An Evaluation of the Risk of Variant Creutzfeldt-Jakob Disease from Exposure to Cattle-Derived Protein Used in Cosmetics

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Introduction

The discovery of a cow with bovine spongiform encephalopathy (BSE) in Washington State in December 2003 triggered action to put in place additional safeguards against BSE. Even though the cow was born in Canada, the fact that the cow was discovered in the U.S. and had been sent to slaughter and rendering before it was identified as positive indicates a vulnerability in the U.S. BSE protective net.

While BSE is usually identified with either food safety or animal health, cosmetics, because of the ways they are used, provide another route for BSE infectivity to enter the human system. Cosmetics may contain a wide range of cattle-derived ingredients, many of which may carry the BSE agent. FDA prepared this assessment of the risks to public health if cattle-derived ingredients are used in cosmetics.

This qualitative risk assessment follows the generally accepted framework for risk assessments endorsed by the Codex Alimentarious Commission, the U.S. National Academy of Sciences, and other authoritative bodies. The framework divides risk assessment into four components: (1) hazard identification, (2) exposure assessment, (3) hazard characterization (or dose-response assessment), and (4) risk characterization. The risk assessment uses scientific evidence to the extent that it exists. The agency has determined that this qualitative risk assessment is appropriate to the circumstances.

Risk Assessment

Hazard Identification

In April 1996, British scientists reported a previously undetected new variant of Creutzfeldt-Jakob disease (vCJD) in young patients, with symptoms somewhat different from sporadic CJD (Refs. 1 and 2). All cases of vCJD had histopathologic evidence of spongiform changes in the brain, but also showed formation of "florid" plaques (a core of amyloid protein with surrounding halos of vacuoles) not typically seen in other forms of CJD (Ref. 3). Clinically, vCJD usually begins with a psychiatric presentation, such as depression, anxiety, nightmares or hallucinations. These symptoms are followed by memory impairment, then dementia in the late stages. The clinical course may last up to two years before death occurs (Ref. 4).

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Because scientific evidence suggests that the presence and infectivity of abnormal prion proteins in vCJD share characteristics with abnormal prion proteins found in cattle with BSE, scientists have concluded that exposure to the BSE agent is the most plausible explanation for the occurrence of vCJD (Refs. 5 - 8). Monkeys (genetically the closest animal model to humans) inoculated with samples of brain from BSE-infected cattle have been found to develop a TSE that is histopathologically similar to vCJD (Ref. 9), as have mice inoculated or fed with BSE-infected tissue (Ref. 10). In addition, studies have shown that abnormal prion proteins from vCJD patients are molecularly similar to abnormal prion proteins from BSE-infected cattle and different from abnormal prion proteins from patients with CJD and other spongiform encephalopathies (Ref. 4).

Prions are predominantly found in the central nervous system, portions of the intestine, and tonsils of cattle with BSE. Cosmetic ingredients can be derived from some of these tissues. Although large prion doses are known to have a shorter incubation period before the disease develops, even low doses may cause vCJD if infectious prions survive digestion and the host survives long enough to complete a longer incubation period. Although most scientists believe that vCJD in humans is caused by consumption of cattle-derived food products contaminated with the agent that causes BSE (Refs. 11-14), exposure from cosmetics derived from cattle protein is another potential route of exposure.

Exposure Assessment

BSE in the United States

On December 23, 2003, USDA diagnosed a positive case of BSE in an adult Holstein cow in the State of Washington.

Use of Cattle Protein in Cosmetics

Cosmetics may be made from a variety of cattle-derived ingredients. These ingredients include albumin, brain extract, brain lipid, cholesterol, fibronectin, sphingolipids, collagen, keratin, and tallow and tallow derivatives. However, tallow derivatives, particularly fatty acids and glycerin, are the predominant bovine ingredient used by the cosmetic industry and contain very little protein, and are therefore unlikely vehicles for the transmission of prions. Cattle-derived ingredients serve many functions and may be used as skin conditioning agents, emollients, binders, and hair and nail conditioning agents.

Absorption of Prions from Cosmetics

There are several routes through which cosmetics contaminated with the agent that causes BSE could transmit disease to humans. Transmission of the BSE agent to humans through intact skin is believed to be unlikely; however, cosmetics may be ingested or applied to cut or abraded skin or to conjunctival tissues that can provide direct routes for infection.

It is well-documented that central nervous system tissue, including the optic nerve, carries infectivity in animals with TSEs and humans with vCJD, and serves as an efficient route of transmission. In mice, intraocular injection of scrapie caused infection along the optic nerve, which eventually spread into non-neural tissue via the lymphatic system (Ref. 15). In addition to intraocular injection, infectivity has been transmitted to animals via the conjunctiva of the eye (mucosal tissue). Scott et al. (Ref. 16) found that scrapie was induced in 42 percent of rodents by dropping a high concentration of infectivity onto the conjunctiva. Klitzman et al. (Ref. 17) suggested that kuru, a human TSE disease found only among the Fore people of New Guinea, might have been transmitted by rubbing infected human brain into eyes or cut skin, while handling and consuming infected brain during funeral rituals.

Cut or abraded skin also has been proposed as a route for contracting TSE diseases. The transmission of kuru through cut skin has been suggested and was mentioned previously. Taylor et al. (Ref. 18) and Ingrosso et al. (Ref. 19) demonstrated increased transmission of scrapie via oral mucosal tissue. In one study, 100 percent of mice with experimentally damaged oral mucosal tissue developed scrapie through ingestion of infected material, while only 71 percent of mice with intact mucosa developed the disease (Ref. 18). In addition, Pammer et al. (Ref. 20) and Sugaya et al. (Ref. 21) noted that epithelial cells, dendritic cells, and keratinocytes (the primary cell types found in the epidermis) have been found to contain infectious prion protein, indicating that these cells are potential targets for peripheral infection with a TSE disease.

Use of BSE-contaminated cosmetics could provide a means of human infection via several routes discussed above. Many cosmetics are typically applied in the area of the eye (mascara, eye brow pencil, eyeliner, eye lotion, and eye makeup remover) and almost any cosmetic, including shampoo, can get into the eye via eye rubbing or incorrect application. Any cosmetic product, but particularly shaving creams and gels and lotions, may be applied to cut or abraded skin. Cosmetics that are ingested, such as lipstick, dentifrices, mouthwash, and breath fresheners, would have an oral route of infection, and the ingested fraction would have the same risk as prion-contaminated meat and other food products derived form cattle. Furthermore, the presence of cattle derived ingredients is not generally obvious to the consumer, since the source of the ingredient (i.e. cattle derived) does not need to be placed on the label.

Hazard Characterization

Prions with a particular abnormal tertiary structure are apparently able to generate a similar misconformation in normal proteins, which can in turn cause further misconformations. This allows propagation of the disease and is also important for understanding the relationship between dose, response, and the incubation required for the disease to develop. Once the prions have entered the brain, the prion concentration grows with a relationship that has been described as exponential (Ref. 14).

In cattle, there is a minimal incubation period of six months to a year required for the development of the disease, regardless of the size of the initial dose, although incubation periods of 4 or more years appear to be more common (Refs. 11 and 12). The lag period may reflect the fact that transmission from food to brain may be preceded by symptomless amplification of infectious prions in the intestine and lymphoreticular tissues. While cattle at this stage would be clinically normal and may have negative BSE test results, various tissues could be infectious (Refs. 11 and 12).

Despite widespread exposure in the U.K. to BSE-contaminated meat products, only a very small percentage of the exposed population has been diagnosed with vCJD to date. However, ongoing experiments indicate that the infectious dose for cattle is very low. One gram of affected bovine brain homogenate is sufficient to cause BSE in more than 50 percent of calves exposed by mouth. Five years after oral consumption of lower doses of brain material, 2 of 15 calves fed 0.1 gram had onset of BSE, and 1 of 15 fed 0.01 gram had developed the disease. This experiment is ongoing (Ref. 22). There is thought to be a 10- to 10,000-fold increase in the amount of infectious material needed to cause illness in humans as compared with cattle, because of the species barrier (Ref. 23).

Risk Characterization

This is not a quantitative risk assessment. However, it does sketch out the logical structure that a quantitative model could use if one were constructed. Some conclusions can be drawn without a quantitative analysis. Since there is considerable uncertainty associated with the premises outlined in the present analysis, it follows that there will also be considerable uncertainty associated with the risk estimate. In the exposure assessment, there are considerable uncertainties associated with the origin of protein used in making cosmetics, the effect of processing on prion concentration, and the transmission rates for dermal and ocular exposure. Particularly large uncertainties associated with the dose response assessment include the magnitude of the species barrier and the length of the incubation period.

With exception of the uncertainty associated with estimates of the dermal and ocular transmission rates, most of the uncertainties associated with a risk assessment of BSE prions in cosmetics are also associated with the risk from food consumption. For example, the number of BSE-affected cattle and the variability in human susceptibility will impact the risk of both food- and cosmetic-associated vCJD.

Some of these uncertainties may concomitantly affect both sides of a cost-benefit analysis. In particular, if there is not substantial use of cattle-derived protein in making cosmetics, then there will be little exposure, and also little economic consequence from regulating use. Conversely, high use would require substantial substitution and alternative means of animal-by-product disposal.

Conclusions

A form of spongiform encephalopathy that occurs in humans (vCJD) is thought to result from the same protein (a prion) that causes BSE in cattle. Although the primary source

of exposure is likely to be due to the ingestion of beef and other food derived from cattle, other routes of exposure may also be important. Although small doses require longer incubation periods for clinical signs to develop, small doses of infectious prions can potentially cause disease. Cosmetics that contain protein derived from bovine sources are a potential source of exposure. It has been demonstrated experimentally that TSEs may result from ocular absorption of protein, and systemic absorption of protein may also occur when cosmetics are applied to lacerated or abraded skin. As a result, it may be concluded that there is some risk of occurrence of vCJD from the use of cattle-derived protein in cosmetics. However, since there are large uncertainties associated with the quantitative estimates of many of the important variables, any quantitative estimate of the risk or rate at which the disease may be expected to occur would be correspondingly imprecise.

The risk of BSE from cosmetics may be reduced through the control of exposure. Aside from the derivation processes used on tallow, the effectiveness of cosmetic manufacturing processes for inactivating BSE prions is unknown. The surest way to prevent transmission of BSE-prion through cosmetics is to avoid the use of high-risk cattle-derived protein in the manufacture of cosmetics.

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