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*Review*

# Review of the Zoonotic Importance of *Salmonellosis* and Associated Risk Factors

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**ABSTRACT**

*Salmonella* is one of the most common and significant human and animal food-borne pathogens that cause salmonellosis, which has high medical and monetary costs. *Salmonella* has a big impact on public health because it can spread zoonotic and foodborne-diseases to people. Many domestic and wild animals intestinal tracts serve as the main reservoir for *Salmonella*, which can result in the direct or indirect contamination of a variety of foods with fecal organisms. *Salmonellae* are etiological agents of diarrheal and systemic infections. They can be shed in large numbers on the faces of clinical cases and carrier animals, causing contamination of the environment and frequently resulting in subclinical infections. Infection in food animals often leads to contamination of meat, eggs, milk and cheese. The organism can also spread through direct contact with infected humans, animals, or feces contaminated environments. Infected food handlers may also act as a source of contamination for foodstuffs, because of the increasing antibiotic resistance of organisms and companion animals, animals are an important source of *Salmonella* infection for humans. *Salmonella* can colonize its hosts by invading, adhering, and bypassing the host's intestinal defense mechanisms, such as gastric acid, thanks to a variety of virulence markers and determinants, including flagella, capsule, plasmids, adhesion systems, and secretion systems. Diagnosis is based on the isolation of the organism either from tissues collected aseptically at necropsy or from faces, rectal swabs or environmental samples, food products, and feedstuffs; prior or current infection of animals by some agents may also be diagnosed serologically.

**Keywords**
Salmonellosis; Animals; Zoonosis; Diagnosis; Transmission.

## INTRODUCTION

*Salmonella* is a gram-negative, rod-shaped, facultative anaerobe, flagellated bacterium that belongs to the *Enterobacteriaceae* family.[1] Salmonellosis is considered one of the most important life-threatening bacterial zoonotic diseases of humans as well as animals and poultry species. There are more than 2500 serovars of *Salmonella* worldwide. In humans, *Salmonella enterica Typhi* (*S. Typhi*) and *Salmonella enterica Paratyphi* (*S. Paratyphi*) cause typhoid fever and paratyphoid fever, respectively.[2] Salmonellosis is an infectious disease in humans and animals, clinically characterized by septicemia, acute enteritis, or chronic enteritis. Animals may be infected without being overtly ill. Since *Salmonellae* are primarily intestinal bacteria, they may be continuously or sporadically excreted in the feces, contaminating the environment. The bacterium causes infections ranging from subclinical carrier status to acute fatal septicemia.[3]

*Salmonella* infections are considered one of the major causes of diarrheal diseases globally, and although most cases are mild and occasionally self-resolving, life-threatening clinical illness is common.[4] It is a potential cause of acute and chronic diarrhea and death in numerous animal species and human beings.[5] The disease is also considered an important food-borne illness with significant public health ramifications.[6] In both more and less developed countries, salmonellosis is regarded as the most common food-borne zoonosis. It is also associated with many other disease syndromes; including septicemia, and acute and chronic enteritis.[7] Bacterial virulence factors have a crucial role in systemic infections. The virulence of *Salmonella spp.* is associated with a combination of chromosomal and plasmid factors.[8] Virulence factors are encoded by several genes located on the bacterium's chromosome, the so-called housekeeping genes, which give specific and basic characteristics to bacteria from the same family. These genes can be found

in the so-called pathogen city islands, or mobile genetic elements such as transposons, plasmids, and bacteriophages. These genes confer advantages for bacteria, such as resistance to antimicrobials, adaptation to the host cell, and the ability to overcome host defense mechanisms.[9]

*Salmonella* infections are often acquired through ingestion of contaminated food of animal origin and contact with infected animals or contaminated environments.[10] Salmonellosis in young children may have different causes than it does in older populations. According to Patrick et al,[11] identified potential risk factors of salmonellosis in young children include having a child riding in a shopping cart next to meat or poultry, exposure to reptiles, attending a childcare center with infected children, consumption of powdered infant formula, eating eggs, undercooked ground beef, chicken or animal produce, the family transmission of *Salmonella* and traveling abroad. *Salmonella* source attribution is being performed in several countries to ascertain the main food-producing animal reservoirs towards which control efforts should be directed and to assess the impact of such interventions.[12] *Salmonella* epidemiology is complex and dynamic, necessitating a multi-tiered approach to control that takes into account the various reservoirs, pathways, and risk factors at play.[13]

Contact with infected people, frequently in a family setting, contact with animals, frequently young animals, exposure while traveling, as well as decreased host resistance due to advanced age, underlying diseases, or prior antimicrobial exposure, are the most crucial risk factors for *Salmonella*.[14] Salmonellosis in humans is typically transmitted *via* the gastrointestinal route. Another possible route of transmission is contact with infected animals. In addition, pets, including reptiles that are frequently kept close to people, help spread the illness.[15] Salmonellosis is a costly disease to dairy producers on account of mortality, treatment expenses, reduced milk yield, and weight loss within the herd. Infected cattle can be either clinical or subclinical, shedding *Salmonella* in their feces.[16] Therefore, the objectives of this review papers are:

- To determine the possible risk factors and the spread of salmonellosis in both humans and animals.
- To highlight salmonellosis's potential zoonotic effects.

## MORPHOLOGICAL CHARACTERISTICS AND EPIDEMIOLOGY OF SALMONELLOSIS

### Characteristics and Morphology

*Salmonella* is a genus of rod-shaped (*bacillus*) gram-negative bacteria that belongs to the *Enterobacteriaceae* family and is the most common cause of food poisoning in humans worldwide.[1] The two species recognized within this genus; are *S. enterica* and *S. bongori*.[17] *Salmonella spp.* are non-spore-forming, predominantly motile enterobacteria with cell diameters of between 0.7 and 1.5 m, lengths of 2 to 5 m, and peritrichous flagella (all around the cell body). They are chemotrophs, obtaining their energy from oxidation and reduction reactions using organic sources. They are also facultative anaerobes, capable of generating adenosine triphosphate (ATP) with oxygen (aerobically) when it is available, or using other electron acceptors or fermentation (anaerobically) when oxygen is not available.[18] Due to the lack of access to safe water and unhygienic food handling practices by food handlers, *Salmonella* is an intestinal parasite infection that poses the greatest public health risks worldwide, particularly in developing nations.[19]

Certain serotypes of the intracellular pathogen *Salmonella* cause disease. Most infections are due to ingestion of food contaminated by animal feces, or by human feces, such as by a food-service worker at a commercial eatery. *Salmonella* serotypes can be divided into two main groups-typhoidal and non-typhoidal. Non-typhoidal serotypes can be transferred from animal to human and from human-to-human. They usually invade only the gastrointestinal tract and cause salmonellosis, the symptoms of which can be resolved without antibiotics.[20] Salmonellosis is caused by *Salmonella spp.* and is the third leading cause of death among food-transmitted diseases. This pathogen is commonly disseminated in domestic and wild animals, and the infection's symptoms are characterized by acute fever, nausea, abdominal pain, and diarrhea. Animals are the primary source of *Salmonella*, and animal-based foods are the main transmission route to humans. *Salmonella* is a genus of gram-negative, facultatively anaerobic, rod-shaped bacteria of the family *Enterobacteriaceae*.[21] According to Ferrari et al,[22] classification is done using the three groups of surface structures that are expressed on the bacterial lipopolysaccharide (LPS), flagella, and capsular polysaccharide.

### Epidemiology and Geographic Distribution

The epidemiology of salmonellosis is complex, which often makes the control of the disease difficult. The epidemiological patterns of infection and disease differ greatly between geographical areas depending on climate, population density, land use, farming practices, food harvesting and processing technologies, and consumer habits. Additionally, because the biology of the serovars varies so greatly, it is impossible to avoid complexity when thinking about salmonellosis, *Salmonella* infections, or *Salmonella* contamination.[23]

*Salmonella spp.* is one of the most important food-borne pathogens and the third leading cause of human death among diarrheal diseases worldwide. The prevalence and diversity of *S. enterica* serovars in animal-based foods (beef, pork, poultry, and seafood) throughout the five continents Africa, Americas North, Latin America, Asia, Europe, and Oceania.[22] The prevalence of salmonellosis in the different agroecological areas has shown that this is due to the accessibility and waste disposal as well as hygienic practices of the society.[21]

### Pathogenesis

*Salmonella spp.* are facultative intracellular pathogens. *Salmonella* can invade different cell types, including epithelial cells, M-cells, macrophages, and dendritic cells. As a facultative anaerobic organism, *Salmonella* uses oxygen to make ATP in an aerobic environment (i.e, when oxygen is available). However, in an anaerobic environment (when oxygen is not available), *Salmonella* produces ATP by fermentation; by substituting one or more of four less efficient electron acceptors than oxygen at the end of the electron transport

chain: sulfate, nitrate, sulfur, or fumarate.[24] The ability of *Salmonella* strains to persist in the host cell is crucial for pathogenesis, as strains lacking this ability are non-virulent.[25] Following the engulfment of *Salmonella* into the host cell, the bacterium is encased in a membrane compartment called a vacuole, which is composed of the host cell membrane. Under normal circumstances, the presence of a bacterial foreign body would activate the host cell's immune response, resulting in the fusion of the lysosomes and the secretion of digesting enzymes to degrade the intracellular bacteria. However, *Salmonella* uses the type III secretion system to inject other effector proteins into the vacuole, causing the alteration of the compartment structure. The remodeled vacuole blocks the fusion of the lysosomes, and this permits the intracellular survival and replication of the bacteria within the host cells. The capability of the bacteria to survive within macrophages allows them to be carried in the reticuloendothelial system (RES).[26]

*Salmonella* pathogenicity islands (SPIs), gene clusters located at the large chromosomal deoxyribonucleic acid (DNA) region and encoding for the structures involved in the invasion process, are where the remarkable genetics underlying this brilliant strategy can be found.[27] The epithelial cells lining the intestinal wall are typically penetrated by the bacteria when they enter the digestive tract through contaminated water or food. SPIs encode type III secretion systems, multi-channel proteins that allow *Salmonella* to inject its effectors across the intestinal epithelial cell membrane into the cytoplasm. The bacterial effectors then activate the signal transduction pathway and trigger the reconstruction of the actin cytoskeleton of the host cell, resulting in the outward extension or ruffle of the epithelial cell membrane to engulf the bacteria. The morphology of the membrane ruffle resembles the process of phagocytosis.[28]

### Entrance Molecular Mechanism

The mechanisms of infection differ between typhoidal and non-typhoidal serotypes due to their different targets in the body and the different symptoms that they cause. Both groups must enter by crossing the barrier created by the intestinal cell wall, but once they have passed this barrier, they use different strategies to cause infection.[29]

**Switch to virulence:** While traveling to their target tissue in the gastrointestinal tract, *Salmonella* is exposed to stomach acid, to the detergent-like activity of bile in the intestine, to decreasing oxygen supply, the competing normal gut flora, and finally to antimicrobial peptides present on the surface of the cells lining the intestinal wall. *Salmonella* can detect all of these types of stress, respond to them by forming virulence factors, and as a result, control when they transition from their normal growth in the intestine into virulence.[30]

**Mechanism of entry:** Non-typhoidal serotypes preferentially enter M-cells on the intestinal wall by bacterial-mediated endocytosis, a process associated with intestinal inflammation and diarrhea. They are also able to disrupt tight junctions between the cells of the intestinal wall, impairing the cells' ability to stop the flow of ions, water, and immune cells into and out of the intestine. The combination of the inflammation caused by bacterial-mediated endocytosis and the disruption of tight junctions is thought to contribute significantly to the induction of diarrhea.[31]

*Salmonellae* are also able to breach the intestinal barrier *via* phagocytosis and trafficking by CD18-positive immune cells, which may be a mechanical key to typhoidal *Salmonella* infection. This is thought to be a more-stealthy way of passing the intestinal barrier, and may, therefore, contribute to the fact that lower numbers of typhoidal *Salmonella* are required for infection than non-typhoidal *Salmonella*. Much of the success of *Salmonella* in causing the infection is attributed to two types III secretion systems (T3SS), which are expressed at different times during the infection. The T3SS-1 enables the injection of bacterial effectors into the host cytosol. These T3SS-1 effectors stimulate the formation of membrane ruffles, allowing the uptake of *Salmonella* by non-phagocytic cells. *Salmonella* further resides within a membrane-bound compartment called the *Salmonella*-containing vacuole (SCV). The acidification of the SCV leads to the expression of the T3SS-2. *Salmonella* must secrete T3SS-2 effectors to effectively survive in the host cytosol and cause systemic illness. In addition, both T3SS are involved in the colonization of the intestine, the induction of intestinal inflammatory responses and diarrhea. These systems contain many genes which must work cooperatively to achieve infection.[32]

**Host adoption:** *S. enterica*, through some of its serotypes such as *Typhimurium* and *Enteritidis*, shows signs of the ability to infect several different mammalian host species, while other serotypes such as *Typhi* seem to be restricted to only a few hosts.[33]

Some of the ways that *Salmonella* serotypes have adapted to their hosts include loss of genetic material and mutation. In more complex mammalian species, immune systems, which include pathogen-specific immune responses, target serovars of *Salmonella* through the binding of antibodies to structures such as flagella. Through the loss of the genetic material that codes for a flagellum to form, *Salmonella* can evade a host's immune system.[34] By directly base pairing with the messenger ribonucleic acids (mRNAs) of the flip gene that encodes flagellin and encouraging degradation, the mgt leader RNA from the bacteria's virulence gene (*mgtCBR* operon) reduces the amount of flagellin produced during infection. Pathogenic serovars of *S. enterica* were found to have certain adhesins in common that have developed out of convergent evolution. This means that, as these strains of *Salmonella* have been exposed to similar conditions such as immune systems, similar structures have evolved separately to negate these similar, more advanced defenses in hosts. Still, many questions remain about the way that *Salmonella* has evolved into so many different types, but *Salmonella* may have evolved through several phases. *Salmonella* most likely evolved through horizontal gene transfer, the formation of new serovars due to additional pathogenicity islands, and an approximation of its ancestry. So, *Salmonella* could have evolved into its many different serotypes through gaining genetic information from different pathogenic bacteria. The presence of several pathogenicity islands in the genomes of different serotypes has lent credence to this theory.[35]

*Salmonella Newport* has signs of adaptation to a plant colonization lifestyle, which may play a role in its disproportionate as-

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sociation with a foodborne-illness linked to produce. A variety of functions selected for Newport persistence in tomatoes have been reported to be similar to those selected for *Typhimurium* from the animal hosts. The *papA* gene, which is specific to the Newport strain and has homologs in the genomes of other *Enterobacteriaceae* that can colonize plant and animal hosts, contributes to the strain's fitness in tomatoes.[36]

**Resistance to oxidative burst:** A hallmark of *Salmonella* pathogenesis is the ability of the bacterium to survive and proliferate within phagocytes.[37] Phagocytes produce DNA-damaging agents such as nitric oxide and oxygen radicals as a defense against pathogens. Thus, *Salmonella spp.* must face attacks by molecules that challenge genome integrity. Mutants of *S. enterica* lacking RecA or RecBC protein function are highly sensitive to oxidative compounds synthesized by macrophages, implying that successful systemic infection by *S. enterica* requires RecA- and RecBC-mediated recombinational repair of DNA damage.[38]

### Zoonotic Importance

Salmonellosis is a common human intestinal disorder primarily associated with *Salmonella*-contaminated meats and poultry.[38] Infections with *Salmonella* in food-producing animals present a serious public health concern because food products of animal origin are considered to be a significant source of human infection. The most common sources of infection are eggs and related products, and meat from poultry and other food animal species. Milk and dairy products have also been associated with outbreaks of salmonellosis in people. In addition, contamination of fruit and vegetables by infected water may also be a source of infection.[39] Human salmonellosis is one of the most common and economically important zoonotic diseases. The Centers for Disease Control and Prevention (CDC) estimates that salmonellosis causes more than 1.2 million illnesses each year in the United States of America, with more than 23,000 hospitalizations and 450 deaths.[40] *Salmonella* infections are most frequently contracted through the consumption of contaminated foods, such as soft cheeses made from unpasteurized milk, meat, poultry, fresh fruit and vegetables, eggs, or egg products. *Salmonella* can also be spread to people through contact with infected birds, livestock, reptiles, amphibians, and dogs and cats. These animals may carry the bacteria even when healthy.[41]

Many serovars, including some that are host-adapted such as *S. Choleraesuis* and *S. Dublin*, have been shown to cause serious diseases in humans. Abattoir workers, animal attendants, and veterinarians may be infected directly during their work when in contact with infected animals. Laboratory personnel may also acquire the infection if safe working practices are not implemented. To avoid laboratory infections, biosafety and biosecurity measures in veterinary diagnostic and animal facilities should have followed Biosafety and Biosecurity Standards. Biosecurity: Standard for managing biological risk in the veterinary laboratory and animal facilities).[42]

### Transmission

Animals are the primary source of this pathogen, and animal-based foods are the main transmission route between animals and humans. *Salmonella* bacteria can last in contaminated eggs and frozen oysters for months, as well as days in groundwater or seawater. To control and monitor, it is crucial to comprehend the global epidemiology of *Salmonella* serovars.[43]

### Salmonellosis Risk Factors

Risk factors for *Salmonella* infections include a variety of foods. Meats such as chicken and pork can be contaminated. A variety of vegetables and sprouts may also have *salmonella*. Lastly, a variety of processed foods such as chicken nuggets and pot pies may also contain these bacteria.[44] Consumption of food purchased from places other than supermarkets was the main modifiable risk factor for salmonellosis.[45] Other established risk factors include recent contact with a diseased patient or carrier, eating ice cream, flavored iced drinks, or food from street vendors, and raw fruit and vegetables grown in fields fertilized with sewage.[46] Poor waste disposal and hygiene of workers in food handling and preparation activities would provide an obvious infection route. The clinical characteristics of salmonellosis in large animals vary depending on the various management systems used; the intensity of stocking; whether or not the animals are housed; and the epidemiological characteristics of the different *Salmonella spp.*[47]

### Animal Risk Factors

The size of the challenge dose and the animal's immunological status, which in turn depends on colostrum intake in neonates, prior infection, and stressor exposure, particularly in older animals, determine the animal's response to infection with a *Salmonella spp.*[23]

### Environmental and Management Risk Factors

Intensification of husbandry in all species is recognized as a factor contributing significantly to an increase in the new infection rate. Any significant change in management of the herd or a group of animals can precipitate the onset of clinical salmonellosis if the infection preexists in those animals. Temperature and wetness are most important, as *Salmonellas* are susceptible to drying and sunlight.[48]

### Pathogen Risk Factors

*Salmonella* are facultative intracellular organisms that can withstand the bactericidal effects of antibodies while living in the phagolysosome of macrophages. *Salmonellas* are more tolerant of different environmental factors than other members of their family. They multiply at temperatures between 8 °C and 45 °C, at water activities above 0.94, and in a potential of hydrogen (pH) range of 4-8. They are also able to multiply in an environment with a low-level of or no oxygen.[49]

**Human source:** Environmental and personal hygiene is one of the knowledge and practice restrictions of humans from beef/dairy farms and abattoir food processing plants. On the other hand, food getting contaminated depends largely on the health status of the food handlers.[48] In both developed and developing nations, in-

cluding Ethiopia, foodborne diseases are a public health concern. Contamination can happen at any stage of the food supply chain, including during production, processing, distribution, and preparation. In dairy farms and industries that process food, high standards of employee hygiene must be upheld.[49]

**Other sources:** International trade and its introduction through international travel, as well as the trade in food, livestock, and animal feed, all present challenges; **Water source:** *Salmonellae* can be found in contaminated water; inanimate objects. A further ambiguity in the environment surrounding food processing is the rise in antimicrobial resistance to *Salmonella* in recent years due to the widespread use of antimicrobial drugs in the human and veterinary sectors.[26]

### Clinical Sign and Symptom

The clinical symptom of salmonellosis are associated with hospitalization, another infection or debilitating conditions in adults, or exposure manifested by watery or mucoid diarrhea with blood in severe cases, vomiting, fever, anorexia, abdominal cramps, fever, occasionally nausea and vomiting, lethargy and progressive dehydration. After a short incubation period of a few hours to one day, the bacteria multiply in the small intestine, causing intestinal inflammation (enteritis). Most people with salmonellosis develop diarrhea, fever, vomiting, and abdominal cramps 12 to 72-hours after infection.[50] Diarrhea is often watery and non-bloody but may be mucoid and bloody. In most cases, the illness lasts four to seven days and does not require treatment. In some cases, though, diarrhea may be so severe that the patient becomes dangerously dehydrated and must be hospitalized. At the hospital, the patient may receive fluids intravenously to treat the dehydration and may be given medications to provide symptomatic relief, such as fever reduction. In severe cases, the *Salmonella* infection may spread from the intestines to the bloodstream, and then to other body sites and can cause death, unless the person is treated promptly with antibiotics.[51]

Typhoid fever occurs when *Salmonella* bacteria enter the lymphatic system and cause a systemic form of salmonellosis. Endotoxins first act on the vascular and nervous apparatus, resulting in increased permeability and decreased tone of the vessels, upset thermal regulation, vomiting, and diarrhea. In severe forms of the disease, enough liquid and electrolytes are lost to upset the fluid balance, cause an electrolyte imbalance, decrease the circulating blood volume and arterial pressure, and cause hypovolemic shock. Septic shock may also develop. The shock of mixed character (with signs of both hypovolemic and septic shock) is more common in severe salmonellosis. Oliguria and azotemia develop in severe cases as a result of renal involvement due to hypoxia and toxemia.[52]

### Diagnosis, Treatment and Prevention

**Diagnosis:** Diagnosis is based on the identification of *Salmonella* either from faces or tissues collected aseptically at necropsy, environmental samples or rectal swabs, feedstuffs, and food products; prior or current infection of animals by some serovars may as well be detected serologically. If reproductive organs are infected, abortion or concepts occurs, it is essential to culture vaginal swabs, placenta, fetal stomach contents, and embryonated eggs.[53] Organisms may be identified using a diversity of techniques that may include pre-enrichment to resuscitate sub-lethally damaged *Salmonellae*, enrichment media that comprise inhibitory substances to inhibit competing organisms, and selective agars to differentiate *Salmonellae* from other enterobacteria. Various biochemical, serological, and molecular tests can be used on the pure culture to allow for reliable verification of an isolated strain. The organism has antigens named somatic (O), flagellar (H), and virulence (Vi), which may be identified by special typing sera, and the serovar may be assigned by reference to the antigenic formulae in the KaufmanWhite scheme. Many laboratories may require sending isolates to a reference laboratory to ensure the full serological identity and to verify the phage type and genotype of the strain, where suitable.[54]

**Treatment:** There are increasing rates of antibiotic resistance throughout the world, so the choice of antibiotics should be a careful one.[55] Salmonellosis is generally self-limited and usually does not require specific treatment. Animals with severe diarrhea might require rehydration, sometimes with intravenous fluids. Antibiotics are not recommended for uncomplicated cases and are only used if the infection spreads or is highly likely to spread from the intestines to the bloodstream and other organs,[45] but, for systemic infection in animals and humans with septicemia, antimicrobial therapy is warranted, and should be based on the antimicrobial susceptibility of the cultured isolate.[56] Chloramphenicol, trimethoprim-sulfa, fluoroquinolones, and aminoglycosides are usually effective against *Salmonella.* Variable resistance to erythromycin, clindamycin, ampicillin, and cephapirin greatest resistance is seen with streptomycin and tetracycline. Animals with the severe clinical disease may require additional supportive therapy as well, including colloid support.[54]

**Control:** To control bacteria reducing the number of *Salmonellae* harbored in the animals will substantially reduce human exposure. All animal feeds are treated to kill *Salmonella* before distribution to prevent the spread of infection. Food animal flocks and herds are routinely tested for *Salmonella* and those found to be positive are sent for special slaughter followed by heat treatment of the meat. Vaccination of livestock in most developed countries contributes to the greater outcome for eradication unlike, in the developed world which is not effectively used and is still a problem to control the bacteria.[21]

## CONCLUSION AND RECOMMENDATIONS

Infection with *Salmonellae* is of great zoonotic and public health importance. So, a collaboration between human and veterinary practitioners is very crucial to increase awareness and education about the disease's importance, especially among susceptible risky groups. Salmonellosis is a highly contagious bacterial disease in animals and humans with a significant economic impact. Animal and human salmonellosis around the globe and these outbreaks have been linked with consumption of *Salmonella* contaminated foods of animal origins such as poultry and related derived products, pork, cattle, sheep, goats, fish, etc. *Salmonella* like many other enteropathogenic bacteria has evolved by utilizing a variety of viru-

lence markers and other cellular machinery to colonize the host by attaching, invading, and bypassing the host's gastrointestinal defense mechanisms. Animals are a primary reservoir for non-typhoidal *Salmonellae* associated with human infections, and contact with animal feces either directly through animal handling or manure or indirectly through fecal contamination of foods is the principal vehicle of human infection. Animal health experts can be an important link to reducing the incidence of non-typhoidal salmonellosis in humans by assisting in the development and implementation of control strategies to reduce the carriage of *Salmonellae* by food-producing and companion animals. Based on the above conclusion the following recommendation forwarded:

• Research should direct toward identifying and characterizing novel virulence determinants required by the organism to establish or maintain an infection. These studies may generate novel antibiotic targets or suggest more unusual therapeutic agents be used in conjunction with traditional antibiotic therapy.
• Vaccine development, for example targeting flagella or pili as antigens, may also allow preventing infection in those who are most at risk.
• For effective control collaboration between human and veterinary practitioners is very crucial to increase awareness and education about the disease's importance, especially among susceptible risky groups.

## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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