

Vaccination of Cattle against *Escherichia coli* O157:H7

DAVID R. SMITH¹

¹College of Veterinary Medicine, Mississippi State University, Mississippi State, MS 39762-6100

ABSTRACT Human infection with Shiga toxin-producing *Escherichia coli* O157:H7 (STEC O157) is relatively rare, but the consequences can be serious, especially in the very young and the elderly. Efforts to control the flow of STEC O157 during beef processing have meaningfully reduced the incidence of human STEC O157 infection, particularly prior to 2005. Unfortunately, despite early progress, the incidence of STEC O157 infection has not changed meaningfully or statistically in recent years, suggesting that additional actions, for example, targeting the cattle reservoir, are necessary to further reduce STEC O157 illness. Ideally, preharvest interventions against STEC O157 should reduce the likelihood that cattle carry the organism, have practical application within the beef production system, and add sufficient value to the cattle to offset the cost of the intervention. A number of STEC O157 antigens are being investigated as potential vaccine targets. Some vaccine products have demonstrated efficacy to reduce the prevalence of cattle carrying STEC O157 by making the gut unfavorable to colonization. However, in conditions of natural exposure, efficacy afforded by vaccination depends on how the products are used to control environmental transmission within groups of cattle and throughout the production system. Although cattle vaccines against STEC O157 have gained either full or preliminary regulatory approval in Canada and the United States, widespread use by cattle feeders is unlikely until there is an economic signal to indicate that cattle vaccinated against STEC O157 are valued over other cattle.

INTRODUCTION

Human infection with Shiga toxin-producing *Escherichia coli* O157:H7 (STEC O157) is relatively rare, but the consequences can be serious, especially in the very young and the elderly. Outcomes associated with STEC O157 infection include hemorrhagic colitis, renal failure, and death (1–5). In 2012, the overall laboratory-confirmed annual incidence of STEC O157 in the United States was 1.1 cases per 100,000 population (6).

However, the incidence in children less than 5 years of age was 4.7 cases per 100,000 population (6).

Infection from STEC O157 occurs directly or indirectly via fecal-oral transmission (7). People are exposed to STEC O157 through a variety of sources, including direct contact with human or animal feces and indirect contact via contaminated food, water, or soil (8). The primary route of transmission of STEC O157 is contaminated food (9, 10); however, large outbreaks have been associated with contamination of municipal water supplies (11–14). Important environmental hazards for human exposure to STEC include daycare facilities, nursing homes, children playing with a sick friend, swimming pools, contaminated food and water, and direct exposure to animal environments such as farms, petting zoos, or livestock exhibitions (9, 10, 15). Approximately one-third of human infections are attributed to consumption of ground or nonintact beef (16). Some of the earliest and most notorious outbreaks of STEC O157 infection were associated with the consumption of undercooked ground beef sandwiches, resulting in the infection being commonly known as “hamburger disease” (2, 17–19).

STEC has been recovered from many animal species, but ruminants are particularly prone to colonization

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Correspondence: David R. Smith, dsmith@cvm.msstate.edu

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(20). Of ruminants, cattle populations are widely recognized as an important reservoir of STEC O157 for human exposure in the United States (8, 21).

A variety of vehicles, other than food, have been important in the fecal-oral transmission of STEC strains to humans, including fomites such as dust (22) and water (11–14) and vectors such as flies (23–27). Other animals, besides cattle, have caused important STEC outbreaks in humans because they served as vehicles for fruit or vegetable crop contamination. For example, a large STEC O157 outbreak in the United States and Canada was due to consumption of spinach that was contaminated in the field by feces from feral pigs that had contact with cattle pastures (28). In Oregon, deer were the source of feces that contaminated strawberries with STEC O157, resulting in one death and at least 14 illnesses (29).

Circumstantial evidence supports the contention that cattle are the primary reservoir for human exposure to STEC in North America. First, there is strong correlation between seasonal variability in incidence of human STEC O157 illness, prevalence of ground beef contamination with STEC O157, and prevalence of STEC O157 shedding by cattle in feedlots, all greater in summer months than winter months (30). This relationship may indicate that STEC O157, originating in or on cattle, contaminates ground beef to eventually become the source for subsequent human infection (30). In addition, there is a correlation between the prevalence of carriage of STEC O157 in feces or on hides of live cattle entering the abattoir and subsequent rates of carcass contamination (31, 32). Finally, since 1998 in the United States, human incidence of STEC O157 has decreased (6), largely because of interventions taken in abattoirs to reduce the flow of STEC O157 from live cattle into the beef supply (33, 34). The decrease in incidence since 1998 is greater than the proportion of illnesses attributable to contaminated beef, suggesting that decreasing the bacterial flow from beef prevented secondary cases of person-to-person STEC O157 infection. Unfortunately, the incidence of STEC O157 infection has not changed meaningfully or statistically compared to the average annual incidence during 2006–2008, suggesting that additional actions, for example, at the preharvest level, are necessary to further reduce rates of STEC O157 illness (6).

PREHARVEST ECOLOGY OF STEC O157

Cattle are colonized by STEC O157 primarily at the terminal rectum (35, 36). Colonization by STEC O157 requires attachment to intestinal epithelium and induces attaching and effacing lesions. Following STEC O157

infection in cattle of all ages, inflammation and innate and adaptive immune responses occur (37), supporting the contention that STEC O157 is a bovine pathogen (37, 38). However, this latter point remains controversial because infection does not result in clinically observable signs of illness in adult cattle (39, 40). In any case, not all cattle shedding STEC in their feces are currently colonized; some may be shedding ingested organisms that are simply passing through the intestinal tract (41, 42). The duration of infection in cattle is variable but short-lived, approximating a month (41, 43–45). In field settings, reinfection is common (44).

Prevalence of STEC O157 carriage by feedlot cattle varies widely within and across seasons and is affected by both incidence and duration of shedding (44, 46, 47). The probability of cattle carrying STEC depends on both gut and environmental conditions that change over time. As with all *E. coli* strains, conditions of the bovine gut that favor STEC O157 may increase colonization and duration of shedding. Factors of the environment that favor STEC O157 survival or opportunities for fecal-oral transmission increase the incidence of exposure. This is because pathogenic and commensal *E. coli* strains have two principal habitats: a primary habitat in the lower intestine of warm-blooded animals and a secondary habitat in water, sediment, and soil (48). The suitability of the primary habitat is influenced by factors such as physical characteristics (e.g., pH); the host's diet, immune system, and physiological state; and interactions with other microorganisms in the same region. The suitability of the secondary habitat is also complex and dependent on physical factors, climatic and meteorological factors, nutrients, and interactions with other microorganisms within the ecosystem. In contrast to the primary habitat, which is uniformly warm, approximately 37°C, and nutrient rich, the secondary habitat may have extremes in temperatures and is typically nutrient deficient (48). Environmental conditions that favor survival and fecal-oral transmission have been associated with greater rates of exposure and shedding in feedlot cattle (46, 47).

Transmission heterogeneity, or superspreading, is the phenomenon of a minority of infected individuals being responsible for transmitting the majority of new infections (49, 50). At a given point in time, STEC O157-infected cattle shed the organism at varying concentrations in feces (42, 51, 52). Therefore, some cattle may contribute vastly more STEC organisms into the environment, and possibly to other cattle, than others. Cattle that shed STEC at greater than 10³ or 10⁴ CFU/g of feces, or cattle that are culture-positive for prolonged

periods, have variously been defined by the term super-shedder (42, 51). It has been proposed that super-shedding status is indicative of cattle colonized by STEC rather than cattle experiencing simple pass-through of organisms (42). Because of the greater number of organisms being shed, cattle designated as super-shedders may have an important effect on environmental contamination and subsequent transmission within cattle production settings (53) or in lairage (54). The relevance of super-shedding to STEC O157 control is not clear. Super-shedding of STEC O157 in feces does not appear to be a persistent state, and we do not yet understand if super-shedding is a characteristic of certain cattle or merely a stage of infection that cattle transition through following infection. It has been observed that detection of super-shedding cattle is temporally correlated with periods of high prevalence, and super-shedder cattle appear to be a subset of fecal-culture-positive individuals within the population (42, 55). Super-shedding may not be necessary or sufficient for STEC O157 transmission, even in closed (all-in, all-out type) feeding systems (56). Rather than super-shedding cattle driving transmission of STEC to other cattle, super-shedding may be an outcome of environmental conditions that favor ingestion of the organism (47). When those conditions favor new host infections, then some cattle may become colonized and transiently shed large numbers of organisms, and because of favorable conditions for transmission, the duration of detectable shedding may be prolonged (44).

To reduce the prevalence of STEC O157 carriage by cattle, efforts have been attempted to make either the primary or secondary habitat less favorable to STEC O157 survival or growth (57–59). To date, efforts to make the cattle environment less hospitable to STEC O157, for example, by scraping pen surfaces or cleaning water tanks, have not effectively reduced STEC O157 carriage by cattle (60–62). However, several strategies for modifying the gut environment, including the use of vaccines; chemicals, such as sodium chlorate or antibiotics; and competing microorganisms, such as some strains of *Lactobacillus*, have effectively reduced the probability of cattle shedding STEC O157 in feces (63–66).

VACCINATION OF CATTLE AGAINST STEC O157

The objective of immunizing cattle against STEC O157 is to make the gut unfavorable for colonization, thereby reducing duration of carriage and minimizing shedding

of the pathogen into the cattle environment (58). In theory, the benefit of vaccination within discrete populations (e.g., pens or herds of cattle) is reduced fecal-oral transmission within cattle environments, less contamination of cattle hides, and fewer pathogens carried into the abattoir at harvest. For vaccination to be useful as a preharvest intervention, the benefits must not be undone during subsequent management practices, such as transportation to the abattoir (67) or during holding in lairage (32, 68, 69). Preharvest interventions such as vaccination are not likely to be adopted widely by cattle producers until they are sufficiently valued in the marketplace to offset the cost of implementation.

Some candidate vaccines against STEC O157 have been tested in animal challenge studies or under field conditions of natural exposure. These vaccines either have undefined antigen targets in the form of bacterial extracts or are directed against specific antigens that function to enable bacterial colonization or survival. Unfortunately, because of serotype specificity, vaccines targeting STEC O157 may offer poor cross-protection against other STEC strains (70).

In randomized controlled studies, the strength of effect of a vaccine is often expressed as vaccine efficacy, a form of attributable fraction that measures the percentage of cases prevented by vaccination (71). Vaccine efficacy is calculated as 1 minus relative risk (72). In this case, relative risk is the probability of vaccinated cattle to carry STEC O157 divided by the probability of nonvaccinated cattle to carry the organism. The odds ratio is the statistical measure of association often reported from vaccine field studies because logistic regression is a commonly used method to analyze the data. Regardless of whether the comparison uses odds (i.e., odds ratio) or probability (i.e., relative risk), a value of 1 indicates no difference from the treatment. The further the value is from 1, toward 0 or infinity, the larger the measure of association. If the study is not a case-control study design, then odds ratio can be converted to relative risk after adjustment for marginal probabilities for disease and exposure (73). In studies with measures of fecal concentration, the measure of association may be expressed as the change in concentration due to vaccine treatment, which is often described as a logarithmic (base 10) reduction (74) and sometimes reported as a percentage (e.g., a decrease from 10,000 CFU/g of feces to 1,000 CFU/g of feces is a decrease of 1 log₍₁₀₎ in CFU/g of feces and may be expressed as a 90% reduction in shedding concentration).

Vaccine Challenge Studies

STEC O157 colonizes bovine intestinal epithelial cells by a type III secreted protein (TTSP) system. Components of the TTSP system include:

- Intimin, an outer membrane bacterial receptor
- Translocated intimin receptor (Tir), a receptor injected into the host epithelial cell membrane
- EspA, an injection filament for delivering Tir to the host cell membrane
- EspB/EspD, which form a pore in the host cell membrane (7, 40, 75, 76)

The H7 flagellin is also believed to function in STEC O157:H7 colonization (77–79). For some STEC non-O157 serotypes, the enterohemorrhagic *E. coli* factor for adherence (*efa-1*) is important for colonization of bovine intestines, and STEC O157 carries a truncated form of the gene (80).

Vaccines targeting various STEC O15-specific antigens have been tested in animal challenge studies. Several studies have demonstrated immune response against the antigens but variable results regarding protection against STEC O157 infection. Suckling pigs whose dams were vaccinated with an intimin vaccine were protected from colonization or microscopic evidence of intestinal damage following oral challenge with 10^6 CFU of a Shiga toxin-negative strain of EHEC O157:H7 (81). Calves vaccinated with EspA developed antigen-specific antibody titers but failed to be protected against colonization with STEC O157 following challenge (82). Similarly, subunit vaccines targeting polypeptides of intimin or *efa-1* elicited humoral responses in 2-week-old calves following intramuscular priming and intranasal booster doses, but the vaccine products failed to prevent shedding after STEC O157 or STEC O26 challenge (80). In the same study, a formalin-inactivated STEC O157 bacterin administered intramuscularly with subsequent intranasal booster doses also failed to reduce shedding in challenged calves (80). Two-month-old calves vaccinated intramuscularly with H7 flagellin had reduced rates of colonization and delayed peak bacterial shedding following oral challenge with STEC O157, but the calves did not show a reduction in total bacterial shedding (83). However, a vaccine prepared with intimin, EspA, and Tir did reduce STEC O157 colonization and bacterial counts in calves orally inoculated with STEC O157 (84). Also, lambs that had been vaccinated with intimin, EspA, and EspB shed fewer bacteria in feces than placebo-treated controls did following an oral challenge with STEC O157 (85). Six- to 8-month-old

calves injected intramuscularly with a vaccine product containing intimin and EspB proteins developed an antibody response against the proteins and shed fewer STEC O157 bacteria in the first 13 days post challenge (86). Calves vaccinated with a bacterial supernatant with TTSP had reduced probability, magnitude, and duration of shedding of STEC O157 following challenge (87). In a follow-up study, calves receiving the same vaccine product were 21% less likely to shed STEC O157 in the feces and shed at a $1.4 \log_{(10)}$ lower fecal concentration 3 to 6 days after experimental challenge with 10^9 CFU of STEC O157 (74). Calves injected twice subcutaneously with an inactivated, whole-cell envelope vaccine (STEC O157 bacterial ghosts) demonstrated an antibody response and shed fewer STEC O157 post challenge (88). Vaccination of pregnant cows with intimin, EspA, EspB, and Shiga toxin 2 within 2 months of calving produced elevated serum and colostrum antibodies against intimin and EspB and a moderate increase in EspA antibodies (89). Calves fed the dam's colostrum had significantly increased serum immunoglobulin G titers against intimin and EspB, but not EspA (89).

Siderophore receptor and porin (SRP) vaccines are targeted against bacterial cell membrane proteins used by gram-negative bacteria for iron transport in conditions of low iron supply (90). By limiting its uptake of iron, STEC O157 is placed at a competitive disadvantage relative to other gut microbiota (91). In a study of beef calves orally inoculated with STEC O157, the SRP vaccine reduced fecal prevalence and bacterial concentration to a level that approached statistical significance (90).

Vaccine Field Studies

The outcomes of experimental challenge studies may not predict the efficacy of a STEC O157 vaccine as it is used under field conditions because factors affecting rates of transmission, sources of pathogens, and dose-loads of exposure are complex and temporally dynamic in cattle production settings (44, 46, 47). Only a few STEC O157 vaccine products have been evaluated for efficacy in the conditions of natural STEC O157 exposure within cattle production systems. An uncharacterized bacterial extract did not reduce STEC O157 carriage in feedlot cattle (92). Another uncharacterized STEC O157 vaccine, administered to pregnant beef cattle during the last trimester of gestation, significantly increased antibody titers in the dam and subsequently the calf, but the study had insufficient power to evaluate efficacy at preventing shedding of STEC O157 by the calves (93). Calves

suckling cows that had been vaccinated against SRP antigens had significantly greater antibody titers against STEC O157 SRP at branding (i.e., 30 to 60 days of age), but neither the passively acquired antibodies nor active immunization significantly prevented STEC O157 shedding by the calves at feedlot entry (94).

Two vaccine products, one targeting TTSP, the other SRP, have been tested extensively in dry-lot beef feedlots under conditions typical of the Central Plains regions of the United States and Canada. These products were the subject of several systematic reviews and meta-analyses that found sufficient evidence to conclude that both vaccines effectively reduce the probability of feedlot cattle to shed STEC O157 in feces (63, 95). One meta-analysis of fecal shedding found the overall odds ratios (and 95% confidence intervals) for detecting STEC O157 in the feces of vaccinated cattle relative to non-vaccinated cattle to be 0.38 (0.29–0.51) and 0.42 (0.20–0.61) for TTSP and SRP vaccines, respectively (63). Given the overall fecal shedding prevalence of 15% observed in the TTSP studies (63), the odds ratio of 0.38 converts to a relative risk of 0.42 and vaccine efficacy of 0.58 (96). Another meta-analysis looked at all outcomes and reported that two doses of TTSP vaccine had odds ratios of 0.49 (0.40–0.60) for preharvest outcomes and 0.45 (0.34–0.60) for preharvest and at-harvest outcomes combined (95).

Details from individual studies provide additional information about the efficacy of STEC O157 vaccine products, although some details, such as antigen concentrations, have not always been reported. Using steers screened to be negative for STEC O157 carriage before the study start, researchers found that steers vaccinated twice with either 2 or 3 ml of SRP vaccine were 14 and 47% less likely than placebo-treated steers to have STEC O157 detected in either feces or rectoanal mucosa swab samples, respectively (97). Feedlot cattle receiving a 2-ml, two-dose SRP vaccine regimen did not differ from controls in STEC O157 carriage over the postvaccination period except for the last day of the study (91). In a trial testing a 2-ml, three-dose SRP vaccine regimen against placebo-treated cattle, the vaccine was 85% effective in reducing the probability of detecting STEC O157 in feces and reduced STEC O157 concentration 1.7 logs compared to controls 56 days after the last dose of vaccine (91). In a vaccine trial conducted in a commercial feedlot, the SRP vaccine demonstrated 53% vaccine efficacy in reducing STEC O157 prevalence and 73% efficacy in reducing the prevalence of high shedders, defined as cattle shedding $>10^4$ CFU/g of feces (98). In that study, pens of cattle receiving vaccination

had significantly reduced feed efficiency and rate of gain, which may represent an additional cost of the intervention (98).

Vaccinating feedlot cattle with a TTSP vaccine product failed to be efficacious in a large initial vaccine field trial (99). However, the vaccine product was reformulated and efficacy improved (99). Vaccine efficacy of a three-dose regimen of TTSP vaccine to reduce the probability of feedlot cattle shedding STEC O157 has ranged from 43 to 73% in several randomized controlled trials (87, 100–102). In addition, the vaccine was 92% and 98% effective in reducing the probability of colonization of the terminal rectum when two- (103) or three-dose (104) regimens, respectively, were used. Two doses of the same vaccine product significantly reduced carriage of STEC O157 by feedlot cattle (103, 105, 106), and it appears that two doses of vaccine may be sufficient to induce an effective immune response (95). However, three doses of vaccine were more effective than two doses in trials with direct comparisons (100, 107). This vaccine does not appear to affect growth performance (104, 107) or carcass quality (104, 106, 107).

The duration of immunity after vaccination is unknown because the evaluation period in feedlot studies has been relatively short, typically with postvaccination observation periods of between 60 and 100 days (63, 108, 109). Increasing or decreasing immunity would be evident as a statistical interaction between vaccine treatment and time elapsing since vaccination on the probability of cattle carrying the organism. This interaction has not been reported. Even though vaccine efficacy appears to persist sufficiently long enough for cattle on finishing diets, duration of immunity remains an important unmet area of investigation for beef and dairy young-stock and breeding cattle (109).

Cattle are typically managed as groups (e.g., pens or herds of cattle), which are fed and housed together. Similarly, cattle management practices such as vaccination are usually applied to the group, partly for ease of management and to provide protection to the group rather than simply the individual. The ability of groups to resist infection, or to limit the extent of infection within the group, is termed herd immunity (110). Herd immunity is a function of individual resistance to infection and the dynamics of transmission within the group (110, 111). Individuals lacking immunity may be protected from infection because of group-level factors; for example, the majority of individuals with immunity change the likelihood of exposure to those without (110).

The probability of cattle carrying STEC O157 in the gut or on their hides is affected by group-level factors. For example, the distribution of fecal prevalence of STEC O157 within pens of feedlot cattle tends to be greater or lesser than expected by binomial distribution around the mean (46), suggesting that, at a given point in time, cattle within pens behave similarly with respect to STEC O157 shedding (i.e., most cattle shedding or most not). Factors explaining the probability of cattle shedding the agent or having evidence of oral exposure are associated with characteristics of the pen environment that either favor survival of the organism (e.g., warm or wet) or increase opportunities for ingestion (e.g., mud or dust), indicating that sometimes the pen environment favors fecal-oral transmission and sometimes it does not (44, 46, 47, 112). Therefore, it is important to evaluate group-level effects of vaccinating cattle against STEC O157. There is evidence that fecal-oral transmission of STEC O157 is reduced within pens of vaccinated cattle. Herd immunity was demonstrated in a longitudinal STEC O157 vaccine study as non-vaccinated cattle housed with vaccinated cattle were less likely to shed STEC O157 compared to cattle penned in the same feedyard where none of the cattle received vaccine (107). Vaccinated cattle housed together in large commercial feedyard pens were less likely to have oral exposure to STEC O157 compared to nonvaccinated cattle housed together in pens in the same feedyards, based on culturing ropes hung on feedbunk rails for cattle to chew (103). Culture of STEC O157 from ropes is correlated to fecal shedding prevalence (112), and more directly measures opportunities for oral exposure (113).

The value of considering the effects of group-level vaccination when designing a STEC O157 cattle vaccination program was demonstrated by the greater efficacy in reducing hide contamination when all cattle in a region of a feedyard were vaccinated compared to the efficacy observed when vaccinated and unvaccinated cattle were commingled within pens (106). Efficacy against hide contamination is important because the hides of cattle are the primary source of STEC O157 carcass contamination (32, 69, 114, 115). It was hypothesized that vaccination of all cattle within a region of a feedyard, or the entire feedyard, would result in a greater reduction in the load of organisms deposited by cattle into the environment and less subsequent contamination of hides than when vaccinated cattle are commingled in pens of nonvaccinated cattle (106). This finding illustrates that the goal of a cattle vaccination program against STEC O157 is to reduce environmental

pathogen load to minimize ingestion of the organism or hide contamination, and this may be accomplished most effectively by administering the vaccine to all cattle within a production system (106).

Whatever efficacy a vaccine may have before harvest, it can be undone by events occurring during subsequent stages of the food system, such as cross-contamination of cattle hides with STEC O157 during transportation or while cattle are in lairage (32, 67, 116). However, the efficacy of preharvest interventions has persisted into the abattoir. In a randomized clinical trial to test a STEC O157 cattle vaccine, there was a significant increase in the prevalence of hide contamination between the time immediately before loading at the feedyard versus just before hide removal in the abattoir. However, vaccination treatments had equal efficacy for reducing hide contamination in the feedyard and at the abattoir. The preservation of vaccine efficacy into the abattoir may have been the result of efforts to load cattle by treatment groups into clean trucks for transportation to the abattoir (106). Therefore, to preserve vaccine efficacy, it may be necessary to devise methods for cattle handling so that preharvest benefits are retained post harvest.

Modeling STEC O157 Vaccine Usefulness

Ultimately, the reasons for vaccinating cattle against STEC O157 are to (i) benefit public health by preventing human STEC O157 infection and (ii) reduce costs to the beef industry due to recalls, lost product value, and liability. There is value in preventing human illness from direct contact with cattle or their environments, but this is a less common source of human illness compared to infections acquired through contaminated food, including beef, milk, and vegetable crops (9, 10). The primary value of vaccinating live cattle is the benefit to the post-harvest sectors of the food system and the consumers of food products. An intervention is not likely to be used if the costs of the intervention exceed the benefits to the food industry or public health. Mathematical models provide a conceptual framework for understanding pathogen transmission dynamics. Models can help identify knowledge gaps, give insight into new research questions, and predict the usefulness of intervention strategies (117).

From a public health policy perspective, one might compare the cost of human illness to the cost of a preharvest intervention. If the marginal costs of vaccinating cattle were equivalent to the marginal benefit to public health, then as the cost of a vaccine intervention increased, fewer cattle would be vaccinated, and as a result, fewer human illnesses would be prevented. Similarly, the

number of cattle that must receive an intervention to prevent a single human illness increases as the effectiveness of the product decreases (16). From a beef industry perspective, preharvest interventions might be valued on the basis of how cattle carrying STEC O157 into the abattoir affect subsequent food safety costs. For example, because an important source of STEC O157 carcass contamination is the hide (32), and fecal shedding prevalence above 20% has been associated with higher prevalence levels of hide contamination (118), postharvest sectors of the beef industry might benefit from preharvest interventions that supply cattle at harvest with less hide contamination and reduced, less variable, fecal shedding prevalence that does not overwhelm subsequent postharvest interventions.

Quantitative or qualitative models have been used to investigate the value of vaccinating cattle and other methods of intervention. Many models predict benefit to both public health and the beef industry from vaccinating cattle against STEC O157. For example, a model simulating ground beef contamination in Argentina predicted that vaccinating cattle and online hide washing would have the greatest impacts on reducing STEC O157 prevalence and concentration in ground beef product and the resulting numbers of human infections, hemolytic-uremic syndrome, and STEC O157-associated mortalities per ground beef meal (119). A stochastic simulation model based on U.S. beef production systems and risk for infection through consumption of ground beef also concluded that vaccination of cattle would have a strong impact on decreasing the number of human STEC O157 illnesses, the number of contaminated beef production lots, the likelihood of STEC O157 detection by regulatory testing, and the probability of outbreaks due to ground beef servings from the same lot (120). A simulation model was used to investigate infection transmission in pastured cattle systems. The modelers concluded that vaccine efficacy of 60% would be particularly effective in reducing levels of infection in a herd (121). Stochastic simulation of the distribution of pen-level fecal shedding prevalence in U.S. commercial beef feedyards predicted that vaccination of summer-fed cattle with a 58% effective product would eliminate pens of highest prevalence, resulting in a prevalence distribution similar to what is typically observed in winter-fed cattle. This model showed that a major effect of vaccination is reduced variability in shedding prevalence (122). The opinions of experts were used in a best-worse scaling evaluation to gain consensus on the effectiveness and practicality of on-farm methods to reduce human exposure to STEC O157

(123). Intervention methods were evaluated for effectiveness and practicality. By this process, vaccination of cattle was considered the most effective, and hand washing the most practical, method to reduce human exposure to STEC (123).

CONCLUSION

Ideally, preharvest interventions against STEC O157 should be

- Efficacious—cattle are less likely to carry the organism because of the intervention
- Useful—able to be practically applied within the beef production system
- Economical—add sufficient value to the product to offset the cost of the intervention

A number of STEC O157 antigens are being investigated as potential vaccine targets. Some vaccine products have demonstrated efficacy to reduce the prevalence of cattle carrying STEC O157 by making the gut environment unfavorable to colonization. However, in conditions of natural exposure, efficacy afforded by vaccination depends on how the products are used to control environmental transmission within groups of cattle or throughout the production system (106). Preharvest benefits from vaccination may be nullified unless steps are taken to prevent cross-contamination of cattle or beef product throughout the food system (68). Although cattle vaccines against STEC O157 have gained either full or preliminary regulatory approval in Canada and the United States, it is not yet clear if they will be widely adopted by cattle feeders because there is not yet an economic signal to indicate that cattle vaccinated against STEC O157 are valued over other cattle.

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