos estudios, así como las perspectivas de futuro.

Palabras clave
References


