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Update on *Salmonella* spp contamination of pet food, treats, and nutritional products and safe feeding recommendations

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Recently, there have been several recalls of commercial pet foods and treats in the United States because of contamination with *Salmonella* spp. This contamination creates a risk that pets ingesting these food items can become clinically ill or may become carriers of *Salmonella* organisms, but it is also a public health concern for pet owners who handle the food products and interact with these pets. As recalls and media attention make the public more aware of the potential for *Salmonella* contamination, clients may rely more heavily on veterinarians for advice in choosing safe diets for their pets and minimizing the risk of salmonellosis in their households. By keeping current on recalls and understanding the basics of how contamination with *Salmonella* spp can lead to disease, veterinarians can provide accurate and educated nutritional recommendations to clients as well as suggestions on public health and hygiene to minimize the risk of salmonellosis in their clients' households.

Salmonella Prevalence and Classification

Salmonella spp are gram-negative bacilli in the family Enterobacteriaceae that are capable of colonizing the intestinal tracts of most vertebrates. The prevalence of *Salmonella* organisms in the feces of companion animals has been assessed, with most studies[1–3] finding a prevalence of < 5% in healthy dogs. The prevalence of *Salmonella* spp in the feces of healthy cats is reported to range from 1% to 18%.[4] Two studies that involved dogs examined at veterinary teaching hospitals because of diarrhea found a prevalence of 1%[5] and 2.8%.[5,6] A larger study[7,8] that involved 1,626 healthy dogs in Florida found a prevalence of 15%. A higher prevalence of fecal shedding of *Salmonella* spp in racing sled dogs and Greyhounds has been reported.[9] In that study,[9] up to 69% of clinically normal sled dogs had *Salmonella* spp isolated from fecal samples obtained prior to a race, and *Salmonella* spp were isolated from 63% of dogs with diarrhea during the race and 57% of dogs without diarrhea during the race. In a study[10] of Greyhounds, 61% of dogs with diarrhea, 11% of dogs without diarrhea, and 56% of diet samples tested had positive results for *Salmonella* spp. In populations of dogs such as those in these 2 studies,[9,10] feeding practices (including provision of raw or undercooked diets that may be contaminated with *Salmonella* organisms) are a concern.

Abbreviation

SPI *Salmonella* pathogenicity island

Nomenclature for *Salmonella* spp has changed over the years as technology has evolved, which has resulted in classification of this genus into 2 distinct species, *Salmonella enterica* and *Salmonella bongori*. There are > 2,400 serotypes of *S enterica*, which are classified on the basis of their agglutination reactions to the somatic (O) and flagellar (H) antigens, whereas there are only 20 serotypes for *S bongori*.[11] Most disease in humans and companion animals is caused by *S enterica* serotypes Enteritidis or Typhimurium.

Contaminated Food Products

Salmonella spp are almost exclusively acquired by ingestion of food or water contaminated with infected feces. Consumption of infected raw meat is presumably the most common source of infection with *Salmonella* spp. Some pet owners elect to feed their pets commercially prepared raw meat diets or to include raw meat in homemade diets (ie, meat acquired from a butcher and subsequently prepared by the owner). Meat from both sources may be contaminated with *Salmonella* organisms if appropriate precautions are not taken during processing, handling, and storage. Feeding commercially produced or homemade raw diets can increase the risk for pet dogs to shed *Salmonella* organisms in their feces.[12,13] In 1 study,[14] commercial raw food diets that contained chicken were 5 times as likely to be contaminated with *Salmonella* organisms as were raw food diets that did not contain chicken. Raw food diets are a likely source of infection for racing Greyhounds and sled dogs and may explain higher fecal shedding in these breeds.[9,15] Many Greyhound and sled dog owners believe that feeding raw meat improves performance; however, investigators in 1 study[15] found that 45% of commercial raw meat used in diets fed to Greyhounds had positive results when tested for *Salmonella* spp (most often *Salmonella* Typhimurium), and antimicrobial resistance was common in these *Salmonella* isolates cultured from meat.

Dry commercial pet foods, treats, vitamins, and nutritional (supplement-type) products can also become contaminated with *Salmonella* spp. Although thorough cooking will kill *Salmonella* organisms, not all products are cooked,

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and there are many steps during the production process after cooking at which there could be cross-contamination with *Salmonella* spp or other fecal bacteria. Handling or consuming these products (or fomites contaminated with *Salmonella* spp from these products) can lead to illness or a carrier state in pets or their owners. Alternatively, canned food is vacuum-sealed and sterilized at a temperature of 121°C for a minimum of 3 minutes to kill pathogenic bacteria.[16] Once this process is complete, the contents of the can are considered commercially sterile and safe. Cross-contamination of *Salmonella* spp to food within sealed cans after sterilization would be extremely unlikely or impossible. However, as with all products, once canned foods are opened, they can be cross-contaminated with bacteria within a consumer's home.

Pig ears have become a popular chew treat for dogs in North America, with over 200 million purchased yearly; however, contamination of this treat with *Salmonella* spp has been identified.[17–19] Pig ears and other dried animal parts typically are frozen, cleaned, and flavored during processing, but they are not cooked. This processing routine may allow contamination with *Salmonella* organisms from the original pig carcasses to survive on pig ears. After a 1999 outbreak of human infections with *S enterica* serotype Infantis in Canada, an epidemiological investigation linked the outbreak to pig ears intended for consumption by dogs; 51% of pig ears purchased at retail stores were contaminated with *Salmonella* spp.[17] The illness rate in dogs was not reported in that study.[17] A similar study[18] in the United States found that 41% of dog treats derived from pig ears and other animal parts purchased from retail stores were contaminated with *Salmonella* spp, including *Salmonella* Infantis isolates indistinguishable from those in the Canadian outbreak. Education and recommendations for improved hygiene have led to a decrease in the prevalence of pig ears contaminated with *Salmonella* spp in Canada to 4% by 2007.[19] Irradiation of pig ears and individual packaging, rather than storing pig ears in bulk bins, are 2 recommendations for minimizing cross-contamination with *Salmonella* spp.[19]

Pet treats containing dried beef were contaminated with *S enterica* serotype Newport and found to be responsible for human illness in a 2002 outbreak.[20] All *Salmonella* isolates carried the bla_{CMY-2} gene, which encodes the antimicrobial resistance enzyme AmpC β-lactamase, CMY-2.[20] Although pet owners handling these dog treats became infected with multidrug-resistant *Salmonella* organisms, fecal samples from pets owned by these owners had negative results for *Salmonella* spp and no illness was reported in these pets.[20]

In 2004 to 2005, a third outbreak of human illness was traced back to contact with salmon and beef pet treats contaminated with *S enterica* serotype Thompson. Eleven people were infected in that outbreak.[21] It remains unclear whether patients acquired *Salmonella* organisms from direct contact with the pet treats or from zoonotic fecal-oral contact from their pets because no canine feces were tested for *Salmonella* Thompson during the epidemiological investigation of that outbreak. Infected pets may have clinical signs or no clinical signs and be carriers shedding *Salmonella* organisms in their feces that are capable of infecting their owners or others with whom they come into contact. In the *Salmonella* Thompson outbreak, 1 dog owned by an infected person had diarrhea, whereas pets owned by other infected people remained healthy.[21] Spread of *Salmonella* organisms between pets, owners, and veterinary staff has been documented in 3 outbreaks (unrelated to contaminated food or treats), presumably as a result of fecal-oral contact with diarrheic cats.[22] In future outbreaks, fecal samples from pets owned by humans with salmonellosis should be tested to investigate the zoonotic potential and role of fecal-oral transmission. However, despite the fact that DNA fingerprinting can confirm that humans and pets share the same bacterial strain, it remains challenging to prove transmission (in either direction), rather than concurrent exposure to a contaminated food product, in any contamination outbreak scenario.

In 2006, a multistate outbreak of *S enterica* serotype Schwarzengrund began that was epidemiologically traced back to contaminated dog and cat food produced by a single manufacturer at a plant in Pennsylvania.[23] The manufacturing process at that plant included the use of time and temperature conditions validated to kill *Salmonella* spp. The food then was moved to an enrobing and flavoring room where it was sprayed to enhance palatability. It is believed the contamination occurred at that stage because the outbreak strain of *Salmonella* spp was detected in the enrobing and flavoring room.[24] To the author's knowledge, that was the first report of a documented outbreak of human illness attributable to dry dog or cat food. In total, 79 people, mostly children, were infected in 21 states, and all recovered from their illness.[24] Although the same strain of *Salmonella* spp was isolated from fecal samples of 5 dogs consuming food manufactured at that plant, no pets became ill with salmonellosis during the outbreak.[25]

The FDA regulates pet foods, treats, and nutritional products in the United States. Outbreaks resulting from *Salmonella*-contaminated food products have led to increased awareness, recommendations for prevention, and surveillance by the FDA and individual manufacturers to ensure the safety of these products. When contamination is detected in a food product, the manufacturer will initiate a product recall to minimize risk of exposure and infection for consumers. The FDA maintains 2 websites that contain up-to-date information on pet food and product recalls for pet owners and veterinarians.[26,27] Manufacturers often voluntarily recall more products than have positive test results for *Salmonella* spp in an attempt to ensure the safety of consumers. This precautionary measure may include all products made at the facility involved, as was seen in a July 2010 recall that included over-the-counter and veterinary-exclusive dry dog and cat diets.[27] At other times, manufacturers will recall only the item that had positive results when tested for *Salmonella* spp, as was seen in a July 2010 recall of beef filet square treats for dogs.[27] These recalls have not been isolated events. During the past year, there have been recalls because of concerns of possible *Salmonella* contamination of beef treats by 3 manufacturers, pig ears by 1 manufacturer, raw diets by 2 manufacturers, and dry pet food by 1 manufacturer.[27]

Vitamins and nutritional products can also become contaminated with *Salmonella* organisms, most likely as a result of cross-contamination during production. In April 2010, a nutritional product for joint health of dogs was voluntarily recalled because of possible contamination with *Salmonella* spp from a hydrolyzed vegetable protein component.[27] Then in July 2010, 56 veterinary nutritional products were recalled by a single manufacturer because of concerns about *Salmonella* spp. Those 56 nutritional products were sold nationally by various retailers under numerous brand names and included multivitamins, cranberry tablets, ear powder, glucosamine, coprophagia treatment, fresh breath treatment, a calcium product, gas prevention

tablets, and calming tablets.[27] Similar to the situation for contaminated foods, pets consuming contaminated nutritional products and owners handling these products have the potential to become ill with salmonellosis. To the author's knowledge, no illnesses in humans or domestic animals relating to these recalled products have been reported.

Host Immunity

Salmonella organisms must overcome numerous host defenses along the gastrointestinal tract before they can establish infection. This host immunity explains the reason that there are fewer clinical cases of salmonellosis in companion animals than would be expected on the basis of exposure or fecal prevalence. Acid in the stomach kills most bacterial species, but *Salmonella* spp can survive exposure to a pH of 3 because of acid-tolerance systems and production of acid-shock proteins.[28] Despite this tolerance, only a small fraction of ingested *Salmonella* organisms survive the stomach. In the intestines, antibacterial properties such as bile salts, organic acids, and peristalsis help prevent colonization. The normal gastrointestinal microflora also play an important role as competitors to colonization of *Salmonella* spp.

Puppies and kittens are more susceptible to infections than are adult dogs and cats because their immune systems are not yet fully developed. Infections can be fatal when acquired by fetuses in utero or by neonates from the contaminated fluids of dams. Deficiencies of methionine or choline during pregnancy can increase the susceptibility of a dam's offspring to salmonellosis.[29] Because of their effects on the normal intestinal flora, stress and selection pressure from antimicrobial treatment are also theorized to increase the rate of colonization, infection, and clinical illness attributable to *Salmonella* spp in dogs and cats.[4,28,30]

Pathogenesis

Salmonella organisms that survive initial host defenses colonize the ileum and attach to the tips of villi. There is invasion at enterocytes or at specialized membranous epithelial cells (M cells) within Peyer's patches. Contact of *Salmonella* organisms with enterocytes triggers signal transduction pathways that result in profound rearrangement in the actin cytoskeleton of enterocytes, which leads to endocytosis of *Salmonella* organisms into cells.[31]

Salmonella organisms induce a secretory and inflammatory diarrhea that is caused by a number of factors. No toxins have been associated with induction of salmonellosis. Enterocyte invasion stimulates increased vascular permeability and edema within villi, injury and sloughing of enterocytes, effusion of a large amount of neutrophils and protein-rich fluid into the intestinal lumen, and formation of a pseudomembrane and diarrhea.[32] The host inflammatory response results in the production of prostaglandins and leukotrienes and also leads to increased chloride secretion into the intestine, which is followed by secretion of water. Fecal shedding of *Salmonella* organisms typically continues for 3 to 6 weeks.[4]

Salmonella organisms that survive the host defense mechanisms of the gastrointestinal tract can spread extraintestinally by invading phagocytic host cells in the intestinal lymph nodes, which is followed by systemic dissemination that causes bacteremia and endotoxemia. The reticuloendothelial system is responsible for removing these bacteria, but *Salmonella* spp often survive in phagocytes within the liver and spleen and cause persistent infections. In times of stress or immunosuppression, organisms can reemerge and cause recurrence of clinical disease and shedding.

Virulence and Resistance Traits

Numerous virulence factors have been identified in *Salmonella* spp and contribute to the ability of these bacteria to be taken up by enterocytes and cause intestinal disease. The ability of *Salmonella* organisms to survive and replicate inside host macrophages is a critical component of their capacity to cause systemic disease.[33] There are 5 SPIs. Each SPI is a region of chromosomal DNA with clusters of virulence genes. The SPI-1 is present in all *Salmonella* spp and encodes a type III secretion system that is required for the uptake of *Salmonella* organisms into intestinal cells.[34] The SPI-2 genes, which are present in *S enterica* but not *S bongori*, are required for survival in host phagocytes by specifically interfering with nicotinamide adenine dinucleotide phosphate oxidase and preventing phagocyte-dependent oxidative killing.[35] The SPI-3 and SPI-4 play a role in survival within macrophages, whereas SPI-5 contains genes encoding proteins required for secretion of intestinal fluids and electrolytes as well as for recruitment of neutrophils.[36] Some strains of *Salmonella* Enteritidis and Typhimurium also contain plasmids whose genes increase the ability to cause systemic disease.[37] Other important *Salmonella* virulence factors include fimbriae that allow attachment and colonization of the intestinal tract and that are critical in establishment of infection, and lipopolysaccharide that induces inflammation and can trigger fever and endotoxic shock and result in death. More studies are needed to determine the association between virulence traits and differences in clinical manifestations of salmonellosis so that identification of these traits can have clinical applicability.

Antimicrobial resistance is common in *Salmonella* isolates, including those from contaminated food products, in part because of various strategies for exchanging genes that carry resistance factors. In Calgary, 26% of *Salmonella* isolates from pig ear treats were resistant to 4 or more antimicrobials, with the most common profile being that of resistance to ampicillin, cephalothin, streptomycin, sulfamethoxazole, and tetracycline.[19] Multidrug resistance was also detected in up to 50% of *Salmonella* isolates cultured from contaminated raw dog foods.[14] *Salmonella* Typhimurium DT104, which has been isolated from dog treats, contains chromosomally encoded genes for resistance to 5 antimicrobials (ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline).[18] *Salmonella* strains may also contain class 1 integrons, which encode genes for multidrug resistance and are capable of transferring these genes between the chromosomes and plasmids; class 1 integrons have been identified in *Salmonella* isolates from dog treats.[18] Plasmids can also carry resistance genes, such as the bla_{CMY-2} gene encoding cephalosporin resistance via AmpC β-lactamase, which was found in all *Salmonella* isolates from contaminated pet treats in another study.[20] In vitro conjugation evaluations have revealed transfer of this plasmid both within and between genera of the fecal flora, specifically between *Escherichia coli* and *Salmonella* spp.[38] These findings suggest that consumption of *Salmonella*-contaminated food products may lead to increased antimicrobial resistance within normal gastrointestinal flora.

Clinical Salmonellosis

Many adult animals exposed to *Salmonella* spp become nonclinical carriers rather than developing clinical illness.[1–3,7,8] Puppies, kittens, stressed or immunosuppressed animals, animals with concurrent illness, animals receiving antimicrobial treatment, or animals that ingest a high dose of organisms may become clinically ill. Animals with *Salmonella*-induced gastroenteritis become ill 3 to 5 days after exposure and develop fever, malaise, anorexia, vomiting, signs of abdominal pain, and diarrhea that may contain fresh blood.[4] Cats that prey on wild birds may develop songbird fever, which is gastroenteritis attributable to infection with *Salmonella* Typhimurium and is characterized by fever, anorexia, vomiting, hemorrhagic diarrhea, and lethargy. Bacteremia and endotoxemia are clinically important in extremely young or immunosuppressed animals, and they may develop with or without concurrent signs of gastroenteritis.[4] Bacteremia can lead to infection of distant organs, such as the lungs, liver, or brain. In utero infections can cause reproductive failures or birth of weak, infected offspring.

In the United States, there are a reported 1.4 million cases of nontyphoidal salmonellosis in humans each year, which results in 400 human deaths/y.[39] Infection of humans with *Salmonella* spp is characterized by diarrhea, fever, and abdominal cramping that develops 12 to 72 hours after exposure and typically lasts for 4 to 7 days.[23] Although most people recover without treatment, salmonellosis is most severe and can spread systemically and be fatal in infants, the elderly, and immunosuppressed people.[23]

Public Health Recommendations

The FDA and manufacturers continue to provide surveillance to ensure the safety of pet food and treats. Pet owners can take precautions to minimize the risk of infection within their homes. Veterinarians play an important role in educating clients about the risks of *Salmonella* spp and can provide practical steps that can be implemented to keep their clients and patients healthy. The following are safety recommendations for pet owners to minimize the risk of *Salmonella* infection for the pets and family members in their homes.[12–15,19,24,40,41]

- Avoid feeding raw food diets to pets.
- Purchase individually packaged pig ears, rather than those from bulk bins.
- Ensure packaging of pet food products is in good condition prior to purchase; return product to store if it appears tainted, discolored, or malodorous.
- Store pet foods, treats, and nutritional products in accordance with label instructions, preferably in a cool, dry environment.
- Save original pet food packaging material, including the date code and product code of all food products, for product identification in case of food contamination.
- Discourage children, the elderly, and immunosuppressed people from handling pet food, treats, or nutritional products, if possible.
- Wash hands with soap and water before and after handling pet food, treats, or nutritional products.
- Use a clean scoop to dispense pet food into bowls.
- Wash water and food bowls of pets as well as feeding scoops routinely with hot soapy water in a sink other than in the kitchen or bathroom.
- Avoid feeding pets in the kitchen.
- Discourage all people from consuming pet foods, treats, or nutritional products.

Ample evidence exists for the risk of *Salmonella* contamination in raw food diets; thus, it is advised that pet owners avoid feeding raw food diets to pets.[12–15] For other uncooked items, such as pig ear treats, veterinarians can help educate owners about the potential risks and advise owners to purchase individually prepackaged pig ears rather than those from bulk bins that have a greater potential for exposure as a result of cross-contamination.[19] Purchased dry pet foods should be inspected for quality and disposed of or returned if they appear tainted, malodorous, or discolored. Pet foods and treats should be stored in accordance with label instructions, preferably in a cool, dry room protected from pets, rodents, and insects. Dry food can be stored in its original bag and placed inside a plastic container to provide extra protection. The original packaging material, including the date code and product code of all food products, should be saved for product identification if food contamination is ever suspected.[40]

Pets should be fed in a room other than the kitchen to minimize cross-contamination of pet food and food intended for human consumption. An epidemiological review of the *Salmonella* Schwarzengrund outbreak revealed that children who fed a pet in the kitchen had an increased risk of illness, compared with the risk for control children.[24] Because children, the elderly, and immunosuppressed people more commonly develop salmonellosis than do healthy adults, these individuals should avoid contact with pet food, food bowls, and pet treats, if possible. Instead of the use of the pet's bowl to obtain food from a bag, a clean scoop should be used to dispense food, and it should be cleaned routinely.[41] Although no direct association was found in the *Salmonella* Schwarzengrund outbreak[24] between illness and children who put pet food in their mouths, it is recommended that humans should not consume pet food or treats.

It is recommended that people should wash their hands after feeding pets and after all contact with pet food or pet treats. Bowls for pet food and water should be washed in hot soapy water at regular intervals to minimize contamination of their surfaces. This should not be performed in the kitchen (to prevent cross-contamination of food intended for human consumption) or the bathtub (to prevent infection of children during bathing).[24] It is also recommended that people wash their hands after contact with all pets because even subclinical carriers may be shedding *Salmonella* organisms and can infect other household members.

Conclusion

Veterinarians are a trusted source of nutritional information for pet owners and can influence the dietary choices for pets. It is important that veterinarians continue to reassure pet owners of the safety of pet foods and treats produced in the United States. Veterinarians also have a responsibility to disseminate accurate information about potential contamination risks, such as *Salmonella* spp, so that appropriate precautions can be implemented. Although the risk of salmonellosis from contaminated pet foods and treats is low, adhering to safety recommendations will help to minimize the risk of infections with *Salmonella* spp for pets and family members.

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