Salmonella enterica Serotype Enteritidis and Eggs: A National Epidemic in the United States

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Beginning in the 1970s, the incidence of Salmonella enterica serotype Enteritidis (SE) infection and the number of related outbreaks in the United States has increased dramatically. By 1994, SE was the most commonly reported Salmonella serotype, with an incidence of >10 laboratory-confirmed infections per 100,000 population in the Northeast. Intensive epidemiologic and laboratory investigations identified shell eggs as the major vehicle for SE infection in humans, and that the eggs had been internally contaminated by transovarian transmission of SE in the laying hen. Three key interventions aimed at preventing the contamination and growth of SE in eggs have included farm-based programs to prevent SE from being introduced into egg-laying flocks, early and sustained refrigeration of shell eggs, and education of consumers and food workers about the risk of consuming raw or undercooked eggs. Since 1996, the incidence of SE infection in humans has decreased greatly, although many cases and outbreaks due to SE contaminated eggs continue to occur.

Salmonellosis is a common infection in the United States, with an estimated 1.4 million human cases occurring yearly [1]. Beginning in the 1950s, an internationally recognized standard method of serotyping, the Kauffman-White scheme, based on O (somatic) and H (flagellar) surface antigens, has been used to subtype Salmonella enterica in the United States; the species now includes >2500 different serotypes [2]. However, 4 serotypes account for almost one-half of all human isolates reported in the United States, namely Salmonella Typhimurium (19%), Salmonella Enteritidis (14%), Salmonella Newport (9%) and Salmonella Javiana (5%). Classification by serotype is useful, because different Salmonella serotypes may demonstrate unique reservoirs and pathogeneses. Although some Salmonella serotypes with similar antigenic characteristics may have broad host ranges, the different characteristics of the O and H surface antigens on these bacteria can serve as markers for potential reservoirs of each serotype. For example Salmonella Typhi is strictly a human pathogen, causing invasive enteric fever, whereas most other Salmonella serotypes cause mainly gastrointestinal syndromes without bloodstream invasion. Salmonella Gallinarum is an important chicken pathogen, but rarely causes illness in humans. Other serotypes are known to be associated mainly with other animals, such as swine (Salmonella Choleraesuis), cattle (Salmonella Dublin), and reptiles (Salmonella IV 44:Z,3,-, formerly known as Salmonella Marina). As our experience with different Salmonella serotypes increases, we learn more about their different reservoirs and epidemiologies. Such is the case, over the past 25 years, for Salmonella enterica serotype Enteritidis (SE). In this time, SE has become the first or second most common Salmonella serotype in many countries. The epidemiology of SE tells the story of a pathogen that has found a niche reservoir in commercially produced shell eggs and that causes major epidemics in the United States and many other countries. Although relatively high rates of human SE infection persist, and human outbreaks of SE infection continue to occur, control measures aimed at preventing SE contamination of shell eggs in the United States have had a major impact on decreasing the human health burden of illness from this organism.

INVESTIGATING THE SOURCE OF SE

A rapid increase in the incidence of human SE infection in the United States began in the Northeast in the late 1970s, and SE infection spread to the mid-Atlantic states by the mid-1980s. As a result, public health investigators have concentrated on studying the serotype’s epidemiology. The Salmonella Enteritidis Working Group, composed of public health officials in departments of health in the northeast states and in the Centers...
for Disease Control and Prevention (CDC), conducted intense investigations of outbreaks of SE infection in the Northeast in 1986 and 1987 [3]. During this period, 65 outbreaks of SE infection were investigated that involved at least 2119 cases, 257 hospitalizations, and 11 deaths. In these investigations, eggs or egg-containing foods were implicated in 77% of 35 outbreaks of SE infection in which a food vehicle was identified. Although eggs were already known to be a source of SE infection in humans, these investigations established the shell egg as the most important vehicle for the ongoing SE epidemic in the United States.

The accumulating evidence that eggs were the most important source of human SE infection raised questions about how eggs were contaminated. Egg-laying hens were known to potentially harbor Salmonella species in their intestinal tracts; in the 1960s, egg-associated salmonellosis was linked to external contamination of the shell by SE during passage through the hen cloaca. Moreover, internal contamination of the egg was thought to occur only by penetration of SE through the eggshell, via microscopic cracks, after the egg had been laid. Intensive control measures at that time to examine eggs for cracks and to wash and disinfect them were thought to have eliminated egg-associated salmonellosis as a public health problem.

The subsequent reemergence of SE suggested that the egg contents were being contaminated by another route. The hypothesis that SE might be transmitted directly to the internal contents of the egg prior to the laying of the egg was supported by earlier studies that demonstrated the transovarian transmission of S. Gallinarum [4]. Although this serotype is rarely associated with human illness, it causes significant morbidity and mortality in chickens, and it shares O antigen characteristics with SE (both belong to serogroup D1) [2]. The transovarian transmission of SE to eggs was further supported by the recovery of SE isolates from intact eggs and from the ovaries of laying hens [5, 6]. Confirmation of transovarian transmission was provided by experimental studies performed at the US Department of Agriculture’s (USDA) Agricultural Research Service [7]. In these experiments, pathogen-free birds were orally inoculated with an experimental strain of SE. Within 3 weeks after inoculation, the experimental strain of SE was recovered from up to 91% of hen cloacal swabs and from up to 41% of egg shells. Importantly, the internal contents of eggs (albumen and yolk) were contaminated by SE in up to 71% of sampled eggs. Subsequent study of the internal organs of inoculated hens indicated that up to 66% of ovary and oviduct sample cultures yielded SE [8].

The farm environment can be a rich source of SE, as well as other avian-adapted Salmonella serotypes, such as S. Gallinarum [9]. Salmonella serotypes have been isolated from insects, rodents, and wild birds living on or around hen houses. Chicken manure and other abundant, moist, organic materials serve as additional reservoirs in which Salmonella species can survive and grow for long periods. The high density of chicken populations on farms serves to spread infection among chickens in flocks through direct contact with infected birds and with the contaminated environment [7]. Thus, the chicken farm environment harbors numerous niches for Salmonella, making its control in the farm environment a vexing problem. In addition, SE infection in chickens is often silent—with no evident morbidity or mortality among infected chickens—so there may not be any outward indication of SE infection among chickens in farm flocks or in the eggs they produce [9].

**SURVEYS OF FARMS AND EGGS IN THE UNITED STATES**

In 1991, and again in 1995, microbiologic studies of SE infection in hens from egg-laying flocks were conducted by the USDA’s Food Safety and Inspection Service [10]. A combined total of 711 flocks were surveyed in these 2 studies; for each flock, a cecum sample was collected from 300 “spent” hens (i.e., at the end of the hens’ egg production) at the time of slaughter. SE was identified in 35% of flocks tested, with the highest proportion (52%) of these SE-positive flocks located in the northern United States. A microbiological assessment of SE environmental contamination of egg-producing farms was conducted by the USDA’s Animal and Plant Health Inspection Service in 1999 [11]. Two hundred farms in 15 states were selected. In total, 7% of farms tested yielded SE in at least 1 sample, with a range of prevalence by region from 0% to 17%. Among farms with SE isolated from the environment, contamination was widespread: positive samples were obtained from egg belts (48%), elevators (45%), walkways (18%), and manure (17%).

In 1991, the USDA’s Animal and Plant Health Inspection Service also conducted a microbiologic survey of egg-processing plants (i.e., plants that produce pasteurized liquid egg, powdered egg white, or egg yolk products) [12]. Bulk tanks, which contained raw, liquid whole eggs, were sampled at 20 plants. Eggs destined for these egg-processing plants were often those that did not meet the grading quality or handling process required for consumer-grade shell eggs. Nonetheless, all eggs were washed and sanitized before processing. Of 278 liquid whole egg samples, 169 (61%) yielded Salmonella, of which 38 (14%) were the SE serotype.

Despite the high frequency of SE in egg-laying flocks, the frequency of SE contamination of individual eggs is low. Ebel and Schlosser [10] estimated this frequency to be ~1 in 20,000 eggs, on average, in the United States. However, the frequency of SE contamination in eggs depends on the intensity of infection among hens in a flock and the timing of egg production relative to infection. As indicated in studies by Gast and Beard [7], eggs produced soon after an SE infection are much more...
likely to harbor SE. Thus, in regions where flocks are likely to be heavily colonized by SE, and at times soon after infection spreads, the proportion of SE-contaminated eggs that are produced may be much higher. In an outbreak of SE infection associated with a restaurant, the frequency of SE-contaminated eggs served was estimated to be as high as 1 in 12 [13]. The overall low frequency of SE-contaminated eggs may be misleading, because the total number of eggs produced in the United States is so large (~65 billion each year). Therefore, even with a low frequency of contamination, the number of SE-contaminated table eggs was estimated to be 2.2 million per year in the mid-1990s [10], which constitutes a significant number of potential human exposures to SE.

THE HUMAN FACTOR

A key factor enabling the egg to be an efficient vehicle for human infection is the manner in which people handle and eat eggs. Eggs are one of the few animal products that are frequently eaten raw or undercooked. Raw eggs are often components of homemade and restaurant-produced ice creams, salad dressings, mayonnaise, and beverages such as egg nog and special diet or health drinks. Other types of foods containing eggs are only lightly cooked, such as mousse and hollandaise sauce. Breakfast eggs are often cooked such that, when eaten, the egg white and yolk are soft or runny. SE infection has been associated with eating raw or undercooked eggs in case-control studies of sporadic infections. Hedberg et al. [14] found that patients with sporadic SE were over 5 times more likely to have eaten raw or undercooked eggs in the 3 days before their illness, compared with healthy control subjects. The extent to which eggs were not cooked was directly associated with illness.

Infection with SE is also associated with eating outside the home. In a review of outbreaks of SE infection from 1985–1999, 62% of outbreaks of SE infection occurred in restaurants or other commercial establishments [15]. One reason that commercial or other large-scale food preparation settings may be more frequently associated with illness is the practice of pooling large numbers of eggs for use in scrambled egg dishes and omelets or as components of batters [16]. When pooling eggs, 1 or a few contaminated eggs can contaminate a large amount of food in conditions that may accelerate proliferation, and thus expose a large number of consumers to high quantities of SE-contaminated egg dishes.

BURDEN OF SE IN THE UNITED STATES

In response to the growing number of outbreaks of SE infection in the United States, the CDC established the *Salmonella Enteritidis* Outbreak Reporting System in 1985. This system collects summary information concerning all reported outbreaks of SE infection in the United States, including number of cases, hospitalizations, and deaths; the identified food vehicle; and the place of preparation and consumption.

There was a total of 997 reported outbreaks of SE infection in the United States from 1985–2003 (figure 1), which resulted in 33,687 illnesses, 3281 hospitalizations, and 82 deaths. The number of reported outbreaks of SE infection in the United States increased from 26 in 1985 to a high of 85 in 1990, with a gradual decrease thereafter to 34 outbreaks in 2003. In addition, the number of cases in outbreaks each year has decreased, from a high of 2656 in 1990 to a low of 578 cases in 2003. The 1 exception was 1994, a year in which >4000 cases were attributed to an outbreak of SE infection caused by consumption of a contaminated, nationally distributed ice cream product [17].

A food vehicle was confirmed in ~44% of outbreaks of SE infection in the United States. Among outbreaks of SE infection with a confirmed food vehicle from 1985–2003, 75% of outbreaks had vehicles that were either primarily egg-based or that contained egg ingredients. Although the number of reported outbreaks of SE infection has decreased, the proportion of out-
breaks of SE infection attributed to egg consumption was approximately consistent from year to year (figure 2). Outbreaks of SE infection that were not egg associated were due to a wide variety of other foods, including poultry products (chicken and turkey), raw almonds, alfalfa sprouts, pork, beef, and orange juice.

National surveillance of laboratory-confirmed SE infections is collected at the CDC from reports of Salmonella isolates submitted by each state. The incidence of reported, laboratory-confirmed SE infection began to increase from ∼1.0 case per 100,000 population in the 1980s to 3.9 cases per 100,000 population in 1994. At that time, SE became the most frequently reported Salmonella serotype, representing 26% of all Salmonella serotypes reported in the United States. Since 1996, the incidence of SE has decreased, to 1.7 cases per 100,000 population in 2003; however, SE remains the second most common Salmonella serotype reported (14% of all Salmonella species in 2003). The regional variation in SE incidence has been dramatic. High rates were first seen in the Northeast in the late 1970s, followed by the mid-Atlantic states (figure 3). The incidence of SE infection reached 9.2 and 10.5 cases per 100,000 population in the Northeast and the mid-Atlantic states, respectively, in 1988. The epidemic spread westward, with the Pacific states reaching an incidence of 6.7 cases per 100,000 population in 1994. The overall incidence in the United States decreased 56% from 1995 (3.9 cases per 100,000) to 2003 (1.7 cases per 100,000), with even greater decreases observed in those regions most affected by the SE epidemic.

Surveillance data are based on laboratory-confirmed SE infections. However, laboratory-confirmed SE infections represent an underestimation of the total number of SE illnesses that occur in the United States each year. For an SE case to be considered laboratory confirmed, an ill patient must seek medical care, a sample obtained from the patient must be submitted to a clinical laboratory, the clinical laboratory must isolate the organism from the sample, and the isolate must be sent to a public health laboratory for serotyping (because most clinical laboratories do not perform full serotyping). At each step along this surveillance pathway, a proportion of cases is lost. The CDC estimated these lost proportions by conducting surveys of ill persons, health care providers, laboratories, and public health departments, and has constructed a “surveillance pyramid” for salmonellosis (figure 4). Thus, an estimate of the true burden of diseases can be calculated when each lost portion is accounted for. For Salmonella, it is estimated that, for each laboratory-confirmed case, there are 38 cases that are not ascertained through surveillance [1]. Taking the number of SE cases reported in national surveillance for 2003 (4890), and applying the multiplier of 38, an estimated total of 185,829 cases of SE occurred that year in the United States.

Because it is not possible to determine the source of infection for most individual cases of salmonellosis, it is not precisely known what proportion of individual SE cases are due to consumption of which specific foods. However, from data provided by the Salmonella Enteritidis Outbreak Reporting System and from national laboratory-based case surveillance, the CDC has estimated that 50,000–110,000 SE infections are attributed to eggs each year in the United States (CDC, unpublished data). Despite the broad range of this estimate, these data reveal that SE-contaminated eggs result in thousands of human SE infections each year in the United States.

Antibiotic-resistant Salmonella have been an increasing public health concern [18]. Because salmonellosis is usually foodborne, infection in humans with an antibiotic-resistant Salmonella isolate is associated with the acquisition of antibiotic resistance in food animals. In the United States, 2 fluoroquinol-
olones, enrofloxacin and sarafloxicin, were approved for use in poultry in 1995 and thus have been used extensively. Since 1996, human Salmonella isolates have been monitored for antibiotic resistance by the National Antimicrobial Resistance Monitoring System [19]. During 1996–2003, SE had a relatively low proportion of resistance to any of the individual antimicrobial agents, with one exception: the proportion of isolates resistant to quinolones, represented by naladixic acid, increased from 0.9% to 5.1%. This increase marks the highest prevalence of resistance to quinolones, any Salmonella serotype [19]. On the basis of this and of dramatic increases in fluoroquinolone-resistant Campylobacter species in humans and poultry, the FDA withdrew its approval of the use of fluoroquinolones in poultry in 2005.

THE CONTROL OF SE IN THE UNITED STATES

The decrease in the rate of SE infection in the United States as described by national surveillance systems did not take place in a vacuum; multiple agencies have played important roles in egg safety. Currently, the USDA’s Food Safety and Inspection Service regulates the safety of egg products, such as pasteurized liquid eggs and dried egg products, under the Egg Products Inspection Act of 1970. The National Poultry Improvement Plan is a cooperative program administered by the USDA’s Animal and Plant Health Inspection Service to enhance the health of poultry and safety of poultry products; components that address SE infection of hens and eggs were added to the plan in 1989. The USDA’s Agricultural Marketing Service regulates shell egg grading, handling, and importation, to assure quality, cleanliness, and proper labeling and packaging of eggs that reach consumers. Since 1990, the FDA has had the regulatory authority to conduct inspections and investigations of egg producers. The FDA and the CDC work closely in the context of egg-associated outbreaks of SE infection in humans to trace infected eggs to production flocks, to establish interventions aimed at halting and preventing additional human infections. Also in 1990, the FDA’s Food Code was amended to include shell eggs as a “potentially hazardous food,” indicating that proper cooking time and temperature controls are required to limit pathogenic microorganism growth. The FDA’s safe-handling label and refrigeration regulations followed in this vein. In 1996, the USDA’s Food Safety and Inspection Service, in collaboration with the FDA, initiated a “farm-to-table” risk assessment of SE in shell eggs, which served as the basis for the federal and state Egg Safety Action Plan to address shell egg and egg product safety.

Three key interventions to prevent the contamination of shell eggs by SE have been the development of egg quality–assurance programs on farms, the rapid and sustained refrigeration of eggs from farm to consumer, and the education of consumers and food workers about the risks associated with pooling, handling, and consuming raw or undercooked eggs. Egg quality–assurance programs on farms are comprehensive plans to limit SE contamination and spread in the farm environment. These voluntary programs usually include acquisition of chicks certified free of SE, control of pests (including rodents and flies, which may harbor or disseminate SE), restriction of access to and movement of personnel and equipment among hen houses, use of SE-free feed, cleaning and disinfection of hen houses between successive flocks, and microbiological testing for SE of the farm environment on a routine basis. In most egg quality–assurance programs, repeated isolation of SE from a farm environment results in a diversion of eggs from that farm to egg-processing plants, where all egg products (i.e., pasteurized liquid egg or powdered egg products) are heat treated to reduce bacterial contamination. These programs have been shown to be effective in reducing rates of human SE illnesses in states where the industry has adopted them; for those states, the rates of incidence of human SE illness increased in the years leading up to the adoption of the program, then decreased significantly in each of the successive years after program adoption [20]. The FDA has proposed a regulation that would make egg quality–assurance programs mandatory for medium and large shell egg producers. New technologies, which are currently used by some producers, have been developed to address SE contamination, such as in-shell pasteurization of table eggs. This method of pasteurization applies a relatively low temperature to eggs for a prolonged period (compared with usual pasteurization methods), so as to reduce microbial contamination but to preserve the liquid nature of the egg contents. According to a risk assessment developed by the USDA’s Food Safety and Inspection Service, the number of SE-related illnesses in the United States could decrease by almost 70% if all shell eggs underwent pasteurization to achieve a 3-log reduction of SE infection [21]. Education of food workers and of consumers of the importance of limiting pooling of eggs, and of handling and cooking eggs safely, has also helped to control SE infection.

Physicians can play a role in SE control by educating patients of the risks associated with consumption of raw or undercooked eggs, the need to avoid contamination of other foods with raw

![Figure 4. Estimated total cases of Salmonella enterica serotype Enteritidis infection in the United States, 2003.](http://cid.oxfordjournals.org/)

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eggs, and the importance of hand washing after handling eggs. Medical directors of hospitals and long-term care facilities that care for debilitated and immunocompromised patients (who are especially prone to severe Salmonella infection) should ensure that only pasteurized egg products be served to patients. In addition, physicians caring for patients with possible Salmonella infection should follow the Infectious Diseases Society of America guidelines on submission of diagnostic specimens, including stool specimens [22]. This will not only aid in the treatment of patients, but it will increase the completeness and accuracy of surveillance data that are important in recognizing outbreaks of SE infection and following surveillance trends of the burden of disease.

The SE epidemic in the United States constitutes a major public concern. A confluence of factors likely played a role in the emergence of egg-associated SE in the United States and in many other countries. The abilities of this organism to asymptptomatically infect hen ovaries and to transmit to the internal contents of eggs, and to persist in farm environments, allowed for its unchecked spread in an era of increasingly centralized large farms that house tens of thousands of birds. Furthermore, cross-contamination of foods and the practice of pooling hundreds of eggs for routinely undercooked egg dishes and batters in retail establishments has allowed for a few infected eggs to contaminate large quantities of foods and to therefore cause large numbers of illnesses. In the most notorious instance, tanker trailers that had previously been transporting raw, unpasteurized eggs contaminated the mixture for a nationally distributed ice cream, resulting in an estimated 224,000 human cases of SE infection [17]. Interventions targeted to address these factors have been designed and implemented in many sectors of the egg industry. Although the epidemic levels of SE illness have decreased, there are still many cases and outbreaks of SE infection each year due to SE contamination of eggs. There is still much work to be done to reach the Department of Health and Human Services’ Healthy People 2010 goal to reduce the number of human SE infections in the United States by 50%, compared with the number of infections in 1997.

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References