Mad Cows and Transmissible Spongiform Encephalopathies: The Human Face of the Globalization of Disease

Mad cow disease, or bovine spongiform encephalopathy, [BSE], quickly caught the attention of the public, changed British farming practices, and affected European trade, and even gave rise to a new psychological disorder, “BSE phobia.” English newspaper accounts announcing the disease projected it would claim as many as 500,000 lives. The picture of the British eating their beloved roast beef and, in the process, consuming a pathogen that could cause a devastating neurological disease that is sure death was certainly food for thought. From a biomedical perspective, the origin and spread of transmissible spongiform encephalopathies, (TSEs) diseases caused by proteins called prions, forced a paradigm shift in which an infectious agent without genetic material could be a disease vector. Anthropologically, these encephalopathies bring forth the fact that local cultural practices can have a global impact on the emerging disease process.

TSEs include an array of human diseases as distinct as the relatively rare but fatal degenerative neurological pathologies such as Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, fatal familial insomnia, and kuru in humans. They also cause mad cow disease, scrapies in sheep, and related diseases affecting deer, elk, and mink. The pathogens’ ability to slip their host, cross their species barrier, and jump geographic limits constitutes a central issue for the study of emerging disease in general and transmissible spongiform encephalopathies in particular.

Kuru appeared among the Fore-speaking horticulturists in Papua, New Guinea, presenting one of the most bizarre and intriguing epidemiological problems that has elicited an anthropological investigation. The outbreak, which reached a peak in the 1950s, afflicted women and young children (2,600 individuals were infected). Victims experienced progressive ataxia, dementia, and a loss of locomotor coordination that eventually led to death. As the disease progressed, victims experienced episodes of what appeared to be uncontrolled laughter that led Western scientists to call it the laughing death. In Fore, kuru means “shaking with fear.”

Autopsies of the brains of individuals dying from kuru revealed amyloid plaques that had been partially removed by an inflammatory response, producing interneuronal vacuolation that gave the brain tissue a spongiform appearance. These neurological lesions resembled pathological changes in the brains of both humans who die from Creutzfeldt-Jakob disease and of sheep that die from scrapies.

The Fore assumed that exosorcery witchcraft originating from outside the group was the source of kuru. Biomedical investigators initially assumed it was a genetic disease (one geneticist suggested that it was a dominant gene in females and a recessive one in males) or the result of consuming a toxin. In a classic case of epidemiological and anthropological detective work, Lindenbaum and Glasser were able to demonstrate that kuru was most likely spread by the practice of a ritual that involved consuming a dead relative’s brain. Steadman and Merbs have argued that it is the process of mortuary preparation in which cuts on the hands were the source of the infection.

The infective agent was eventually isolated from the brains of kuru victims and inoculated into chimpanzees to produce the pathology. The long incubation period of the disease made the determination of its etiology extremely difficult. The source of kuru was initially thought to be a “slow” virus because of its long incubation period, which ranges from one year to as long as thirty years. It was a series of cross-species transmission studies that eventually linked kuru to Creutzfeldt-Jakob disease and other TSEs. Ultimately, such encephalopathies were shown to be caused by a proteinaceous infectious particle, or prion.

However, even with the awarding of the Nobel Prize, there are scientists who still contest the evidence that BSE is transmitted by a prion. The Nobel prize in medicine was awarded for Gajdusek’s initial discovery that kuru was spread by an infectious agent and for Prusiner’s determination that the prion was the agent of the disease. Even with the awarding of the Nobel Prize, there are scientists who still contest the evidence that BSE is transmitted by a prion. They point to studies in which homogenates prepared from the brains of victims of this disease were injected into mice. All the mice displayed neurological symptoms and neuronal death, but 55% did not have detectable pathogenic prions.

Prions are unusual in that they lack DNA or RNA, which usually is found in infective pathogens and, indeed, in all known living organisms. When the normal prion, PrP-supC, folds into an abnormal shape, becoming PrP-supSc, it serves as a template for the proliferation of other prions in the brain, thereby causing the pathology. That the same nucleic acid and amino acid sequence gives rise to both normal and abnormal prions is just one of the intriguing facets of the transmissible spongiform encephalopathies. The production of pathogenic prions can have different effects depending on...
the region that is their target. For example, if they affect the cerebrum, judgment may be compromised, whereas in the cerebellum they impair locomotion and, in the thalamus, sleep. Even more intriguing are "strains" of prions that exist without benefit of one of the typical changes in the nucleic acids. The new paradigm will have to explain how the prion can control these processes.

Cannibalism was the vector for kuru among the Fore. Kuru most likely originated from the consumption of a dead relative who experienced the one-in-a-million spontaneous development of Creutzfeldt-Jakob disease. Certainly when cannibalism was prohibited, the prevalence of kuru declined dramatically. Those in biomedicine saw this as a victory for science; the Fore assured themselves that their practices to ward off exosorcery led to the decline of kuru. From an emerging disease perspective, the kuru epidemic was contained.

The exotic nature of kuru and its existence in far-off New Guinea among a tribal people who engaged in cannibalism provided Westerners a safe physical and social distance from this disease. Even when we understood that kuru was related to pathologies such as Creutzfeldt-Jakob disease, it raised few fears. CJD is relatively rare, causing the death of only one in a million individuals, and that provided us further comfort. However, the recent increase in the prevalence of CJD has raised the concern of the public and the medical community. Corneal transplants,43,44 growth hormone therapy,45–47 and the use of dura mater in grafting,48–51 practices that have been described as neo-technical cannibalism, as well as the use of brain probes,52 are believed to have increased the prevalence of this disease. The iatrogenic risk made an individual more vulnerable. Prions are incredibly resistant to standard sterilization procedures.53 Brain sections fixed in formaldehyde or frozen for years appear to have prions that are still capable of producing infection. Even exposure to intense heat and acid does not disrupt the infectivity of prions. Guanidine thiocyanate seems to be the reagent that most effectively disrupts the prion's ability to infect.54

Cannibalism was the vector for kuru among the Fore. Kuru most likely originated from the consumption of a dead relative who experienced the one-in-a-million spontaneous development of Creutzfeldt-Jakob disease. Certainly when cannibalism was prohibited, the prevalence of kuru declined dramatically. Those in biomedicine saw this as a victory for science; the Fore assured themselves that their practices to ward off exosorcery led to the decline of kuru. From an emerging disease perspective, the kuru epidemic was contained.

Mad cow disease in England has an immediate and potentially far-reaching impact. Even though the British Government claimed there was little risk that the disease would be spread to humans,55 they eventually developed a plan for culling infected animals.56,57 It is estimated that 165,000 infected cattle from 34,000 herds have been culled to prevent the epidemic from spreading. Nevertheless, it is estimated that nearly 7,000 cattle will have been infected with BSE between 1997 and 2001.58,59 The outbreak in England was related to the practice of feeding rendered sheep carcasses and recycled dead cattle as meat and bone meal supplements. The outbreak coincided with changes in the processing and rendering of dead animals for cattle feed. Initially, downed sheep and cattle were batch-processed in procedures that used solvents to remove fat. After an industrial explosion, modification of the rendering procedure developed in the United States that excluded the solvent-extraction stage and reduced processing temperatures to 100°C was introduced into the United Kingdom. The changes in extraction and reduction in temperature produced more heat-resistant prions.

Ultimately, BSE did spread to the human population.60 Twenty-one cases of a new variant of Creutzfeldt-Jakob disease (nvCJD) in Great Britain during a three-year period appeared to be related to transmission from cattle.61 The Centers for Disease Control committee states that the "evidence is insufficient to establish a direct link between BSE and nvCJD, but goes on to say that this is "the most likely explanation."62 The clustering of these cases in people under the age of 30 years was a source of concern. The expected number of cases of Creutzfeldt-Jakob disease in this age group is one in five billion individuals.

BSE from the consumption of cattle does not presently appear to be a health threat in the United States. Sheep-tissue products comprises only 0.6% of those from rendered animals in the United States compared to 14% in Britain. In the United States, the prohibition against feeding offal to other ruminants and the more widespread use of plant-based proteins make the infection less of a threat.62 In addition, an effective surveillance program in the U.S. indicates that cattle are BSE free. However, free-ranging mule deer, white tail deer, Rocky Mountain elk,63 cats, and mice64 have been shown to be infected with transmissible spongiform encephalopathies. There has even been the report of a possible case of prion disease related to a hunter's consumption of a tradi-
Agricultural practices in which cattle are fed infected sheep or other infected cattle are the vector for human infection. The international trade in beef; variations in husbandry practices among countries; and the long incubation period for TSEs create the potential for global spread of the disease. However it appears that the British response, which has included culling infected cattle, prohibiting the use of infected sheep as feed, changing the practice of rendering, the use of infected sheep as feed, and other infected cattle as the vector for human infection. The international trade in beef, variations in husbandry practices among countries, and the long incubation period for TSEs create the potential for global spread of the disease.