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Salmonellosis and the GI Tract: More than Just Peanut Butter

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Abstract

Nontyphoidal salmonellosis is the leading cause of foodborne illness in the U.S., causing approximately 1.4 million infections annually. Most cases of salmonellosis are due to ingestion of contaminated food items such as eggs, dairy products, and meats. However, almost any foodstuff can be implicated, including peanut butter, as seen during a recent outbreak of over 600 *Salmonella* infections. Although outbreaks often gain national media attention, the majority of nontyphoidal *Salmonella* infections in the U.S. occur sporadically. Risk factors for salmonellosis include gastric hypoacidity, recent use of antibiotics, extremes of age, and a variety of immunosuppressive conditions. Clinical manifestations of the infection most commonly involve self-limited gastroenteritis; however, bacteremia, endovascular, and localized infections may occur. Most cases of gastrointestinal involvement are self-limited, with antibiotic therapy reserved among persons at risk for complicated disease. Preventive strategies by both industry and among consumers are advocated to further reduce the occurrence of nontyphoidal salmonellosis.

Introduction

Salmonella were named after the Pathologist Salmon over a century ago [1,2]. Although first described in farm animals, it was soon realized that *Salmonella* caused a spectrum of disease among humans. The best known organisms of this genus are S. *typhi* and *S. paratyphi*, the etiologies of enteric fever. Nonetheless, non-typhi *Salmonella* cause over 1 million infections in the U.S. annually and include over 2,500 different serotypes [3]. The increasing importance of these infections is a result of continued outbreaks of nontyphoidal *Salmonella* (including a recent outbreak involving contaminated peanut butter), the high incidence rates of infections worldwide, and the evolution of multiresistant *Salmonella* strains [4-6]. Several excellent reviews have been published focusing on typhoid fever, which is most often acquired among U.S. residents during travel abroad [7-9]. However, the largest burden of *Salmonella* infections within the U.S. are due to nontyphoidal serotypes [10]. The focus of this article is the epidemiology, clinical manifestations, and treatment of nontyphoidal salmonellosis.

Microbiology

Salmonella are Gram-negative, facultative anaerobic bacteria in the family of Enterobacteriaceae. The genus *Salmonella* is divided into two species, *S. enterica* and *S. bongori*. Most pathogenic species of *Salmonella* affecting humans are within the species of *S. enterica*, formerly called *S. choleraesuis*. The taxonomic classification of *Salmonella* is

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complex. *S. enterica* is further subdivided into six subspecies, designated I, II, IIIa and IIIb (formerly *S. arizonae*), IV, and VI; V is now the separate species of *S. bongori* [3]. Over 2,500 serotypes have been reported due to differences in the somatic (O) and flagellar (H) antigens based on the Kauffman and White scheme [11]. Some serotypes are designated by a name (many which have been derived from the location of first isolation.) while other serotypes are designated by a formula. Naming often omits the species and simply lists the serotype. For instance, the term "*Salmonella* Typhimurium" is often utilized, however, its official name is *Salmonella enterica* subspecies *enterica* serotype Typhimurium. In this review, as in most of the literature, the abbreviated names will be used.

Salmonella is typically isolated by sampling of fresh stools. Rectal swabs are less sensitive and are not recommended. Samples can be plated on low-selective media (e.g., MacConkey agar) or more selective medias for *Salmonella* (e.g., Hektoen agar). Highly selective media (e.g., selenite with brilliant green) are typically reserved for known carriers or during outbreak investigations [12]. Invasive infections are typically diagnosed by culturing the bacteria from blood cultures or from wound cultures from the site of infection. Most laboratories have antisera or agglutination tests which can define specific groups of *Salmonella* without necessarily identifying the specific serotype. Serotyping of isolates can often be performed at public health laboratories. During outbreak investigations, more sophisticated testing (e.g., PCR-based fingerprinting, multilocus sequence typing) may be performed to determine the relatedness of the strains within a given serotype. Blood tests for antibodies to O antigens, such as the Widal test, are nonspecific and are not recommended for the diagnosis of either nontyphoidal or typhoidal *Salmonella* infections.

Epidemiology

Nontyphoidal *Salmonella* is the most commonly identified cause of foodborne illness in the U.S., with approximately 1.4 million cases per year [10,13,14]. The number of cases reported each year approximates 45,000; however, this represents only the "tip of the iceberg" as it is estimated that the actual number is 30-fold higher than that reported. The incidence rate of infection in 2002 was 17.7 cases per 100,000 person years [15], with infants and children (<5 years) being at highest risk for the disease. As with most foodborne illnesses, the peak occurrence is during the summer months. The most common serotypes identified are *S.* Typhimurium, *S.* Enteritidis, and *S.* Newport, in descending order [3,16]. Although the rates of *Salmonella* infections in the U.S. rose over the past two decades, they have declined since the late 1990s; however, *Salmonella* continues to account for 30% of all deaths associated with foodborne disease in the U.S., [13] and it continues to be the second most common bacteria isolated from stool cultures during diarrheal illnesses, following *Campylobacter jejuni*.

Salmonella can both colonize and cause infections in humans and animals. Of interest, some *Salmonella* species appear to be better adapted to humans, and vice versa. For example, *S. typhi* does not have an animal reservoir and is solely transmitted by humans, whereas the nontyphoidal serotype *S.* Dublin mainly affects cattle.

Most (>95%) human cases of *Salmonella* involve ingestion of a contaminated food item, in particular, eggs, poultry, ground beef, or dairy products. Although these are the most commonly implicated food items, nearly any food can be contaminated as discussed below. Waterborne infections also can occur, albeit less commonly [17]. In addition, contact with an animal carrying *Salmonella* may result in human infection if careful hand hygiene is not followed. For instance, multiple reports of reptile-associated transmissions have occurred within the U.S. leading to the ban of small turtle sales in the U.S.; however, the risk of acquisition from animals such as iguanas, turtles, and snakes remains and accounts for 3-5% of all *Salmonella* infections in the U.S. [18,19]. Even household pets such as cats, dogs, and rodents may be implicated

[20,21]. Even more surprisingly, simply handling products such as pet food and treats have recently been linked to outbreaks of human infections [21,22]. Finally, *Salmonella* can be acquired by direct personal contact, nosocomial transmission, or contaminated drugs/solutions.

Regarding food exposures and *Salmonella* infections, the predominant source in the 1970s through 1990s were contaminated shell eggs. For instance, the Centers for Disease Control and Prevention (CDC) investigated 65 outbreaks (involving 2,119 cases) of *Salmonella* in the Northeastern U.S. during 1986-1987 and found eggs were implicated in the majority of these cases [23]. Although it was initially believed that eggs became contaminated after hatching, studies have shown that they were in fact infected transovarially before hatching [24,25]. Subsequently, several improvements in the processing of eggs have led to a decline in egg-related cases since 1998 [24,26]. Nonetheless, the egg remains a common source of salmonellosis, particularly when raw eggs are utilized in making such foods as hollandaise sauce, ice cream, Caesar or homemade salad dressings, tiramisu, or egg nog. In addition, if a single contaminated egg is mixed with other eggs to make large quantities of food in restaurant settings, this can result in an outbreak [24]. Besides eggs, a variety of meats (especially poultry, ground turkey, and beef) can be contaminated with *Salmonella* during slaughter, processing, or distribution.

Food items not directly derived from animals have also been contaminated with *Salmonella* (e.g., tomatoes, cantaloupe, unpasteurized orange juice, seed sprouts, and cilantro). Gaining national headlines, contaminated Peanut Butter (Peter Pan and Great Value produced by ConAgra Foods Inc. plant in Georgia) caused a multistate outbreak this year resulting in over 600 patients infected with the serovar, *S*. Tennessee [4]. The median age of patients infected was 52 years (range 2 months to 95 years), and 73% were female. In addition to gastrointestinal symptoms, 45% had dysuria related to this serotype's ability to infect the urinary tract. Overall, 20% required hospitalization, but no deaths were attributed to *Salmonella* infection. This was the first time peanut butter was associated with a *Salmonella* outbreak in the U.S.; the source of contamination was unknown at last report [4]. We searched MEDLINE and EMBASE for foodborne outbreaks of nontyphoidal *Salmonella* infections in the U.S. from 2000 to 2007 using the search terms "*Salmonella*", "United States", and "disease outbreaks". A summary of recent food-associated outbreaks in the U.S. are shown in Table 1 [4,27-42]. In addition to these reports, an outbreak traced to a colonized food handler was also noted [43]. Although outbreaks are an important cause of salmonellosis, the majority (80%) of cases are sporadic.

Foodborne salmonellosis remains a concern, especially in light of the risk of manufactured foods as described in many of the recent outbreaks. Companies may distribute large quantities of food to geographically diverse locations. In addition to the recent peanut butter-associated outbreak, another such example is an outbreak during 1994 which involved over 200,000 cases involving nationally distributed ice cream premix that had been contaminated during transportation using a tanker trailer previously carrying unpasteurized eggs [44]. Moreover, due to the shipment of food items internationally, the possibility of worldwide outbreaks exists.

Beyond the U.S., nontyphoidal *Salmonella* infections are common in developing areas, such as Asia, Africa, and South America, where it is an important cause of infantile and childhood diarrhea. Travelers to these areas can acquire *Salmonella* as a cause of traveler's diarrhea [45].

Pathogenesis

Salmonella infections occur mainly via ingestion of contaminated foodstuffs. Organisms must survive the hostile gastric environment with low pH and avoid lysis by bile salts in the upper small intestine. The organisms attach and invade the distal ileum and proximal colon causing clinical illness. Initial host responses involve neutrophil infiltration, followed by the arrival of

lymphocytes and macrophages. Occasionally, diffuse colitis occurs mimicking inflammatory bowel disease; however, pathologically, these conditions are distinct. *Salmonella* infections may spread beyond the gastrointestinal mucosa into draining mesenteric lymph nodes; adenitis may simulate acute appendicitis. Spread then may continue to the liver, spleen, and systemically, via the bloodstream. A detailed description of the virulence factors of *Salmonella* and the innate and acquired host responses against invasion have previously been described [12,46].

The infectious dose required for clinical illness is unknown, but is estimated at approximately 10^6 organisms [47]. The ingested dose also appears to be a determinant of the incubation period and the severity of the disease, with larger dosages ingested being associated with a decreased time to illness and more severe disease manifestations [48]. Fewer organisms in the range of 10^2 to 10^3 may cause disease; for instance, patients with low gastric pH (given that acidity is an important barrier to *Salmonella* infections) may develop disease after ingesting a smaller quantity of bacteria [49,50]. Hypoacidity often occurs in infants, in pernicious anemia, or with the use of antacid medications.

Other host factors appear to increase the susceptibility to *Salmonella* infections including the extremes of ages and a variety of immunosuppressive conditions, such as the human immunodeficiency virus (HIV), diabetes mellitus, rheumatological conditions, malignancy, reticuloendothelial blockade (sickle-cell disease), and the use of immunosuppressive medications, such as corticosteroids [6]. Chronic granulomatous disease and iron overload are also associated with a higher risk of these infections. Finally, the use of antibiotics during exposure to *Salmonella* may actually increase the risk of clinical illness, as the antibiotics may reduce the “competitive” effect of the normal intestinal flora [5]. Preinfection antibiotics have been noted to be risk factors during outbreak investigations [51,52].

Clinical Manifestations

Clinical manifestations of nontyphoidal salmonellosis include gastroenteritis, bacteremia, endovascular infections, and localized infections. The most common presentation is gastroenteritis which manifests as nausea, vomiting, and diarrhea occurring 6-48 hours after ingestion; a more rapid onset is associated with a higher inoculum or a compromised host. Symptoms cannot readily distinguish *Salmonella* from other GI pathogens such as *Campylobacter* or *Yersinia*. Stools are usually non-bloody and of moderate volume, although this maybe variable. Associated symptoms may include fever, chills, abdominal cramps, myalgias, and headache. Occasionally, severe right quadrant pain occurs mimicking appendicitis [53]. Significantly bloody stools are not characteristic and usually occur more commonly with *Shigella* or enterohemorrhagic *E. coli* (EHEC). Microscopy stool examination usually shows leukocytes and sometimes red blood cells. The peripheral white blood count may be slightly elevated (10,000-15,000 cells/mm^3).

The disease is usually self-limited (three to seven days); prolonged symptoms usually suggest another diagnosis. Occasionally, *Salmonella* mimicking inflammatory bowel disease can occur, but is uncommon [54]. Some cases of gastroenteritis require hospitalization due to the severity of the diarrhea and dehydration; admission occurs at an incidence rate of 2.2 per 1 million persons annually. The elderly and the immunocompromised host have higher risks for severe manifestations. Overall, there are approximately 500 deaths per year due to nontyphoidal salmonellosis in the U.S. [13].

Patients may continue to carry *Salmonella* in their gastrointestinal tracts after the acute infection for a mean duration of four weeks; neonates and children usually shed bacteria longer (seven weeks) [55]. Antibiotics during the acute infection may actually prolong the carrier state [55]. Some patients with nontyphoidal *Salmonella* infections, like those with typhoid fever,

may develop a chronic carrier state, defined as positive stool or urine culture for *Salmonella* at 12 months following the acute illness. Chronic carriage of nontyphoidal *Salmonella* occurs in 0.5% of cases (compared to 3% of those with *S. typhi*) and represents an important public health issue as a mechanism of transmission to other persons. Infants, women, persons with gallstones or kidney stones, and those co-infected with *Schistosoma haematobium* are at higher risk for chronic carriage.

Bacteremia is the most common complication of gastroenteritis, occurring in 1-4% of immunocompetent patients [55]. Some serovars, such as *S*. Choleraesuis and *S*. Dublin, have a particular propensity to cause bacteremia. Adults with *Salmonella* gastroenteritis are more likely to have complicated infections compared to children [56]. Furthermore, several populations are at increased risk for bacteremia, including those at the extremes of age (infants and the elderly) and immunocompromised persons (acquired immunodeficiency syndrome (AIDS), transplant recipients, and patients with malignancy or autoimmune diseases) [12]. HIV-infected persons have up to a 100-fold increased risk for salmonellosis compared to the general population [57]; recurrent bacteremia due to *Salmonella* is classified as an AIDS-defining event. A reduction in the incidence of salmonellosis has been seen among HIV patients, likely due the introduction of potent antiretrovirals (for instance zidovudine has anti-*Salmonella* activity) and the receipt of trimethoprim-sulfamethoxazole, which is protective, not only against *Pneumocystis jiroveci* pneumonia, but also against *Salmonella*. Clinicians should consider evaluating patients with *Salmonella* bacteremia, especially those without a history of gastroenteritis or those with recurrence, for an immunosuppressive illness or anatomical risk factor (e.g., kidney or biliary stone, endovascular lesion) [6]. Follow-up blood cultures to document clearance of bacteremia and a clinical evaluation for potential septic complications have been suggested [6].

Endovascular complications may occur in patients with bacteremia, including seeding of atherosclerotic plaques or aneurysms, especially in the aorta. However, mycotic aneurysm can develop in any arterial vessel; less commonly, venous thrombophlebitis may occur. Vascular complications occur in 10-25% of adults with bacteremia [12,58]. Bacteremia may also lead to localized infections in 5-10% of cases including meningitis, endocarditis, pneumonia, empyema, abscess formation, osteomyelitis, or septic arthritis [12]. Abscesses may develop in association with malignant tumors [59], and patients with sickle cell disease have a prediction to develop *Salmonella* osteomyelitis. Arthritis can occur due to direct infection into the joint which is typically monoarticular. A reactive polyarthritis can also occur after the onset of gastroenteritis; however, this is an immune phenomenon rather than a dissemination infection. Gastrointestinal manifestations of nontyphoidal salmonellosis may include hepatomegaly, splenomegaly, cholecystitis, cholangitis, and splenic and hepatic abscesses, but these are overall uncommon [12,59,60].

Antibiotic Resistance

Although a variety of antibiotics were effective against *Salmonella* before the 1990s, within the last 15 years, resistance to ampicillin, chloramphenicol, and trimethoprim-sulfamethaxozole have been increasingly reported. In 1998, a report of multiresistant S. Typhimurium definitive phage type (DT104) resistant to these antibiotics plus tetracycline and streptomycin was reported in the U.S. [51].

In addition to resistance to the aforementioned antibiotics, nalidixic acid resistance has been reported which has been shown to predict lack of clinical response to the fluoroquinolones. The emergence of this resistance has been directly linked to the rising use of fluoroquinolone antibiotics (e.g., enrofloxacin and sarafloxicin) in animals. The human impact of

fluoroquinolone-resistant *Salmonella* has been already been seen including cases of life-threatening diarrheal illness and has been noted especially in cases from Southeast Asia [61].

In 2000, another concerning isolate was identified - a *S*. Typhimurium infection in a child that was resistant to 13 antibiotics, including extended spectrum cephalosporins, aminoglycosides and aztreonam [62]. Interestingly, the organism was shown to be acquired from livestock on the family's farm. Hence the rising antimicrobial resistance noted among human cases of salmonellosis appears to be a direct result of increasingly resistant strains among farm animals, emphasizing the need for judicious use of antibiotics in all settings, including veterinary medicine and agriculture [6,27]. In this regard, the FDA withdrew its approval of the use of fluoroquinolones in poultry in 2005; other antibiotic restrictions have also been considered. Prudent use of antibiotics in humans is also advocated, as infection with a resistant strain of *Salmonella* is also related to the prior receipt of antibiotics among patients [5].

Rates of resistant *Salmonella* have steadily risen in the U.S.; by 2002, multidrug resistance was noted among 24% of *S*. Typhimurium isolates [63]. As a consequence of rising resistance rates in *Salmonella*, effective treatment for salmonellosis has become more limited, and early empiric antibiotics may fail [5,45]. Several studies have demonstrated that multiresistant bacteria are associated with excess morbidity and mortality. This finding may be due to lack of an effective antibiotic for treatment; in addition, reports suggest that resistant organisms are also more virulent [5,64].

Treatment

Therapy for salmonellosis depends on the location of the infection and the host. Gastroenteritis due to *Salmonella* is typically self-limited and usually does not require antibiotic therapy among immunocompetent persons. Management in these cases is focused on hydration and electrolyte replacement. A meta-analysis did not find that antibiotics decreased the length of illness; in fact, this study found that even short-course antibiotics were associated with an increased risk of relapse and persistent *Salmonella* carriage [65]. The mechanism of these findings may be related to the fact that antibiotics may actually suppress the "protective effect" of endogenous flora [5,6]. Antidiarrheal agents are also not recommended as they may extend the GI transit time and lengthen the clinical course of illness.

Since some patients have an increased risk of developing bacteremia, this population may benefit from antibiotics to minimize the occurrence of complications. For this reason, antibiotics should be considered for infants <3 months of age (some advocated consideration at <1 year of age); persons >50 years; immunosuppressed hosts; those with vascular abnormalities, such as prosthetic valves or grafts; as well as persons with prosthetic joints [6, 12,66,67]. Antibiotics for these groups may include an oral fluoroquinolone, azithromycin, trimethoprim-sulfamethoxazole, or amoxicillin for three to seven days or until after resolution of fevers (Table 2) [12,67]. Given rising antibiotic resistance rates for amoxicillin/ampicillin and TMP-SMX, ciprofloxacin is the preferred agent, but as noted above, resistance has been described with this agent, as well. In 2004, the prevalence of resistance among nontyphoidal *Salmonella* isolates was 2.6% for fluoroquinolones (represented by nalidixic acid) and 3.4% for third-generation cephalosporins [63]. Despite concerns of using fluoroquinolones in children, a trial of ciprofloxacin for the treatment typhoid fever suggested that these agents can be used safely for *Salmonella* infections [68]; of note, fluoroquinolones are not currently approved by the FDA for use in children in the U.S. The antibiotic course among immunocompromised persons or for relapsing disease is often extended to 14 days.

Salmonella bacteremia requires intravenous antibiotic therapy, generally for 7-14 days duration [12]. Due to increasing reports of antibiotic resistance, both a third-generation cephalosporin (e.g., ceftriaxone) and a fluoroquinolone should be utilized until sensitivity data are available.

A single agent should then be chosen, as combination therapy is not known to improve the clinical response [6]. Aminoglycosides and first generation cephalosporins are not useful for *Salmonella* infections. Patients with persistent bacteremia or risk factors for endovascular complications should undergo imaging to exclude these complications; those with documented endovascular infections should receive a six-week course of intravenous antibiotics (usually intravenous ampicillin or ceftriaxone) and surgical management. For instance, those with endocarditis typically require valve replacement and those with a mycotic aneurysm should undergo surgical resection. Localized infections often require surgical debridement along with antibiotics; the course of therapy is dependent on the site of involvement [12].

The chronic carriage state can be treated with amoxicillin (1 gram three times daily for three months), trimethoprim-sulfamethoxazole (1 DS tablet twice daily for three months), or ciprofloxacin (750 mg twice daily for 1 month), similar to the management of *S. typhi* carriers [12]. The latter two antibiotics have superior penetration capabilities and may be the preferred agents. The choice of antibiotic should be based upon sensitivity testing of the colonizing isolate. Patients with concurrent gallstones should be considered for cholecystectomy, and those with concurrent *S. haematobium* infections should first receive therapy with praziquantel.

Prevention

Interventions in the “farm to the table” continuum should be pursued to ensure the sale of uncontaminated food items within the U.S. [27]. Education of food handlers and the general population is a key component of these processes. Foremost is the necessity of good hand hygiene and adhering to food preparation guidelines. These include the avoidance of cross-contamination in the kitchen of raw eggs or potentially contaminated products with other food items.

Consumers should avoid ingesting raw or undercooked eggs and all meats (especially poultry and ground beef) should be well-cooked to an internal temperature of ≥160°F [27]. In addition, eggs and dairy products should be pasteurized before consumption. Vegetables and fruits should be thoroughly washed before ingestion. All persons should wash their hands after touching pets, especially after handling reptiles; avoiding natural pet treats and raw food diets for pets is recommended [21]. Immunocompromised persons or those at the extremes of age should be particularly mindful of these preventive strategies.

Healthcare providers should not prescribed antibiotics for salmonellosis in an attempt to reduce secondary transmission; as noted above, antimicrobials can actually increase carriage times. The best method of reducing spread is good hand hygiene [66]. *Salmonella* cases within the hospital should be managed with the use of barrier precautions to avoid nosocomial transmission.

Follow-up stool cultures among patients who have had *Salmonella* gastroenteritis are not warranted and may be positive for several weeks as noted above. It has been recommended that healthcare workers may return to their jobs after the cessation of diarrhea and the intervention of good hand hygiene [6]. However, local guidelines should be followed regarding laws concerning both healthcare workers and food handlers. Some geographic regions require two negative stools (after antibiotic discontinuation) before food handlers can return to work; local guidelines through the public health department must be followed.

Conclusions

Nontyphoidal *Salmonella* infections continue to occur frequently within the U.S., leading to 1.4 million infections annually. Although most cases occur sporadically, outbreaks continue to gain national attention, including a recent outbreak involving contaminated peanut butter.

Salmonella infections usually produce a clinical illness of self-limited gastroenteritis; however, certain populations, such as immunocompromised hosts, have a heightened risk of complicated disease including bacteremia and localized infections. Preventive strategies regarding food preparation and consumption are advocated to further reduce the occurrence of *Salmonella* infections. However, due to the ubiquitous nature of *Salmonella*, sporadic cases and outbreaks are likely to continue to occur; consequently, clinicians should be familiar with the clinical manifestations and the treatment recommendations of nontyphoidal salmonellosis.

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Table 1

Foodborne Outbreaks of Nontyphoidal Salmonellosis in the U.S., 2000-2007

Reference No.	Year of Outbreak	Serotype	Food Product	No. Cases*
27	2000	*S*. Typhimurium	Milk	23
28	2000-2002	*S*. Poona	Cantaloupes	155
29	2001	*S*. Kottbus	Alfalfa sprouts	31
30	2001	*S*. Enteritidis	Eggs	741
27	2002-2003	*S*. Newport	Ground beef	59
31	2003	*S*. Typhimurium	Raw milk	62
27	2003	*S*. Typhimurium	Ground beef	165
32	2003	*S*. Typhimurium	Egg salad	18
33	2004	*S*. Typhimurium	Ground beef	31
34	2004	*S*. Javiana and others	Roma tomatoes	429
34	2004	*S*. Braenderup	Roma tomatoes	125
35	2004	*S*. Enteritidis	Almonds	29
36	2005	*S*. Newport	Tomatoes	72
36	2005	*S*. Braenderup	Tomatoes	82
36	2006	*S*. Typhimurium	Tomatoes	190
37	2006	*S*. Oranienburg	Fruit salad	41
38.	2007	*S*. Wandsworth	Veggie booty snacks for kids	65
39	2007	*S*. Schwarzengrund	Dry pet food, Mars Petcare US	62
40	2007	*S* l4,[5], 12:i:-	Pot pies, Banquet brand	238
41	2007	*S*. Typhimurium	Cake mix	26
4	2007	*S*. Tennessee	Peanut butter	628
42	2007	*S*. Typhimurium	Raw milk and cheese	29

* Number at last reporting per references; some numbers combined if outbreak same food item and serotype. Some cases investigated by the CDC occurred in Canada.

Table 2

Treatment Recommendations for Nontyphoidal *Salmonella* Infections

Location fo Infection	**Therapy***
Gastroenteritis	Usually no antibiotic therapy required Patients with risk factors** for the development of complicated disease should receive antibiotics for 3-7 days -Ciprofloxacin 500-750 mg po bid -Amoxicillin, trimethoprim-sulfamethoxazole, or azithromycin may be options depending on susceptibility testing results
Bacteremia	Cef triaxone 2 g iv daily plus ciprofloxacin 400 mg iv q12 until susceptibility testing is available. De-escalate to one agent (usually ceftriaxone). Treatment course is 7-14 days.
Localized Infections (e.g. osteomyelitis, meningitis)	Intravenous therapy; consider surgical debridement See reference #12 for specific antibiotic recommendations
Chronic Carrier	Ciprofloxacin 750 mg po bid × 1 month Other options: amoxicillin 1000 mg po tid × 3 months or trimethoprim-sulfamethoxazole DS 1 po bid × 3 months

* Other options listed in the text

** Infants <3 months of age (some advocated treatment if <1 year of age), persons >50 years, immunosuppressed hosts, those with vascular abnormalities such as prosthetic valves or grafts as well as prosthetic joints.