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Methods to reduce the risk of *E.coli* O157:H7 shedding in cattle

Background

E. coli O157:H7 belongs to the Shiga toxin-producing *E. coli* (STEC) and is a bacterium that often colonizes the guts of cattle, although many animal species harbor it in their digestive tract. There are other STECs besides *E. coli* O157:H7, although much less studied, and the terms are used interchangeably here. This pathogen can cause serious disease in people, especially in the elderly, children or immune-compromised. Cattle shedding STEC, on the other hand, do not show signs of disease because they lack the receptor that binds the toxin produced by the pathogen. People get exposed through various routes, such as direct contact with animals or infected persons or through water sources, but the most important route is via contaminated food [1]. Some of the foods most commonly associated with *E. coli* infections are ground beef as well as vegetables, such as Romaine lettuce, which was implicated in one of the most recent outbreaks in the US [2]. Interventions at the slaughter plant and consumer education about properly cooking meat have led to a decrease in the number of cases of human STEC infections over the past 20 years [3]. Nevertheless, there is some concern that cattle may be a possible source of STEC contamination of vegetable crops [4]. Strategies to prevent fecal shedding of STEC in live cattle is therefore desirable to complement food safety measures at the slaughter plant and during food preparation. The pathogen lives both in the environment as well as in the host and cattle shed STEC at different rates depending on factors such as ambient temperature or diet [5]. So-called super-shedders, i.e. cattle shedding at least 1000 colony forming units (CFU) / g of feces, play an important role in transmission among cattle, but the mechanisms that lead to super-shedding are not well understood [6]. Possible targets for reduction of STEC shedding are thus the environment and the guts of cattle. Vaccines targeted at *E. coli* O157:H7 have been explored as a means of reducing the survival and shedding of STEC from cattle guts. Let's look at the different targets in more detail.

External environment:

Management factors are important for biosecurity and animal health and may help reduce the burden of STEC, however, they will not eliminate *E. coli* O157:H7 from the environment.

- **Season**: STEC burden is higher in **warmer summer months** [7, 8], likely because conditions are more favorable for STEC replication in the environment. Season is one of the most reliable predictors for STEC shedding across studies and efforts to minimize STEC shedding from cattle should be intensified during the warmer months.
- **Stress:** Weaning and transport have been associated with increased STEC shedding [9, 10] and there is evidence that the stress hormone norepinephrine stimulates *E. coli* O157 growth [11]. Low-stress handling may be helpful in reducing STEC shedding.
- **Manure:** Super-shedders are thought to be the biggest contributors to pen contamination and transmission. 20% of *E. coli* O157:H7 shedding cattle are responsible for 80% of infections in cattle [12]. Unfortunately, we still don't have the means to easily identify and mitigate super-

shedders. However, reducing manure as a source of transmission through pen cleaning and proper stocking density may help reduce overall STEC shedding.

- **Water troughs**: *E. coli* O157:H7 is commonly found in pen water troughs and survives in this environment, especially at colder water temperatures [13]. Addition of disinfectants such as chlorine at 2 to 5 ppm (2 to 5 ml chlorine per 1000 L of water), 0.1% caprylic acid or trans cinnamaldehyde have been effective in reducing or inactivating *E. coli* O157:H7, but palatability and water intake by cattle may be impaired [14, 15]. In addition, organic matter such as algae and feces inactivate disinfectants quickly. Overall, water trough management, while important for cattle health and welfare, has not been identified as an efficient means to reduce STEC shedding.
- **Other species:** Rodents, insects, birds (starlings, cowbirds, egrets, wild geese), pigs, sheep and deer have all been shown to carry STEC or to increase the risk of cattle shedding STEC if found in cattle proximity [16-21]. While reducing contact of these species with cattle can have many benefits, the direct effect on STEC shedding is probably limited [22].

Internal environment:

Feeds that are associated with **increased** STEC shedding:

- **Distillers grains**: multiple studies have shown increased *E. coli* O157 shedding with feeding brewer's grains [23], dried distiller's grains [24] or wet distiller's grains [25]. The suggested mechanism is that distiller's grains are highly rumen digestible, leading to less starch passing to the hindgut and resulting in a higher fecal pH, which may be more hospitable to *E. coli* O157 [26]. However, the relationship between hindgut starch fermentation, pH and STEC survival is more complex than this and study results with other feed stuffs show different relationships [27].
- **Fasting:** fasting leads to a decrease in the amount of volatile fatty acids in the ruminant digestive tract and has been associated with an increase in STEC shedding [22].

Feeds that are associated with **decreased** STEC shedding:

- **Orange peel:** when fed at 10% dry matter to sheep in a mixture with dried orange pellets, fresh orange peel reduced *E. coli* O157:H7 in the intestinal tract of experimentally infected sheep [28].
- **Cottonseed:** Feeding whole cottonseed was associated with decreased shedding of *E. coli* O157:H7 in dairy calves [29].
- **Tasco**: a brown seaweed (*Ascophyllum nodosum*) feed additive marketed to improve intestinal health has been shown to reduce *E. coli* O157:H7 in feces by 11% [30]. This product is available in the US through Tasco's distributor Nutrablend.
- **Essential oils:** citrus oils have shown antimicrobial activity against *E. coli* O157:H7 in vitro, but controlled studies in live animals are still lacking [27].

Probiotics

Probiotics are beneficial bacteria such as *Lactobacillus acidophilus* or *Propionibacterium freudenreichii.* These bacteria work by crowding out harmful bacteria and/or promoting host immunity. Studies have shown that products containing certain probiotics can successfully reduce *E. coli* O157:H7 shedding in

cattle. Bovamine Defend® is a product that has performed well in multiple studies at reducing the risk of shedding [31, 32].

Vaccines

There is currently one vaccine conditionally licensed in the U.S. named Escherichia Coli Bacterial Extract vaccine with SRP® that is targeted against *E. coli* O157. It is marketed by Zoetis and available through veterinarians. It is labelled for vaccination of healthy cattle 5 months or older. Three doses are recommended, however the duration of immunity is unknown and there is a 60 day slaughter withdrawal period. The SRP in the vaccine's name stands for Siderophore Receptors and Porins, which are transport proteins in the *E. coli* cell surface that are necessary for iron transport into the bacterial cell. The vaccine elicits an antibody response against bacterial SRP proteins. In a field trial, cattle that received three doses of vaccine were 84.7% less likely to shed STEC, and those vaccinated that did shed had a 98% reduction in fecal bacterial concentration compared to a placebo group [33]. In a second study, where only 2 doses were given, overall shedding was reduced by 53% and the number of high shedders (shedding more than 10,000 CFU/g feces) was reduced by 77% [34]. Unlike in the first study, the second study saw a small reduction in average daily gain by 2.7% in vaccinated animals, which was contributed to the additional processing when giving the booster injection compared to control animals. In the first study all animals received three injections, either vaccine or placebo.

Vaccines for *E. coli* O157:H7 are not intended to improve the well-being or performance of cattle as *E. coli* O157:H7 is considered a commensal in cattle, not causing disease. So far, the cattle industry has shown little interest for the vaccine, because there is no perceived marketable benefit. It is also important to understand that while they seem to reduce shedding, *E. coli* O157:H7 vaccines are unlikely to eliminate all shedding of STEC from cattle.

Another point to ponder is that any of the prevention measures outlined may become futile from a meat safety standpoint, if treated cattle are mixed with untreated cattle during transport to slaughter through the spread of contaminated feces on hides [6].

Future possibilities

The addition of sodium chlorate to cattle feed or drinking water has shown promising results in *E. coli* O157:H7 reduction but its use in food producing animals is still under review by the FDA [35]. Bacteriophages are viruses that target bacteria and are already in use for reduction of *E. coli* on cattle hides at the slaughter plant. Studies in live animals have shown that phages can reduce *E. coli* O157:H7 shedding in ruminants but large-scale therapy is thought to be difficult to implement [36, 37]. Other bacterial targets for vaccines are being investigated.

Summary

E. coli O157:H7 is shed by many healthy cattle and does not cause disease in cattle. However, it is a pathogen for people and can lead to serious disease and even death if consumed. No measure will be able to completely eliminate shedding from cattle, but reduction is possible through management, nutrition or vaccination. The decision to apply any of the measures highlighted should be based on feasibility and a cost/benefit analysis in discussion with a nutritionist and/or veterinarian.

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