

Prospects of Pre-Harvest Control of Bacterial Foodborne Disease Agents

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Recently, food safety has emerged as a significant consumer and government issue. The 1993 disease outbreak associated with *Escherichia coli* O157:H7-contaminated hamburger in the western United States pushed food safety right to the top of the news and USDA's agenda. The tragic outbreak, which affected more than 600 people and killed 4 children, highlighted a glaring weakness in our system of food inspection: ignorance of the ecological relationship between on-farm practices in animal agriculture and the occurrence of foodborne pathogens of human disease.

The Challenge to a Comprehensive Food Safety Program—The Case for Pre-Harvest Control

Food safety has traditionally been a problem dealt with by processing plants, retailers and ultimately consumers. Essentially, we treated the on-farm component of food safety as non-significant or believed the hazards were ubiquitous and that the prevalence of these hazards could not be affected by changes in farm management. This attitude regarding the importance of pre-harvest factors in food safety has made a turn in the last few years as research has begun to demonstrate links between on-farm ecologic niches (present because of farm management decisions) and the prevalence of several important foodborne pathogens.

Several foodborne pathogens or hazards, including *Salmonella enteritidis* in layers, *E. coli* O157:H7 in cattle, *Yersinia enterocolitica* in swine, and the non-host adapted *Salmonella sp.* in cattle, are not ubiquitous in the livestock population. As an example, *E. coli* O157:H7, which was first recognized as a human pathogen in 1982 (although there is good evidence that a pathogenic relationship existed prior to that date). Although other sources have not been ruled out, it would appear that the pathogen has a primary reservoir in cattle (Griffin et al., 1991). As a caveat, it has not been established beyond doubt that cattle are a reservoir rather than incidental hosts. What is also unknown is the prevalence of the pathogen in the cattle population.

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Recent work at Washington State University has attempted to establish prevalence estimates of *E. coli* O157:H7 in cattle. Surveys have been conducted of dairies, feedlots and cow-calf operations. The dairy survey included 3,570 fecal samples from 60 northwestern herds and yielded a prevalence of *E. coli* O157:H7 of 2.8/1000; 1,412 fecal samples from 25 cow-calf herds revealed a prevalence of 7.1/1000; 600 fecal samples from 20 pens of feedlot cattle revealed a prevalence of 3.3/1000. The 95% confidence intervals of these prevalence estimates broadly overlap. Additionally, the bacteria is not randomly distributed between premises and seems to cluster on particular farms and in particular groups of animals. These observations suggest that *E. coli* O157:H7 is part of the dynamic coliform flora which colonizes cattle herds rather than individuals.

Some of the important foodborne pathogens do not cause significant disease in the reservoir species. *E. coli* O157:H7 in cattle and *Salmonella enteritidis* in poultry are examples (Anon. 1994; Ebel et al., 1992). This is particularly problematic from a public health standpoint since infected herds and flocks experience no evident marker conditions. Some other pathogens, particularly *Salmonella sp.*, may cause disease of variable severity but the disease is short term.

Although the foodborne pathogens may be persistent on the farm, they may only be transient components of an individual animal's intestinal flora. Feeding experiments with *E. coli* O157:H7 in young calves demonstrated variable length and amount of shedding. The duration of fecal shedding ranged from 2 to 45 days (personal communication T. Besser, Washington State University, 1994). A similar shedding pattern has been shown to be true for salmonella infections in cattle (Wray et al., 1987).

Finally, research with dairy operations with endemic herd infections of non-host adapted *Salmonella sp.* in cattle (Gay et al., 1993; Clegg et al., 1983; Pacer et al., 1989) and to some extent *E. coli* O157:H7, have linked management factors to the persistence of the hazards on the farm. These observations for herds with endemic *E. coli* O157:H7 infections have led to speculation that expansion of the niche for the agent have involved one or more geographically-widespread changes in the way that cattle are maintained. As the hypothesis goes, this would have caused a slight shift in the exceedingly complex ecosystem of the gastrointestinal flora to the advantage of *E. coli* O157:H7. Such an orchestrated change in the gastrointestinal ecology of cattle, occurring widely in the industrialized world over a short time span, may seem unlikely; yet several candidate factors are worthy of consideration. For example, waste management has undergone wide-

spread changes in dairy herds and, to a lesser degree, in feed-lots. Several byproduct feeds previously rarely used in cattle feeds have come into widespread use in recent years. Certain feed additives, such as ionophores, were not used commercially prior to the 1970's but are now used very commonly in cattle production in both beef and dairy cattle. These speculations can also be applied to the occurrence of other farm-based foodborne pathogens such as the *Salmonellae*.

These observations, coupled with the consumer expectation of a practically hazard-free food have pushed the agenda for developing a comprehensive control plan for food safety that includes the pre-harvest sector. It has become clear that in order to satisfy this expectation, the entire chain in the food production cycle (including the farm) must be accounted for and appropriate quality measures instituted to assure consumer confidence in the product.

A Traditional Approach to Pre-Harvest Food Safety—Can It Work?

The traditional approach to disease control on farms has been trace-back testing, on-farm testing to identify carriers, and then implementation of a "control" program with the ultimate goal of disease eradication. Usually, these control plans have some combination of culling and vaccination. An underlying premise of these plans is that animals with disease can be reliably and consistently detected with some test (clinical signs, serology or microbiology). Other assumptions in traditional disease control schemes are that infected animals are persistently infected and that there are no animal or inanimate reservoirs (other than the livestock host) for the hazard.

The implementation of these disease control programs is highly dependent on two factors. First, the ability to monitor national livestock populations through marker diseases or some sort of ongoing universal testing program. Second, the ability to trace back to a small number of affected herds and eradicate the agent by a program of test and removal. At this time, that seems to be the direction in which the regulatory agencies are moving, or at least are administratively being directed to move, in their pre-harvest efforts. An example of this occurred in May of 1994; the USDA Food Safety and Inspection branch released several requests for proposals to develop methods of detection of foodborne pathogens. Clearly, some of this initiative is driven by public pressure; but it also is a natural reaction of these agencies to support models of control which have been used in the past.

It is important at this juncture of program development that critical questions be asked regarding the goals of the program and what role can be defined for testing. Ultimately, in order to answer these questions, we need to decide whether the ecology of the pathogens of interest fit the assumptions of our traditional disease control model.

In fact, the assumptions of our traditional model are routinely violated by the foodborne pathogens with livestock hosts. As already mentioned, many of the pathogens do not cause significant clinical disease in the reservoir host. With other foodborne pathogens, particularly the non-host adapted species of salmonella, reservoir animals occasionally become chronically or persistently infected, but most of these infections are transient (Wray et al., 1990; Clegg et al., 1983). In

these cases, herds that are persistently infected are likely to be recycling the bacteria between animals in the herd. The results of an investigation of one dairy herd in California suggested that the *Salmonellae* in the herd were production system-adapted rather than host-adapted (Gay et al., 1993). This is an important point since the hazard persists in the herd, not because of biologic host/pathogen interaction, but because of a production system or management scheme that promotes an ecologic niche for the hazard.

Given these constraints, it would seem that the traditional approaches to disease control that have been used with some success by the livestock industry (i.e. our tuberculosis, pseudorabies and brucellosis programs) will not be an effective model for a pre-harvest food safety program. Whereas our goal in disease control has been eradication, the role of pre-harvest food safety will more likely be as a component of the farm-to-table quality management program and to limit the pathogen load traveling from the farm to the processing plant.

The role of testing in pathogen reduction will be limited. Although having more effective rapid tests might improve the speed at which we can identify herds, it is clear that these tests on their own cannot aid our understanding of the pathogens' ecology nor result in any actual policy decisions. At this point in our understanding of the pathogen farm ecology, trace-back testing from the slaughter plant to the farm will be of no value. Since we are mostly uncertain as to why any of these pathogens may appear on a farm, trace-back cannot result in any actions unless quarantine becomes an option. Given the large number of farms on which one or more foodborne agents exist—often at a very low prevalence within the herd—quarantine of all farms endemic for one or more foodborne agents does not appear a viable option.

It has been suggested that we should be testing post-harvest to ensure that no contaminated product reaches the consumer. This testing would focus on detecting specific pathogens, which in many cases are present in low numbers. An alternative would be systemic monitoring based on indicator organisms—such as total coliforms. This method has far more scientific relevance in a quality assurance system than monitoring for specific pathogens. In either system, testing would be the primary component of a quality assurance program. Quality assurance is simply guaranteeing that a product achieves some minimum level of quality (Nadkarni, 1991). The result of not meeting minimum standard is discarding the product or product lot. This is a wasteful method to ensure quality, but more importantly: How does an industry choose to interpret a negative test result? "If particular organisms are found to be non-detectable in a given sample drawn from a consignment of food, this result is only of statistically-limited significance for the sampled consignment" (Mossel et al., 1992). In a litigious society, or even a society with expectations of low risk from their food, test-based quality assurance is an ill-conceived notion.

Designing a Pre-Harvest Food Safety Program

An alternative approach for designing pre-harvest food safety programs is to view the problem as a total quality management issue, i.e. define the quality goals, identify the fac-

tors or critical control points associated with breakdown of quality, and develop programs to support the critical control points. In the area of pre-harvest total quality management, one of the goals will be on-farm pathogen reduction. Unfortunately, we are only beginning to develop the methods to design the studies necessary to understand the ecology of the pathogens of public health concern. A starting point would be to work with management strategies that have been structured from experience and common sense to control the host-adapted *Salmonellae*. Sensible manure management, preventing cross-contamination of feed equipment with manure handling equipment, wildlife control, and rational use of antibiotics (Smith et al., 1992). While these ideas are a start at pathogen reduction, this is not the solution to implementing rational pre-harvest quality programs. At this time, our limited knowledge of the farm biology of the foodborne pathogens does not allow us to define critical control points nor to implement science-based programs for on-farm pathogen reduction. Ameliorating this knowledge gap will require that we fund focussed, farm-based research with at least three pre-harvest research areas that warrant attention: epidemiologic/ecologic longitudinal studies, focussed epidemiologic studies on dietary or physiologic stress and shedding of pathogens, and the efficacy of competitive exclusion.

Epidemiologic/ecologic studies would capitalize on the natural "experiments" provided by the diversity among livestock operations. Where some farms are endemic for a particular agent and others lack the agent, there must be identifiable reasons for this diversity. By carefully collecting data on a variety of differences in housing, feeding, waste management, etc., solid clues can be gained as to the critical factors involved in creating a niche for a particular pathogen. The approach is not necessarily limited to pathogen presence/absence but could also be used in a quantitative mode to determine associations with level of contamination or percent of animals contaminated at harvest. The ultimate goal is to identify management changes which would close or reduce the niche for the foodborne pathogens on the farm. Candidate factors identified in such natural experiments would then be targeted by prospective studies to confirm relationships and to set the stage for intervention trials and ultimate industry-wide implementation. The role of testing in this scenario of pathogen reduction is strategic testing to identify herds with particular hazards. Using on-farm risk assessment and perhaps prevalence surveys, breakdowns in control points would be identified and appropriate management strategies implemented. Limited work has been done in this area by researchers at Washington State University and by Veterinary Services (USDA:APHIS) regarding *E.coli* O157:H7 and at Penn State, University of Pennsylvania, and USDA:APHIS regarding *Salmonella enteritidis*, but funding has been notably difficult to obtain.

A second pre-harvest ecologic approach to controlling foodborne pathogens would focus on the effect of management-related stress to the animals and its influence on pathogen shedding and spread on the farm. The times of most interest would likely include the week prior to slaughter, weaning periods, parturition and times of housing changes, particularly resulting in the formation of new social groups. The hypothesis of the research would be: Changes in the gastrointestinal tract during most of a meat or milk-producing animal's

life are secondary to changes occurring in the tract during times of stress. Research in this area might allow us to define critical control points and the determinants of the shedding. As an example, the stress of handling associated with marketing animals has been suggested as a critical time that influences the GI tract bacterial ecology. Potentially, the contamination level of the haircoat, an important source of bacteria on carcasses, would be considered a critical control and monitoring point. Epidemiologic research would reveal the tools to manage the risk and might include modifications of diet, transportation and housing.

A final possibility for pre-harvest research for reduction of foodborne pathogens would be competitive exclusion (CE). CE is based on observations, made over many years, that the normal intestinal flora of adult animals plays a key role in resistance to colonization by exogenous enteropathogens (Dubos et al., 1964; Hentges, 1983; Tancrede, 1992). It was first used as a pre-harvest food safety tool by Nurmi and others in the early 1970's (Nurmi et al., 1992). Thus far, use of CE has been limited to controlling salmonella in poultry, but the concept has appeal for other foodborne agents (Nurmi et al., 1992). As presently used (mainly in Europe), CE consists of inoculation of chicks with mixed bacterial cultures (via aerosol or in water) which have been obtained, directly or indirectly, from the gastrointestinal tracts of adult chickens. Several large studies have generated a wealth of data supporting the efficacy of CE (Wierup et al., 1988; Wierup et al., 1992). The mechanisms of action of CE against salmonella are exceedingly complex and appear to require the interaction of a number of mainly anaerobic bacterial species (Hinton et al., 1991a; Hinton et al., 1991b; Nurmi et al., 1992; Corrier et al., 1993). For an *E. coli*, CE might take advantage of the natural competition for nutrients and binding sites which exist among diverse *E. coli* strains in the gastrointestinal tract (Freter, 1983). Given the practicality and affordability of CE, efforts are needed to determine the nature of the foodborne pathogens' niche in the ecosystem of meat-producing animals GI tracts and to identify possible microfloral species that might be used for CE.

The goal of any pre-harvest research should be focussed on hazard reduction and not eradication of the hazards from the farm. It is clear that pre-harvest measures are an important part of the food safety story, but it is only one of the pieces in a comprehensive plan for food safety. It is also clear that we cannot rely on testing to ensure the safety of our food. Testing has an important role in monitoring the yet-to-be-identified critical control points, but testing will not take the place of considerate research aimed at understanding the farm ecology of the foodborne pathogens.

The varied responses to the growing problem with foodborne disease are similar to those for many other emergent problems we face as a society. The pessimists—much in the majority—look through the eyes of tradition and see no road to resolution. Others trust in the magic of "high tech" even though they can't articulate credible hypotheses of how a particular high-tech product or technique would lead to resolution. Finding a solution for the emerging foodborne pathogens will require a much better definition of the problem, especially as regards its reservoir; and the solution which finally emerges may not conform to traditional visions of how infectious diseases ought to be controlled.

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