

The Ecology of Shigatoxic *E. coli* O157 and Prospects for On-farm Control

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The impetus for considering pre-harvest efforts for shiga-toxicogenic *E. coli* O157 (sometimes termed *E. coli* O157:H7, and denoted in the remainder of this paper as simply O157) has been the growing recognition that the risk of foodborne disease associated with O157 cannot be eliminated at processing, retailing, or consumer levels. This has led to the multiple hurdles model (Figure 1) in which some reduction is made at each level. Since reductions are multiplicative, the overall effect is one of great reduction in risk.

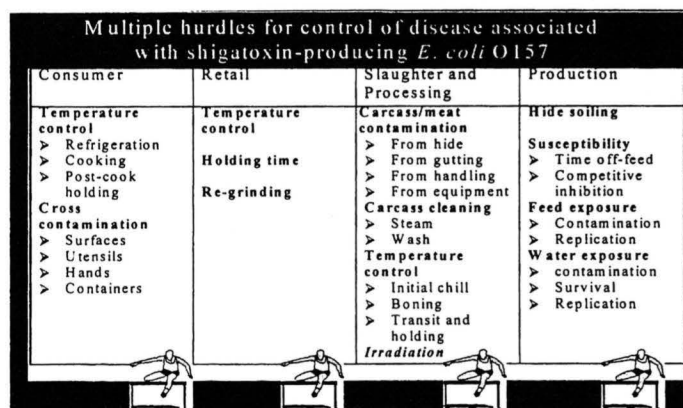


Figure 1. The widespread adoption of the multiple hurdles approach has been due to the recognition that absolute control is not possible at any level.

The primary reason to suspect that risk reduction is possible through pre-harvest efforts is the fact that cattle entering the slaughter plant are the main source of O157 for contamination of meat. In a survey of feedlot cattle in holding pens at a slaughter plant, about 2% were found to be positive. Among a small number of post-killed cattle at 8 slaughter plants about 5% were fecal

positive and additional animals had evidence of hide contamination. For a slaughter plant receiving and processing 2000 head per day (for example), dozens of O157 colonized/contaminated cattle would be received per day. It seems very clear that incoming cattle represent the main source of O157 contamination of beef. If the prevalence of O157 in incoming cattle could be reduced by, say, 4-fold; this would be expected to reduce contamination levels farther along in the food chain.

Identification of effective control strategies at the farm level requires that we understand the ecology of O157. The key features identified so far are as follows:

O157 exists, at least intermittently, on a majority of cattle farms.^{4,5,7,11,12} It is distributed across the U.S. in both dairy and beef cattle.^{4,12} The percent of cattle with O157 detectable in their feces is typically less than 5%.^{1,4,5,7,11,12,21} The agent has been detected at a similar, or slightly higher, prevalence among cattle being held at slaughter plants and on the external surface of the hides of recently slaughtered animals.¹⁰ O157 has been found in feces from several species other than cattle, including deer, sheep, dogs, horse, flies, and birds.^{6,15,17-19} A long-term reservoir species, if one exists, has not been identified. Colonization of cattle with O157 is typically of short duration (1-2 months), and long term carriers have not been found.^{1,2} O157 is not associated with any recognizable disease in cattle, but instead appears to behave as transient *E. coli* 'normal flora'.^{1,2,9} A minority of cattle can be colonized by low doses of O157 (<250 cfu), and these animals amplify the infection and transmit O157 to other cattle.² Growing cattle 3-18 months of age have a higher prevalence of O157 than either younger (suckling) calves or adult cattle,^{4,5,7} which is likely reflective of a less stable *E. coli* flora among younger animals.⁹ O157 prevalence in a herd is not as-

sociated with manure application to grazing land.¹¹ Tentative associations with other management factors have been observed but have not yet been tested in targeted studies.^{3-5,11,13} The typical pattern of O157 shedding in a herd followed over time is one of epidemics of shedding interspersed with longer periods with rare or no shedding animals.^{7,11} These epidemics occur mainly during warm weather, suggesting that environmental proliferation may play an important role in the epidemiology of this agent (Figure 2).^{5,7,14} O157 can multiply prolifically in cattle feeds when moisture is added, as commonly occurs in mixed rations.¹⁶ O157 has been found in water troughs on numerous farms. O157 persists at least 4 months in water trough sediments and may even multiply in this environment, suggesting that water troughs could be a long-term reservoir which maintains O157 in herds during periods of low infection prevalence.^{6,8} Considerable strain diversity among O157 isolates can be detected, between and even within some herds. Specific strains of O157 can persist on particular farms for at least 2 years.²⁰ Regional transmission of O157 appears to occur, since indistinguishable strains have been found in herds > 500 km apart. Isolates from non-bovine species are closely related or identical to bovine isolates.²⁰

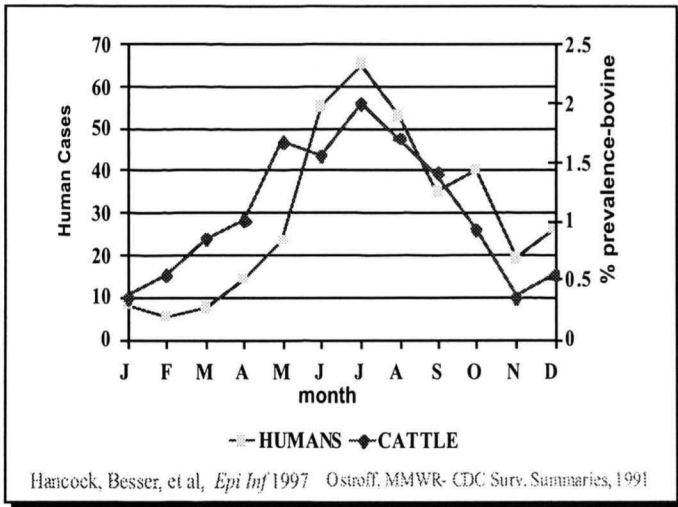


Figure 2. Fecal *E. coli* O157 shedding increases markedly in warm months as does the incidence of human disease associated with this agent.

In considering possible control strategies (Figure 3), it is important to recognize that O157 is not subject to eradication, either from whole regions or from individual herds. This is so because O157 is ubiquitous in cattle and widespread in nature, including in birds, deer, and other wildlife. This feature is not unique among infectious agents. Indeed, it is a reality for most foodborne disease agents including *Campylobacter*, *Salmonella*, *Listeria*, and others. Although recognition of

Levels of possible farm-level control

- Eradication
- Establishment of biosecurity in herds
- Ecological measures to reduce contamination level
 - Animal feed safety
 - Animal water safety
 - Factors affecting host susceptibility

Figure 3. Although eradication or establishment of biosecurity for individual herds may be the ultimate form of control of an infectious agent, they are not feasible for O157, a ubiquitous, multi-host agent. Although ecological measures would not be expected to result in eradication, they do hold the promise of great reductions in prevalence among cattle entering slaughter plants.

our inability to eradicate these agents has led to pessimism about control in general, several ecological measures could provide significant reductions in the prevalence of O157 (and perhaps other agents) among cattle presented at slaughter.

Two very promising areas for ecological control relate to feed and water management (Figure 4), specifically, by undertaking measures that would lead to reductions in total enteric bacterial intake in feed and water. We are investigating strategies to maintain a low intake of enteric bacteria in water troughs; simple cleaning does not accomplish this in summer because sediments that accumulate within 24 hours support robust growth. Our current efforts are focused on chemical treatments of troughs (e.g., chlorine). In mixed rations, our early data indicate that naturally occurring propionic acid is strongly inhibitory to growth of enteric bacteria (including *E. coli* and *Salmonella*). We are currently investigating this relationship to determine if added propionate, or other natural chemical, would prevent replication of enteric bacteria in feeds in warm months. Although some contamination of feed is probably unavoidable (due to handling equipment, flies, birds, etc.), the natural variation we see among farms indicates that the greatest determinant of dose is whether or not the ration supports bacterial growth.

A third ecological approach relates to increasing host resistance to colonization. One possible means of accomplishing this is strategic colonization (via inoculation) with bacteria that compete with O157 for nutrients or binding sites or otherwise inhibit its ability to

450 kg feedlot steer at 32 C

Intakes

15 kg feed (70% DM)

78 liters of water

		Water <i>E. coli</i> concentration/ml				
		4	16	64	256	1,024
Feed	10	462,000	1,398,000	5,142,000	20,118,000	80,022,000
<i>E. coli</i>	100	1,812,000	2,748,000	6,492,000	21,468,000	81,372,000
concentration	1,000	15,312,000	16,248,000	19,992,000	34,968,000	94,872,000
/gm (as fed)	10,000	150,312,000	151,248,000	154,992,000	169,968,000	229,872,000
	100,000	1,500,312,000	1,501,248,000	1,504,992,000	1,519,968,000	1,579,872,000

Figure 4. Total daily intakes of generic *E. coli* for a finishing steer consuming water and feed of different *E. coli* concentrations. The range of levels shown for feed and water are within the range of farm-to-farm variation that has been observed in cattle operations. Although the habits of cattle (grooming, etc) dictate a certain inevitable *E. coli* intake, it appears that most of the farm to farm variation in dose is due to feed and water contamination levels. The concentrations in both feed and water increase in some herds seasonally which hypothetically accounts for the sharp increases in prevalence during warm months.

colonize. This is called competitive exclusion (CE). The effectiveness of CE has been well documented for *Salmonella* in broiler chicks, and several lines of evidence suggest it might be effective for O157 in cattle. As with salmonella in poultry, the GI flora of adults appears to be relatively inhibitory to O157 colonization. The sharply higher prevalence of O157 in recently shipped feedlot cattle is probably due to floral disturbances which could potentially be impacted with CE. Research on CE targeting O157 is underway in the lab of Mike Doyle at the University of Georgia.²²

Summary

Cattle colonized or contaminated with O157 represent the main source of this organism in slaughter plants. Although complete elimination of O157 from cattle populations does not seem possible, substantial reductions in prevalence would be expected to result in a lower rate of contamination with the organism throughout processing and down to the consumer. Data available at present point to two broad methods by which this could be accomplished: reducing O157 exposure dose to cattle by improved feed and water management and by enhancing resistance of cattle to colonization by competitive inhibition.

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CAUTION: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

Human Warnings: Not for human use. Injection of this drug in humans may be fatal. Keep out of reach of children. Do not use in automatically powered syringes. Exercise extreme caution to avoid accidental self injection. In case of human injection, consult a physician immediately. Emergency medical telephone numbers are 1-800-722-0987 or 1-317-276-2000. Avoid contact with eyes.

Note to Physician: The cardiovascular system appears to be the target of toxicity. This antibiotic persists in tissues for several days. The cardiovascular system should be monitored closely and supportive treatment provided. Dobutamine partially offset the negative inotropic effects induced by Micotil in dogs. β -adrenergic antagonists, such as propranolol, exacerbated the negative inotropy of Micotil-induced tachycardia in dogs. Epinephrine potentiated lethality of Micotil in pigs.

For Subcutaneous Use in Cattle Only. Do Not Use in Automatically Powered Syringes.

Indications: For the treatment of bovine respiratory disease (BRD) associated with *Pasteurella haemolytica*. For the control of respiratory disease in cattle at high risk of developing BRD associated with *Pasteurella haemolytica*.

Description: Micotil is a solution of the antibiotic tilmicosin. Each mL contains 300 mg of tilmicosin base as tilmicosin phosphate in 25% propylene glycol, phosphoric acid as needed to adjust pH and water for injection, q.s. Tilmicosin phosphate is produced semi-synthetically and is in the macrolide class of antibiotics.

Actions: Activity — Tilmicosin has an *in vitro* antibacterial spectrum that is predominantly gram-positive with activity against certain gram-negative microorganisms. Activity against several mycoplasma species has also been detected.

Ninety-five percent of the *Pasteurella haemolytica* isolates were inhibited by 3.12 μ g/mL or less.

Microorganism	MIC (μ g/mL)
<i>Pasteurella haemolytica</i>	3.12
<i>Pasteurella multocida</i>	6.25
<i>Haemophilus somnus</i>	6.25
<i>Mycoplasma dispar</i>	0.097
<i>M. bovirhinis</i>	0.024
<i>M. bovoculi</i>	0.048

*The clinical significance of this *in vitro* data in cattle has not been demonstrated.

Directions — Inject Subcutaneously in Cattle Only. Administer a single subcutaneous dose of 10 mg/kg of body weight (1 mL/30 kg or 1.5 mL per 100 lbs). Do not inject more than 15 mL per injection site.

If no improvement is noted within 48 hours, the diagnosis should be reevaluated.

Injection under the skin behind the shoulders and over the ribs is suggested.

Note — Swelling at the subcutaneous site of injection may be observed but is transient and usually mild.

CONTRAINDICATION: Do not use in automatically powered syringes. Do not administer intravenously to cattle. Intravenous injection in cattle will be fatal. Do not administer to animals other than cattle. Injection of this antibiotic has been shown to be fatal in swine and non-human primates, and it may be fatal in horses.

CAUTION: Do Not Administer to Swine. Injection in Swine Has Been Shown to be Fatal.

WARNINGS: Animals intended for human consumption must not be slaughtered within 28 days of the last treatment. Do not use in female dairy cattle 20 months of age or older. Use of tilmicosin in this class of cattle may cause milk residues. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

CAUTION: The safety of tilmicosin has not been established in pregnant cattle and in animals used for breeding purposes. Intramuscular injection will cause a local reaction which may result in trim loss.

How Supplied: Micotil is supplied in 50 mL, 100 mL and 250 mL multi-dose amber glass bottles.

Storage: Store at room temperature, 86°F (30°C) or below. Protect from direct sunlight.

Literature revised December 30, 1996

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