New Perspectives on the Persistent Scourge of Foodborne Disease

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(See the articles by Johnson et al. and Helms et al. on pages 1040–9 and 1050–5, respectively.)

This issue of the Journal includes 2 studies that highlight important emerging foodborne-disease threats from very different perspectives. The wide spectrum of extraintestinal disease caused by potentially foodborne Escherichia coli is often underappreciated. Johnson et al. [1] present provocative data suggesting that antimicrobial-resistant E. coli and extraintestinal pathogenic E. coli (ExPEC) represent a newly recognized group of foodborne pathogens and raise a number of issues that deserve further attention. Helms et al. [2] describe adverse health effects of infection with antimicrobial-resistant Campylobacter strains, much of which are also ultimately traceable to foodborne sources.

The study by Johnson et al. is based on microbiologic examination of food. One of its fundamental observations is the high rate of bacterial contamination of many common food products, including both processed foods and those typically eaten raw. They found, for example, that >25% of samples of cucumber/zucchini and shrimp and >90% of poultry were contaminated with E. coli. Contrary to popular perception, food is not sterile. Others have demonstrated similar findings, although studies of food-handling behaviors have suggested that a substantial proportion of the population either has not received this message or does not understand its implications [3]. Continuing emphasis on safe handling and thorough cooking is worthwhile but clearly will not solve the problem alone. Efforts must continue to better understand the routes by which consumed food becomes contaminated, to appropriately focus preventive strategies.

Their study serves as an important reminder that not all foodborne disease presents with diarrhea and vomiting. The most commonly recognized foodborne pathogens, such as Salmonella species, usually cause gastroenteritis but occasionally have extraintestinal presentations. Other common foodborne diseases—such as botulism and those associated with Listeria species, Vibrio vulnificus, and scombroid poisoning—are usually associated with extraintestinal symptoms. E. coli is one of the most commonly isolated organisms from clinical specimens, and Johnson et al. raise the provocative possibility that a substantial proportion of those infections may disseminate from the food supply. At present, invasive ExPEC is rarely cited on lists of “foodborne diseases,” but, with further investigation, this could change. At present, we have little insight into what proportion of extraintestinal E. coli infections have a foodborne source, and this question deserves more attention.

The study by Johnson et al. is based on molecular and serologic characterization of microbial isolates from foods. These isolates were compared with a collection of referral specimens from urinary tract and invasive infections, some of which may have come from foodborne sources. A natural future step would be a systematic population-based study of invasive E. coli infections, to identify risk factors and clinical and microbiologic characteristics of the subset possibly due to a foodborne source. Unfortunately, the molecular and serologic resources to identify most E. coli serotypes (much less virulence factors or other genotypic or phenotypic characteristics) are currently limited to research laboratories and are not readily accessible to clinicians. The disproportionate attention given to O157:H7 among the panoply of E. coli strains is a simple consequence of the fact that it is the only specific serotype that is readily identifiable in most clinical laboratories.

The study by Johnson et al. also fuels the debate over whether “natural” and antibiotic-free foods are safer than foods not so designated, which seems to be the widespread perception. The reported results are mixed; meat products from natural-food stores were less likely to be contaminated...
with *E. coli* and showed less antimicrobial resistance. Paradoxically, however, poultry labeled as antibiotic free was more likely to be contaminated with *E. coli*. These disparate results demonstrate the complexity of decision-making about the relative risks and benefits of modifications to an elaborate food-supply system (or an individual’s dietary choices).

Potential medical measures for decreasing the burden of extraintestinal *E. coli* infection include the development of ExPEC-specific vaccines, as well as diminishing human colonization through a number of means, including eliminating reservoirs and transmission pathways and treating the host with adhesion-receptor analogues. As we await progress in developing such high-tech interventions, clinicians and public-health programs must continue to advocate the wider implementation of available measures. In the context of an immensely complex food production and delivery system and the apparent ineffectiveness of attempts to improve basic food-safety behaviors in the consumer’s kitchen, means of reducing risk close to the point of consumption should be pursued. Food irradiation is a well-studied technology that could reduce a substantial portion of the microbial contamination described by Johnson et al. Clinicians and the scientific community should work to promote acceptance of this technology while continuing to pursue other preventive measures.

Another important issue raised by the study by Johnson et al. is that of antimicrobial resistance and its prevalence in the microbial flora of food. Antimicrobial resistance in *E. coli* O157, the serotype most commonly thought of as being foodborne, is identified much less often than is resistance in *Salmonella* and *Campylobacter* species and some other foodborne pathogens [4]. Johnson et al. raise the possibility that emerging antimicrobial resistance in *E. coli*, particularly ExPEC, could also become an important foodborne-disease problem. For example, >80% of their *E. coli* isolates from beef, pork, and poultry exhibited resistance to ≥1 antimicrobial agent, and >50% of isolates from poultry were resistant to ≥5 drugs! Although the identification of antimicrobial resistance in food contaminants is becoming increasingly common, compelling evidence that this resistance leads to distinctly poorer outcomes in human foodborne infections has been scant—this is, however, rapidly changing [5, 6]. Recent studies have demonstrated that many infections with resistant *Salmonella* and *Campylobacter* strains, for example, are more severe than infections with antimicrobial-sensitive strains [5, 7, 8].

The study by Helms et al. [2] takes advantage of a unique resource—a national, population-wide disease registry linked to comprehensive microbiologic data—to provide evidence of adverse health events associated with antimicrobial-resistant *Campylobacter* infections. Patients infected with quinolone- or erythromycin-resistant *Campylobacter* strains were substantially more likely to have invasive disease and die than were those infected with susceptible strains. Much remains to be learned in this area. In this case, for example, it is unclear how erythromycin resistance relates directly to adverse outcomes observed within 90 days of infection. In this case, rather than being directly related to therapeutic failure, resistance might be associated with other risk factors that must be elucidated. In the United States, the prevalence of ciprofloxacin-resistant *Campylobacter* strains increased from 13% in 1997–1998 to 20% in 2002 [4], which demonstrates that this is not simply an abstract problem or one confined to other countries.

Taken together, these findings are an important contribution to the growing body of evidence indicating that antimicrobial use in food-animal production must be addressed promptly. A large proportion of the antimicrobial agents used in the United States are used in food animals. It is becoming increasingly clear that antibiotic pressure in food production contributes substantially to the growing problem of resistance in foodborne disease [5, 6]. In other countries, interventions to decrease antibiotic pressure on the farm have demonstrated some success [9, 10]; despite the challenges [11], control measures appropriate to the US food-production system must be pursued vigorously.

As dense with provocative data as these studies are, they raise more questions for further investigation than they can answer definitively. Perhaps the most vexing question is how much human disease is ultimately attributable to the food we eat. Better understanding of which aspects of the food production and distribution process increase or decrease the risk of microbial contamination for specific commodities will be an important foundation for developing preventive interventions. Likewise, developing practical and acceptable recommendations to limit the development of antimicrobial resistance will be challenging in the face of the substantial benefits of antimicrobials to animal producers. Appropriately addressing these complex questions will require the focused attention and cooperation of numerous parties, from the farm, to the bench, to the bedside.

References

5. Angulo FJ, Nargund VN, Chiller TC. Evidence of an association between use of anti-micro-


