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CURRENT SITUATION OF BOVINE SPONGIFORM ENCEPHALOPATHY (BSE)

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1. Introduction

Bovine spongiform encephalopathy (BSE) is a progressive, fatal neurological disease of adult bovines, characterized by the presence of degenerative brain lesions, a long period of incubation, and the absence of inflammatory and immunological reactions. It is induced by a transmissible, unconventional, and very resistant infectious agent called a prion.

This disease was first recognized in Great Britain in 1986, and it belongs to a group of fatal degenerative diseases of the central nervous system, characterized anatomicopathologically by the presence of astrogliosis, intracellular vacuolation, loss of neurons, and formation of occasional amyloid plates in the central nervous system. The abundant cavities or vacuoles in histologic cuts of the brain give them a characteristic spongy aspect, hence the name of the disease. Clinically, it is characterized by a nervous symptomatology, especially alterations of behavior, hyperesthesia, tremors, and ataxia.

On 21 May 1995 Stephe Churchill, a young Englishwoman, 18 years of age, became the first known victim of the so-called variant of Creutzfeld-Jakob disease (vCJD). The case was reported on 28 October in the English scientific journal *The Lancet*. Since then, for almost 100 people the cause of death was listed as vCJD, whose etiologic agent seems to be identical to that of BSE.

The fact that this zoonosis can potentially affect such a broad, complex, sensitive group as consumers has meant that its spread to several countries has convulsed public opinion in old Europe, causing alarm among consumers, opening heated new discussions, provoking numerous and profound political crises, and seriously threatening the future of its cattle stock and burgeoning meat industry.

Furthermore, this disease has called into question the methods of procuring and utilizing proteins considered "of high biological value" in animal feed, has altered the cattle trade and the consumption of meat products, has modified some of our more deeply rooted eating habits, and will have significant repercussions for certain environmental regulations in some countries.

BSE today constitutes one of the principal concerns of the European governments, especially those of the European Union, because of its health and social implications. Numerous meetings of heads of state, presidents, and ministers of public health, agriculture, consumption and the environment, as well as eminent scientists, have been convened, at which important decisions have been adopted and much legislation has been promulgated. All of this has meant heavy economic investment in the development of research programs and surveillance and eradication systems that guarantee control and impede transmission to man.

The intensification of trade in animals and animal products constitutes a risk factor for the spread of this and other epizootics, which has increased spectacularly during recent years; this fact alone raises a whole series of technical issues worthy of continuous study by experts and the authorities responsible for world animal health.

Finally, it has become increasingly evident that these serious epizootics and zoonoses influence the entire constellation of social, political, scientific, sanitary, technical, legal, and economic regulations by which our society is currently governed.

Moreover, it also is clear that BSE has led to numerous scientific and technical milestones in the history of the research on these neurological diseases, both in man and in the affected animal species, and of the programs for epizootic eradication. That history includes the appearance of the most advanced and innovative diagnostic techniques.

The international agreement for the creation, in Paris, of the International Office of Epizootics (IOE), was signed on 25 January 1924 by 24 countries. The organization currently has 157 member countries and has existed longer as an international organization than even the specialized agencies of the United Nations.

The IOE has, among its responsibilities, those of regulating the standards for the prevention and control of epizootics in the world and promoting and coordinating research on subjects related to animal health. Since the appearance of BSE in Great Britain in 1986, it has participated actively in the coordination of commissions and working and "ad hoc" groups, made up of the best scientists in the world, whose results are reflected in the corresponding chapters of the *International Zoosanitary Code* (the *Code*) and of the *Standards Manual* (the *Manual*), as well as in numerous scientific publications and in the periodic health information issued on the status of this disease, which are speedily distributed throughout the world.

2. Etiology and Pathogenesis

Considered by the experts an emerging disease, BSE has a known history, both in man and in animal species. Included in the human pathological processes are kuru, Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker disease (GSS), and fatal familial insomnia. Among those in animals are scrapie or lumbar prurigo of sheep and goats (tremblante, in French and scrapie in English), BSE, various encephalopathies of mink, feline spongiform encephalopathy, chronic cachexia in deer and elk, and several encephalopathies of wild ungulates.

The prototype of all these diseases is, without a doubt, ovine lumbar prurigo, a neurological disease of sheep, characterized by intense pruritus, which was already known in 1732 in the United Kingdom.

In 1920 the Austrian neurologist Hans Creutzfeldt published a description of the first human case of a disease that today takes his name, and a year later another Austrian, Alphons Jakob, also described the disease. In 1957 an endemic human disease was described in a wild tribe of Papua New Guinea; it was called kuru, which in the tribal language means "tremor." In 1966 its experimental transmission to the chimpanzee was induced.

The transmissible character of lumbar prurigo was demonstrated by Cuillé and Chelle in 1936 in Toulouse, France, through intraocular inoculation of healthy animals with material from the spinal cord of sick sheep. An extraordinarily long incubation of between 14 and 22 months was observed. At the end of the 1950s, Hadlow demonstrated the similarity between kuru and ovine lumbar prurigo; the latter is not transmitted to man. The similarity between the neuropathology of CJD and kuru was established by Klatzo in 1959 and, as in the previous case, its transmission to experimental animals was demonstrated in subsequent years. From then on, other diseases were described and classified together as transmissible spongiform encephalopathies (TSEs).

In the early 1960s, the unusual properties of the etiologic agent, still undiscovered, attracted the attention of investigators, who created all sorts of hypotheses, postulating a nature ranging from parasitic to viral,¹ including the so-called viroids,² virinos,³ and unconventional viruses.

The availability of techniques for the preparation of partially purified fractions from the brains of hamsters infected experimentally made it possible to demonstrate their partial resistance to treatments with proteases and insolubility in some detergents. At the same time, the existence of nucleic acids or polynucleotides could not be demonstrated.

In accordance with this and other, previous research, in 1992 Stanley Prusiner of the University of California proposed his prion hypothesis, whose antecedents are found in the experiments carried out in 1967 by J.S. Griffith. The latter suggested, for the first time, that in the etiology of ovine lumbar prurigo, a protein of the host itself could be implicated, without the participation of any viral nucleic acid. Prusiner's prion research

¹ The term "slow virus"(also "lentivirus") was registered by Pjorn Sigurdsson in 1954, to refer to the cases of scrapie and visna in sheep in Iceland, distinguished by a long incubation period, occasionally up to 10 months or more.

² A viroid is a small circular molecule of RNA of only 300 to 400 nucleotides, noncoding, which is replicated by intervention of the enzymes of the host. It produces significant diseases in plants.

³ A virino is an imperfect nucleic acid, covered by a host protein

gradually gained supporters; in 1994, he received the Albert Lasker Award and then in 1997 the Nobel Prize, which signified, without a doubt, the recognition of his hypothesis by the international scientific community.

A prion is a proteinaceous, infectious particle, considered the agent of spongiform encephalopathies in man and animals. It is composed exclusively of a simple protein molecule.

In all healthy organisms of most vertebrates, including human beings, there exist proteins whose abbreviated name is PrPC (cellular or normal prion protein). Taking into account the models of study on lumbar prurigo, the prion was called PrP (prion protein), which differs from the infectious prion, called PrPSc, only in a change in its spatial arrangement, which transforms the protein from normal to pathological. This altered or isomorphous form (incorrectly folded protein) confers two properties on the PrPSc that make it possible to differentiate it from the normal one: partial resistance to digestion by proteases and insolubility in certain detergents.

Its pathogenicity implies the existence of a modified host protein, capable of converting normal proteins into other, similar ones. Ultimately, the PrPSc represents an abnormal conformation of the PrP, capable of generating additional molecules of PrPSc through an autocatalytic process and of accumulating in the brain of the patient.

The conditions that induce the error in the folding establish the different forms of the prionic diseases described:

- Sporadic, appearing without apparent cause and for which there is currently no explanation.
- Hereditary, caused by genetic alterations that facilitate the incorrect folding of the PrPC.
- Infectious, which is explained by the action of the PrPSc on the PrPC which transforms the latter into the former.

The PrPSc are more resistant to physical and chemical treatments than other conventional pathological agents, such as viruses and bacteria, but are not invulnerable. Sodium hypochlorite and, to a lesser extent, caustic soda and formic acid destroy them. They tolerate temperatures above 100 °C, but do not resist incinerating temperatures. It is important to emphasize that—under the European Union's regulations—the classical treatment of meat and bone meals, which involves exposure to 133°C and 3 isobars of pressure for 20 minutes, almost totally inactivates prions.

Prionic diseases are the result of a completely new pathogenic mechanism, based on a post-translational change in the conformation of a self-propagating hydrophilic protein. Upon assuming a composition similar to that of the normal protein, the infectious prion appears not to induce the normal defense mechanisms of the organism, and when it penetrates the host, neither inflammatory nor immune nor cellular reactions occur. When the path of infection is digestive, the agent resists the action of the gastric juices and arrives at the ileum, where Peyer's patches, lymphoid tissue that has cells that capture viruses and bacteria from the intestinal contents, perform the same action with prions. At this point the host is considered infected.

3. Epidemiology

There are diverse speculations on how the infectious agent appeared in cattle. Nevertheless, many epidemiologists agree that it occurred in England as a consequence of using lumbar prurigo-infected sheep carcasses and offal from slaughterhouses in the preparation of meal for livestock feed.

Other hypotheses lean toward a bovine origin, as a consequence of a mutation of the cellular prion proteins, further amplified through the meal. Finally, there are authors who hold that its origin is to be found in African cattle.

In 1900 meat and bone meal began to be utilized in the feeding of ruminants. After World War II, an increase in the production of these meals occurred, particularly in the United Kingdom, and in the 1960s and 1970s there was extraordinary development of conversion plants in the United States.

At first, the original sterilization procedures were discontinuous and involved exposure to high temperatures for specified periods of time. At the same time petroleum-based solvents were utilized for the extraction of fats, with the production, on the one hand, of meat and bone meal and on the other, fats. The disease arose in Great Britain, probably because of a change in the system for producing meal from meat that occurred between 1981 and 1982. In 1980 the price of fossil fuels began to rise and to save energy, continuous manufacturing processes were introduced, involving a reduction in the lengths of time and the sterilization temperature, in addition to the elimination of chemical treatments.

In Great Britain, a country with a high prevalence of lumbar prurigo (with an average of 260 foci/year during the last decade), the remains of sick sheep were used in the manufacture of meat meal prepared with the new techniques, which no longer inactivated the prions and these, which previously had infected only sheep, succeeded in passing through the species barrier and infected and adapted to cattle, cats, and other species.

In general, the cases of BSE appear unpredictably and sporadically, and often just one animal or a very few in a herd are infected. There have also been cases, in large operations, with more than 100 infected animals. The possible means of transmission among animals and between them and man are currently being investigated. The crossing of the placenta is an exceptional probable form of transmission.

4. Progress of the Disease in the United Kingdom and in Other Affected Countries

In April 1985 on a farm in the south of England an adult Frisian cow was observed for the first time with a neurological syndrome called "chronic hypersensitivity with incoordination syndrome," which was described as a change in temperament accompanied by aggressive behavior. By February 1986, nine more cases appeared in the same herd, with the same clinical symptoms. In November, histopathological analysis of the brains of these animals showed great similarity to the brains of animals affected by lumbar prurigo. Since then a similar type of encephalopathy has been diagnosed in several cows and even in an African antelope.

The disease affects adult animals, including those four to five years of age. According to statistics from the International Information and Exchange Service of the IOE, 1992 saw the highest number of cases in the United Kingdom (37,280) and thanks to its program of eradication, the epizootic is on the wane. In 2000 there were 1,101 cases, with a cumulative total of 177,780 to date. Between 1989 and 1990 secondary epizootics were generated in other Community countries as a consequence of the importation of contaminated meat and bone meal from the United Kingdom; in Ireland, with 145 cases reported up to December 2000; in Switzerland, with 33; in France, with 161; and in Portugal, with 142. More recently cases in Spain, Germany, Belgium, Denmark, and the Netherlands were reported. None have been reported up to the present in other countries of the European Union, such as Austria, Sweden, Finland, and Greece.

5. Diagnosis

As in any other disease, the eradication programs revolve around diagnosis. However, BSE presents a series of problems due to the peculiarities of its etiologic agent, pathogenesis, and aforementioned epidemiology. On the one hand, serological techniques cannot be applied, since these infectious agents do not induce an immune response and, on the other, the absence of a nucleic acid associated with the infectious particle prevents the use of PCR. Other, additional problems are the extended incubation period and the

accumulation of PrPSc only in the CNS, particularly the brain and spinal cord. The sample of choice is the obex (medulla oblongata and pons), where, it should be noted, most of the lesions are. Specialized laboratories must be used and for now, detection of the disease is possible only through clinical manifestations of the disease. The diagnostic techniques can be classified into four large groups:

- Anatomicopathological, which make it possible to detect microscopically the histopathological alterations of the CNS characteristic of the disease, that is, vacuolation of the encephalic tissue and astrogliosis. Its low sensitivity is due to the absence of histopathological alterations before clinical signs appear.
- Biological, through inoculation of sensitive laboratory animals (mice and hamsters); it is the most sensitive, but excessively detailed and slow.
- Immunohistochemical, through the utilization of specific mono- or polyclonal antibodies, marked with a stain, that make it possible to detect the presence of the prion in histological section with an optical microscope.
- Rapid techniques, carried out on brain samples from the dead animal, which have been validated by the European Union and are currently applied by several Community countries in their surveillance and eradication programs.

The economic and social impact of this disease, the development of sanitary programs, and the problems posed by the first three diagnostic techniques required rapid, simple alternatives sensitive enough to detect low levels of PrPSc—that is, at the beginning of the incubation period—utilized on a large scale, and that can be used with the live animal. Thus, it was necessary to find the most appropriate solutions, and the recent developments in research to meet these objectives is dizzying.

According to the report issued after the last meeting of the Working Group on Biotechnology of the IOE, held in Paris this past January, a new generation of diagnostic tests based on detection of PrPSc in brain has arisen recently. These are rapid techniques, which are conducted on brain samples and detect the presence of the infectious prion through reaction with the specific antibody, detecting it by color. One of them is based on the immunoelectrophoresis of proteins, which are subsequently recognized by specific antibodies (immunoblotting or Western blotting). The other two are based on the ELISA methodology.

All the antibodies (of very diverse origins) have a great affinity for PrPSc, but are incapable of distinguishing it from the PrPc. Thus, the latter must be eliminated with a

preliminary chemical treatment based in the resistance of the former to digestion by proteinase K. Other methods are based on their differences in solubility in detergents.

The deficiencies in the specificity of these tests do not have just an economic impact. Their main problem is their degree of sensitivity, since that could impact public health. Currently, all the biochemical tests are less sensitive than the biological tests, which means that the sensitivity of any of those must be evaluated against the tests performed on murine models.

Moreover—according to the same report of the above-mentioned group—there are several research projects under way aimed at increasing the sensitivity and specificity of the rapid tests, and experimental tests have begun to detect PrPSc in live animals. These have already been utilized successfully to detect it in lymphatic tissues, such as eyelids and tonsils, from biopsies performed on animals infected with lumbar prurigo. They have not yet been used for cattle. The main problem lies in the distribution of PrPSc in ovine and bovine tissue. PrPSc can be detected in the lymphatic tissue of sheep experimentally infected with BSE, but not in cattle—except, perhaps, in Peyer's patches associated with the distal ileum.

A significant problem still awaiting solution is knowing when it will be possible to detect the presence of PrPSc in infected live animals. Up to the present, it seems that that can be done in infected cattle only some six months before the appearance of clinical symptoms, and the incubation period of the disease is from four to five years on average.

The IOE coordinates efforts to promote research on new diagnostic techniques for BSE, to improve those already existing, to solve the many problems that arise, and to standardize the methods with a view to facilitating the international cattle trade. These are precisely the reasons why the Commission on Standards has begun to plan its activities, so that in the end, the results can be included in the edition of the Manual appearing in 2004.

6. Recent Evolution of the Programs for Surveillance and Eradication

The presence of BSE in some countries of the European Union has generated a large number of directives and decisions directly or indirectly related to its surveillance, control, and eradication. The singular etiological, pathogenic, and epidemiological characteristics of BSE make it impossible for the disease to be eradicated through methods regarded as conventional. Accordingly, as new scientific knowledge has arisen in recent years, Community legislation has evolved rapidly, adopting specific measures to protect consumer health and impede the spread of the disease among ruminants.

The European Commission, the executive organ of the European Union, annually reviews and approves the various sanitary programs applied in the Community countries—programs that are cofinanced up to 50%. The diseases given priority in these programs are selected, taking the following criteria into account:

- The disease must be a zoonosis.
- It must be included in List A of the IOE; that is, it must be highly contagious and cause serious economic losses.
- It must be a problem in the country requesting the program.
- In general, the sanitary programs related to BSE in the European Union involve:
 - Surveillance of spongiform encephalopathies in livestock.
 - Control of substances utilized in animal feed.
 - Inspection of establishments involved in the processing of by-products and carcasses.
 - Control of specified risk materials (SHM) in slaughterhouses.

The movement of livestock has an enormous influence on the spread of BSE, which means that its control in livestock operations is indispensable for prevention, as well as for effective implementation of any sanitary program. To this end, the European Union has also promulgated legislation to develop an effective system for the individual identification of animals, adequate sanitary documentation for trade in the Community and with third countries, and a book of livestock operations. All these measures permit the tracking of meat and meat products from production on the farm to the consumer.

In addition, in accordance with the European Union's "White Book on Food Security," a taskforce has been created. It is made up of veterinary experts who periodically study the evolution of the most significant diseases transmissible from animals to man, among them BSE.

The most recent advances in the European Union in the eradication, surveillance, and control of this disease have occurred in the surveillance system, based on diagnosis of the disease, prohibition of utilization of meat and bone meal in livestock feed, risk management, and the development and validation of rapid techniques for postmortem diagnosis and their application in animals that die accidentally on farms.

Without a doubt, the most controversial has been the decision of the Council of the European Union which, at its meeting in early December 2000, banned the use of meal of animal origin (excluding fish meals) in the feeding of all animal species, except pets, to prevent its accidental mixing with cattle feed. This measure is considered fundamental from the standpoint of sanitary policy; however, due to the long incubation period of the disease, its effectiveness can be evaluated only after five or six years. At the same meeting, a regulation was adopted requiring (beginning 1 July 2001) meat for human consumption from cattle over 30 months of age to be certified as disease-free, including intestines among the specified risk materials (SRM), together with brain, eyes, spinal cord, and spleen (in sheep and goats). In February spinal column was added.

In this decision, the experiences of France and Switzerland have served as very important models. Switzerland does not belong to the European Union and, taking note of the English experience, the Swiss health authorities, already prepared, took preventive action even before the first case of disease appeared in the country. On 8 November 1990, once cases were confirmed (two in the same month), the use SRM (brain, spinal cord, spleen, thymus, intestines, lymphoid tissues, and visible nerves from cattle over six months of age) in food for human consumption was prohibited. In 1990 a measure regarded as basic from the standpoint of veterinary policy took effect in this country (and also in neighboring countries, such as France): a ban on the feeding of ruminants with meal made from meat. For the first time, the authorities discussed their decisions, based on risk analysis, in public.

This ban led to a noticeable decline in the rate of infection in Switzerland, although it has not been possible to prevent all new infections. Of the 363 cows infected with BSE after 1990, 121 were born after the ban on feeding ruminants with animal meals. Since 1996 the animal carcasses, that is, the bodies of the animals slaughtered for sanitary reasons, cannot be made into meat and bone meals in this country, and certain SRM (brain, spinal cord, eyes, and tonsils) must be burned. This regulation is to be applied, moreover, to food from animals of foreign origin.

One of the residual risks identified is that of cross-contamination, that is, the accidental incorporation of prohibited proteins into animal feed, either in the production of mixed feed, during transport, or even during distribution of the feed on the farm. On 20 June 2000, measures were strengthened to reduce cross-contamination in production even further.

Taking into account all the measures adopted, the authorities started with the idea that the risk that existed since 1996 was lower and that while it was necessary to expect infections in animals born in 1996, in those born in 1997 there should have been none, or only in very isolated cases. But these forecasts have also been doomed: last October BSE was diagnosed

in a cow slaughtered on an emergency basis that born in February 1997 in the Canton of Obwald. It was also diagnosed in another, born in November 1996. These two animals were, then, born several months after the strengthening of the measures instituted in 1996.

The Swiss veterinary authorities are now trying to determine the origin of these cases and to discover occasional errors in the eradication operation and eliminate them. Accordingly, in March 2000 with the object of accelerating eradication of BSE, they considered the possibility of adopting a ban on animal meals in the feeding of all animals destined for market as a supplementary preventive measure.

In addition, the survey conducted in France between 7 August and 24 October 2000, covering a total of 15,000 cattle that died on farms or were slaughtered on an emergency basis (population at risk), two years of age or older, in the livestock-producing regions of Gran-Oeste, Lower Normandy, Brittany, and the Loire region, detected 32 positive animals. With this experience, last December that country proposed to the European Union the utilization of rapid diagnostic tests on all cattle over 30 months of age destined for market. That practice was initiated on 1 January of this year and the measure will affect 2.5 million cattle in France alone. Furthermore, the Ministry of Agriculture has announced the creation of 300 new posts to strengthen the veterinary services.

7. Actions and Recommendations of the IOE

Development of the information linked to disease prevention in livestock included in Lists A and B (BSE is included in B) is one of the specialties and the priority function of the IOE. The Sanitary and Phytosanitary Measures, signed in 1994 by the World Trade Organization (WTO) and the IOE, grant the latter a dominant role in animal health in the world, the responsibility to set the sanitary standards that are to govern international trade in live animals and their zootechnical products.

The Code Commission is, without a doubt, the most important of this organization, responsible for the preparation of the *International Zoosanitary Code*, the core of the activities of the IOE and its relations with the World Trade Organization (WTO) and other international organizations, such as the Food and Agriculture Organization (FAO) and the World Health Organization (WHO). The objective of the Code is to safeguard the sanitary safety of the international animal trade and its zootechnical products; its recommendations contribute to their stability and fluidity. Its development is the fruit of ongoing work begun years ago by the IOE, which has brought together the foremost specialists in the world to create new chapters or to review and improve those already existing, based always on the most recent advances in veterinary science.

The Code Commission systematically asks the delegates from the member countries their opinion on the projects that it carries out. The Code is thus the result of a broad consensus of the highest veterinary authorities in the world.

Being based on these principles, the IOE considers that to prevent the spread of this or any other epizootic, there must be an international standard which, in the case of BSE, is included in Chapter 2.3.13 of the Code, whose latest edition is dated May 2000. This chapter establishes the criteria for international certification of the sanitary status of a country or area with regard to this disease. The country or area may be classified: free of BSE; provisionally free, with no cases reported; free, with at least one autochthonous case reported; or with low or high incidence.

Important in the aforementioned chapter is the requirement that the status of a country or an area with respect to BSE can only be determined according to the following criteria:

1. Results of a risk analysis that identifies all potential factors in the appearance of bovine spongiform encephalopathy, as well as its history, in particular:
 - (a) Consumption by the cattle of *meat and bone meal* or of the fried skin cracklings of ruminants.
 - (b) Importation of *meat and bone meal* or of fried skin cracklings potentially contaminated by the agent of transmissible spongiform encephalopathy, or of animal feed that contains those products.
 - (c) Importation of animals or ovules or embryos potentially infected by the agent of transmissible spongiform encephalopathy.
 - (d) Epidemiological situation of the country or of the area with respect to all animal transmissible spongiform encephalopathies.
 - (e) Degree of knowledge of the distribution of the bovine, ovine, and caprine populations of the country or area.
 - (f) Origin of the animal remains, parameters of the systems for processing those remains, and methods for the production of livestock feed.

2. A continuous training program aimed at veterinarians, livestock producers, and the people who work in the transportation, marketing, and slaughter of cattle to urge them to report all cases of nervous disease in adult cattle.
3. Compulsory reporting and examination of all cattle that present clinical signs compatible with those of bovine spongiform encephalopathy.
4. A continuous surveillance and monitoring system for bovine spongiform encephalopathy that pays particular attention to the risks described in Point 1 above and takes into account the directives of Annex 3.8.3. The records related to the number of examinations conducted and their results should be conserved for a minimum of seven years.
5. Examination in an authorized laboratory of the samples of brain or other tissues taken within the framework of the aforesaid surveillance system.

The Code also establishes other interesting aspects of BSE prevention. These include directives for the risk analysis, evaluation of the veterinary services, zoning and regionalization, epidemiological surveillance and continuous epidemiological monitoring, import and export procedures, animal health measures that can be applied before exit and at exit, border posts and quarantine stations of the importing country and the animal health measures that must be applied on arrival, and the principles of veterinary certification, among which are the format of the certificates, the responsibility of the signing veterinarian, conditions for electronic certification, and harmonization of methods.

It is important to point out that no new scientific information has contradicted the validity of the standard contained in Article 2.3.13. Since 1992 the IOE has been updating it periodically through thorough study of the pertinent scientific publications and consultation with the foremost world experts on transmissible spongiform encephalopathies in animals.

The aforementioned chapter indicates, in particular, that the status of a country with regard to BSE only can be determined after a risk assessment in which all the potential factors in the appearance and spread of the disease are taken into account, as well as their evolution over time. Among these factors are the inclusion of meat and bone meal from ruminants in cattle feed, the importation of potentially contaminated products such as those mentioned, the importation of cattle or cattle embryos from affected or potentially affected countries, the epidemiological situation of transmissible spongiform encephalopathies in the animals in the countries subject to evaluation, the origin of animal remains and the parameters established for their processing, the obligation to report every suspected case of BSE in the evaluated country, the establishment of a program for sensitizing professionals in the cattle sector, as

well as a surveillance system, and finally, the existence of an authorized laboratory staffed by personnel trained in the diagnosis of the disease.

Taking into account the current scientific knowledge, the IOE recommends that, whatever the sanitary status of an exporting country with respect to BSE, importing countries not place any restriction on imports or transit through their territories of milk and dairy products, semen, deproteinized sebum and products obtained from it, dicalcium phosphate with no remaining proteins or fat, hides and skins, gelatin, and collagen prepared from hides and skins.

The IOE also has formulated specific recommendations for the importation of cattle, embryos, fresh meats, and meat products in relation to the health status of the exporting country with respect to BSE. Moreover, Chapter 2.3.13 contains recommendations for the international trade of gelatin and collagen prepared from bone, as well as sebum (that may not be deproteinized), destined for use in the preparation of products for human or animal consumption or for cosmetic or pharmaceutical products or materia medica.

Two elements have contributed to progress with regard to surveillance of BSE: on the one hand, rapid, industrial-scale, diagnostic postmortem techniques have been developed and, on the other, certain countries have demonstrated the importance of surveillance, not only of animals with suspicious clinical signs, but also of dead animals or animals that fall victim to accidents in livestock operations. The result of these initiatives in some countries has been an increase in the number of cases detected, which, in practice, basically makes it possible for these countries to apply measures that reduce the risks associated with BSE to the operations.

In addition, the general ban on feeding all animals, including pigs and domestic fowl, meat and bone meal from ruminants is not due to the discovery of a new risk of BSE in porcine and avian species, but to a mechanism for effective management adopted by several countries. Indeed, conditions for the manufacture and distribution of feed made from meat meal and destined for pigs, poultry, or fish in infected countries may have accidentally facilitated cross-contamination of the feed destined for cattle during manufacture or transport or on the farm.

Finally, next May at the General Assembly of Delegates of the IOE, the International Zoosanitary Code Commission will submit proposals to the International Committee aimed at enhancing the Code's directives on the surveillance of BSE and will not fail to raise the issue of meat and bone meal with the Committee.

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