Bacterial Contamination of Animal Feed and Its Relationship to Human Foodborne Illness

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Animal feed is at the beginning of the food safety chain in the “farm-to-fork” model. The emergence of variant Creutzfeldt-Jakob disease has raised awareness of the importance of contaminated animal feed, but less attention has been paid to the role of bacterial contamination of animal feed in human foodborne illness. In the United States, animal feed is frequently contaminated with non-Typhi serotypes of *Salmonella enterica* and may lead to infection or colonization of food animals. These bacteria can contaminate animal carcasses at slaughter or cross-contaminate other food items, leading to human illness. Although tracing contamination to its ultimate source is difficult, several large outbreaks have been traced back to contaminated animal feed. Improvements in the safety of animal feed should include strengthening the surveillance of animal feed for bacterial contamination and integration of such surveillance with human foodborne disease surveillance systems. A Hazard Analysis and Critical Control Point program should be instituted for the animal feed industry, and a *Salmonella*-negative policy for feed should be enforced.

Bacterial enteric pathogens are estimated to cause ~5 million illnesses, 46,000 hospitalizations, and 1458 deaths in the United States each year [1]. Food-producing animals (e.g., cattle, chickens, pigs, and turkeys) are the major reservoirs for many of these organisms, which include *Campylobacter* species and non-Typhi serotypes of *Salmonella enterica*, *Shiga* toxin–producing strains of *Escherichia coli*, and *Yersinia enterocolitica* [1]. Food-producing animals acquire these pathogens by ingestion. Contamination of animal feed before arrival at and while on the farm contributes to infection and colonization of food-producing animals with these pathogens. Pathogens can then be transmitted through the food chain to humans and cause human foodborne illness. Concern about the contribution of contaminated animal feed to human foodborne illness has been heightened by the recent emergence of variant Creutzfeldt-Jakob disease in humans in the United Kingdom. Variant Creutzfeldt-Jakob disease is a prion disease thought to be associated with the feeding of cattle with meat and bone meal derived from sheep infected with transmissible spongiform encephalopathies [2].

**THE ANIMAL FEED INDUSTRY**

There has been major transformation and intensification of agriculture in the United States and elsewhere during the past 50 years. This has led to increasing reliance on a wide range of manufactured feed products as food for animals destined for human consumption. Firms of several types are involved in animal feed production. Rendering plants process animals, meat trimmings, and other slaughter by-products into animal feed ingredients. Protein blenders obtain animal and vegetable protein from various sources and mix or redistribute it as animal feed [3]. Feed mills combine ingredients of animal and plant origin to produce a feed mix suited to animals of a particular species and/or age. For older animals, the combined and ground product of feed mills, sometimes called “ration,” may be used as feed, or it may be heat-treated and compressed into formed pellets (figure 1). For young mammals, protein is used as an ingredient in the manufacture of milk replacer. Some farms that raise food-producing animals are large enough to process their own feed and are often referred to as “miller” operations.
The global trade in animal feed and animal feed ingredients is substantial and far-reaching. More than 100 countries reporting to the United Nations Food and Agriculture Organization recorded importing a total of 2 million tons of meat meal alone in 1999 [4]. In the United States, the animal feed industry is large. During the year 2000, 119 million tons of animal feed were produced, and farmers spent ∼$25 billion on animal feed [5]. In 2000, the leading 85 feed companies alone operated 1,850 mills and had a combined annual feed production capacity of 1.54 million tons [6]. It is estimated that there are a total of ∼8,000 feed mills and 264 protein renderers in the United States [7]. There is considerable potential for contaminated animal feed or animal feed ingredients to move between and within countries. This could result in the widespread and rapid dissemination of a pathogen to geographically dispersed animal herds—and, in turn, to a range of human food products.

RESPONSIBILITIES AND LEGISLATION RELATING TO SAFETY OF ANIMAL FEED

Several federal agencies are responsible for the different components of animal feed safety. Under the Federal Food, Drug, and Cosmetic Act of 1906, as amended, the US Food and Drug Administration (FDA) has the authority to ensure that animal feed is properly labeled, is safe for its intended use, and produces no human health hazards when fed to food-producing animals. In addition, the US Department of Transportation has the authority under the Sanitary Food Transportation Act of 1990 to prescribe regulations to safely transport animal feed. The US Department of Agriculture’s Animal and Plant Health Inspection Service is responsible for ensuring the health and care of animals and for improving agricultural productivity while contributing to the nation’s economy and public health [3].

Food-producing animals are the major reservoir of non-Typhi serotypes of S. enterica, which cause an estimated 1,412,498 human illnesses, 16,430 hospitalizations, and 582 deaths annually in the United States [1]. To illustrate the potential importance of bacterial contamination of animal feed, we review the evidence that contamination of animal feed with non-Typhi serotypes of S. enterica can contribute to the burden of human salmonellosis.

EVIDENCE THAT ANIMAL FEED IS FREQUENTLY CONTAMINATED WITH BACTERIAL PATHOGENS

There is considerable evidence that animal feed is frequently contaminated with foodborne bacterial pathogens. Non-Typhi serotypes of S. enterica were reported in US poultry feed as early as 1948 [8, 9]. Studies from around the world have documented the presence of S. enterica in a wide variety of animal feeds [10–19].

In the United States, the FDA periodically conducts surveys of feed ingredients and feed. In 1993, the FDA tested for the presence of S. enterica in 78 rendering plants that produced animal protein–based animal feed and in samples from 46 feed mills that produced vegetable protein–based animal feed. S. enterica were detected in 56% of the 101 animal protein–based samples and 36% of the 50 vegetable protein–based samples [20]. In 1994, the FDA tested 89 finished feed samples collected from feed mills and from farms where animal feed is mixed and found that 25% of the samples were contaminated with S. enterica (D. G. McChesney and G. Kaplan, unpublished data). Surveys done by the rendering industry...
[21], although limited in their scope, also show that animal protein-based animal feed is frequently contaminated with S. enterica.

**EVIDENCE THAT CONTAMINATED ANIMAL FEED RESULTS IN INFECTION OR COLONIZATION OF FOOD ANIMALS**

It has long been known that infectious agents can be transmitted to animals through contaminated feed. For example, in 1948, workers in the United Kingdom demonstrated that non-Typhi serotypes of S. enterica could be transmitted to chicks through feed contaminated by the feces of infected rodents [22].

Experimental studies confirm that animals given feeds artificially contaminated with non-Typhi serotypes of S. enterica develop colonization or infection with that organism [23]. Furthermore, there are numerous examples of outbreaks of Salmonella infections in animals that were traced to contaminated feeds. These include cattle [13, 24, 25], pigs [26], chickens [27], turkeys [28, 29], and mice [30]. Although it is less well documented, bacteria that can cause human infections but may not cause illness in animals can also be readily transmitted to food animals via contaminated feed and appear on animal carcasses destined for human consumption [31].

**EVIDENCE THAT CONSUMPTION OF INFECTED OR COLONIZED FOOD ANIMALS AND THEIR PRODUCTS RESULTS IN HUMAN ILLNESS**

It has been well established that bacteria from colonized food animals can be transmitted to humans through the food supply. Humans become infected when they ingest contaminated meat or poultry products, raw produce contaminated with animal feces (e.g., from contaminated streams used for irrigation), or other foods, particularly uncooked foods, that have been cross-contaminated by contact with uncooked meat or poultry products. For example, E. coli O157:H7 is shed in the manure of cattle and contaminates beef during slaughtering. Eating undercooked hamburger, a widespread practice, can lead to E. coli O157:H7 infection [32, 33]. Campylobacter jejuni, carried by poultry, can be spread to many poultry carcasses during the water-bath dressing process. Human infections occur when undercooked chicken or cross-contaminated food is consumed [34]. Cattle, poultry, pigs, and other food animals are colonized with non-Typhi serotypes of S. enterica, which have multiple routes into the food supply. Consumption of meat or poultry products contaminated during slaughtering leads to human salmonellosis [35, 36]. Consumption of produce grown adjacent to herds of animals colonized with bacterial pathogens may result in human infections if the crop is contaminated with animal feces [37].

The Foodborne-Disease Outbreak Surveillance System of the US Centers for Disease Control and Prevention collects data on foodborne disease outbreaks reported by state and local health departments. During 1993–1997, 23% of outbreaks of human foodborne illness in which a food vehicle was identified were attributed to eating meat, dairy, and poultry products [38]. That figure does not include outbreaks in which meat and poultry were among several items possibly linked to illness and outbreaks due to cross-contamination of foods by meat or poultry products. In addition to causing outbreaks of illness, meat and poultry products also contribute to a large proportion of sporadic illness [39–41].

**OUTBREAKS OF HUMAN SALMONELLA INFECTIONS TRACED TO CONTAMINATED ANIMAL FEED**

Several incidents have been reported in which human illness was traced back to contaminated animal feed. In 1958, an outbreak of infection with foodborne S. enterica serotype Hadar in Israel was linked to consumption of chicken liver. An investigation of the chicken farm found that bone meal fed to the chickens was contaminated with the same serotype of Salmonella [15]. A milkborne outbreak of infection due to S. enterica serotype Heidelberg in England in 1963 resulted in 77 human illnesses and was traced to a cow with bovine mastitis due to the same organism. Investigation revealed that meat and bone meal fed to the cow was contaminated with the same organism [42]. During 1968, frozen chickens from a packing station in Cheshire, England, were implicated in a large outbreak of infection with S. enterica serotype Virchow [43]. Investigation showed that the hatchery and the majority of rearing farms that supplied the packing station contained chickens colonized with S. enterica serotype Virchow, and the organism was isolated from feed fed to the chickens [44].

In 1970, S. enterica serotype Agona emerged as a public health problem in several countries. In the United States, before 1970, S. enterica serotype Agona infection of humans had been reported only twice, once in 1967 and again in 1968. By 1972, 507 isolates from humans had been reported, and S. enterica serotype Agona had risen to be the eighth most frequently isolated S. enterica serotype. Human infections occurred predominantly in states with poultry-raising operations that used feed derived from Peruvian fish meal. An epidemiological investigation in Arkansas implicated chickens served at a restaurant. The chickens were traced to a farm in Mississippi that used animal feed derived from Peruvian fish meal. The Peruvian fish meal had been contaminated with S. enterica serotype Agona before the animals were infected [11] and was found to be the ultimate source of the increase in the number of infec-
tions with *S. enterica* serotype Agona in the United States as well as in the United Kingdom, Israel, and the Netherlands.

A variety of factors probably contribute to the recent small number of cases of human foodborne illness and lack of outbreaks that have been traced to contaminated animal feed. Although the food vehicle is identified in many foodborne disease outbreaks and although many such outbreaks are attributed to eating contaminated meat or poultry, few investigations trace the source of contamination back through the food supply to the farm of origin. The reasons for this include limited resources and the difficulty of tracing food and animals because of limited identification of animals and limited farm record-keeping. Furthermore, when epidemiological studies of human foodborne disease outbreaks include an investigation to trace back the source of infection to farms, they rarely extend to microbiological evaluation of the quality of animal feed. In addition, surveillance of animal feed for bacterial contamination is not sufficiently developed nor is it integrated with the surveillance of food-producing animals, food, and human illness to detect outbreaks that may be attributable to contaminated animal feed.

**SIGNIFICANCE OF SALMONELLA CONTAMINATION OF ANIMAL FEED FOR HUMAN FOODBORNE ILLNESS**

Because *S. enterica* serotype Agona was rare in the United States before its introduction in animal feed, the increase in the number of infections due to this pathogen was detected by human *Salmonella* surveillance, and its source in animal feed was determined by a series of studies. It is likely that introductions of more-common serotypes occur but are not detected and remain uninvestigated. Determining the overall contribution of contaminated animal feed to human illness, relative to other sources of contamination, is difficult with currently available data. Similarly, it would be difficult to conduct a precise, quantitative risk assessment of the contribution of contaminated animal feed to human illness. Nevertheless, evidence presented here and elsewhere [35, 45, 46] suggests that the contribution of contaminated animal feed to human foodborne illness is likely to be important.

The potential magnitude of the problem can be examined by studying the increase in *S. enterica* serotype Agona infection more closely. Since its remarkable expansion after being introduced in animal feed, *S. enterica* serotype Agona has persisted in the United States, resulting in a substantial disease burden. Between 1970 and 2000, there were 28,322 human *S. enterica* serotype Agona infections reported to the US National *Salmonella* Surveillance System (figure 2). Of these, 40% occurred in infants and children aged <10 years, and 1.5% of isolates were recovered from the bloodstream, a mark of severe disease [47]. It is estimated that only 1 in 38 *Salmonella* infections in humans are reported through the national surveillance system [1]. Therefore, *S. enterica* serotype Agona has probably caused >1 million human illnesses in the United States since it was introduced in animal feed in 1968.

Differences in the *S. enterica* serotypes isolated from ill humans and the serotypes isolated from animal feed are sometimes used as an argument that contaminated animal feed does not contribute substantially to human foodborne illness. For example, of the 15 serotypes most commonly isolated from humans in the United States during 1987–1997 [48], only 3 (*S. enterica* serotypes Enteritidis, Agona, and Montevideo) were also recovered from finished feed, as reported in the 1993 FDA study of finished feed [20]. However, the spectrum of *S. enterica* serotypes isolated from animal feed would not be expected to
match the spectrum of serotypes isolated from ill humans, because organisms multiply in feed after testing, because the infectious doses of different serotypes of *S. enterica* are different for animal species and humans, and because multiple sources of *S. enterica* contribute to colonization of animals and infection of humans. Furthermore, only limited microbiologic surveys of animal feed have been done, and, when *S. enterica* has been isolated, not all isolates have been serotyped. For example, only 35 (23%) of 151 of *S. enterica* isolates collected from animal feed in the 1993 FDA survey of finished feed had their serogroups or serotypes determined [20]. Additional sampling of animal feed would be particularly useful to monitor trends in *S. enterica* contamination. Data regarding such trends could contribute to the assessment of the impact of animal feed interventions and further elucidate the relationship between contaminated feed and human illness. In addition, the recovery of *S. enterica* isolates from animal feed indicates failure to control contamination early in the human food chain.

**LESSONS FROM TYPHOID FEVER CONTROL IN THE UNITED STATES**

The trends in reported human *S. enterica* infections in the United States for 1920–1998 indicate substantial declines in typhoid fever and the rising importance of non-Typhi serotypes of *S. enterica* [36]. Typhoid fever, which is caused by *S. enterica* serotype Typhi, was common during the early 1900s. Humans are the reservoir of *S. enterica* serotype Typhi, which is shed by infected persons in their stool. Typhoid fever was common during the early 1900s, but its incidence declined with the implementation of pasteurization of milk, chlorination of water, and safe canning practices. These interventions controlled the entry of human stool from the human food and water supply. Since the mid-1900s, non-Typhi serotypes of *S. enterica* have emerged as a major cause of human foodborne illness. Food-producing animals are reservoirs for non-Typhi serotypes of *S. enterica*, which infected animals shed in their feces [49]. A sanitary revolution in food-animal production could lead to a decline in the incidence of non-Typhi salmonellosis in humans that would be similar to the decline in the incidence of typhoid fever after the early 1900s. Such a decline would be possible if contamination of animal feed, as well as human food and water, by non-Typhi serotypes of *S. enterica* from animals was reduced or eliminated.

**“FARM-TO-FORK” CONTROL OF HUMAN FOODBORNE ILLNESS IN SWEDEN**

Sweden has a comprehensive so-called “farm-to-fork” *Salmonella* surveillance and control system that recognizes the importance of each step in the feed-animal-food-human chain. Notably, Sweden implemented a Hazard Analysis and Critical Control Point (HACCP) program for animal feed in 1991. Approximately 7000 samples from feed mills are analyzed annually, and 40% of samples are obtained before heat treatment. On average, during 1995–1999, 5 samples per year that were collected at critical control points after heat treatment were found to be positive for non-Typhi serotypes of *S. enterica*. Detection of any such positive sample generates more-extensive sampling and corrective action. Sweden’s integrated surveillance of feed, animals, food, and humans allows investigators to track trends and monitor the impact of interventions [50]. This multifaceted surveillance and control program has been highly successful: it has virtually eliminated *S. enterica* from domestically produced animal feed [51] and red and white meat [52], and it has been associated with a decline in the annual incidence of domestically acquired human salmonellosis from 14 cases per 100,000 population in 1991 to 8 cases per 100,000 population in 2000 [50, 53].

**ADDRESSING SAFE ANIMAL FEED IN THE UNITED STATES**

The 2001 Food Safety Strategic Plan of the President’s Council on Food Safety calls for safety control efforts at every stage “from farm to fork,” including enhancement of national, systematic monitoring of food animal diseases and testing of feeds and feedstuffs for microbial, chemical, and other hazards that pose a food safety risk [54]. Three major measures are needed to address animal feed safety in the United States. First, surveillance of animal feed for microbial contamination is necessary, which must be integrated with surveillance systems for food animals, food, and humans. This measure will monitor and improve our understanding of the flow of feed contaminants through the food chain, will inform policy, and will track the impact of interventions. Second, a HACCP program is needed in the animal feed industry to minimize *Salmonella* contamination by identifying and controlling sources of feed contamination. HACCP is an approach that applies 7 principles to identify, rectify, and prevent problems in food production that could result in foodborne illness. It was initially developed 30 years ago to reduce the risk of contamination of food for consumption by astronauts [55]. Finally, a *Salmonella*-negative standard for animal feed should be implemented. A *Salmonella*-negative policy for animal feed was announced by the FDA in 1991, but it has not been implemented or stringently enforced.

Microbial contamination of animal feed is a significant potential pathway for entry of pathogens into the human food supply, and at present, there is no comprehensive program that addresses it in the United States food safety program. Ensuring that animal feed is free of bacterial pathogens should help reduce human foodborne illness.
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References
