



# A Review of History, Definition, Classification, Source, Transmission, and Pathogenesis of Salmonella: A Model for Human Infection

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Article info	Abstract
Original: 1 June 2018 Revised: 28 June 2018 Accepted: 12 September 2018 Published online: 20 December 2018	Salmonella is one of the most frequently isolated food-borne microorganism. It is a major world-wide public health involvement, accounting for 93.8 million food-borne illnesses and 155,000 deaths per year. The genus Salmonella is a member of the bacterial family Enterobacteriaceae named in recognition of a famous veterinary bacteriologist Daniel E. Salmon (1850 - 1914). The genus consists of more than 2500 serological distinguishable variants in which more than half of them belong to <i>Salmonella enterica subsp. enterica</i> , which accounts for the majority of Salmonella infections in humans. Most of Salmonella serotypes are potentially pathogenic, causing sporadic infections, as well as outbreaks of fatalities, while some are less pathogenic and causing minor infections in both human and most animal species. Preventive measures have been proposed to eliminate the spread of Salmonella infection. While the maintenance of effective food hygiene and water sanitation remain the cornerstones, additional measures such as restriction of indiscriminate use of antibiotics in food animals are important. The aim of this review is to highlight the history, bacterial definition, classification of its species, source of infection and contamination, transmission routes, and finally pathogenesis.

**Key Words:** Bacterial infection, zoonotic disease, food poisoning, contamination, review

## Introduction

### History of Salmonella

Salmonella bacterium was first found by Sohlerin in 1839 [1], and it isolated by Eberth in 1880 from the mesenteric lymph nodes and spleen of a person died from typhoid fever. Salmonella was cultured in 1888 by Salmon and Smith from pigs which had died of hog cholera [2]. Salmonella bacteria as a causative agent for gastroenteritis was isolated by Gartner in 1888 from a fatal case of gastroenteritis in a young man who had eaten raw meat taken from a diseased cow [3]. *S. typhimurium* was isolated by Loeffler in 1892 from an infected mouse [4]. In 1896, Achard and Bensaud isolated an organism to which they gave the name *Bacillus paratyphique* and this organism according to Boycott (1911) was *S. schottmulleri* [5].

The etiological agent of Pullorum disease (*S. pullorum*) was described by Rettger in 1899 and the disease was called fatal septicemia of young chicks [6]. Schottmuller in 1900 showed that 2 distinct types of paratyphoid bacilli existed; these were afterward renamed as *S. paratyphi A* and *B* [7]. The name Salmonella

was proposed for the genus by Lignieres in 1900 in honor of American veterinary bacteriologist Daniel E. Salmon which become formal in 1934 [8,9]. *S. panama* was isolated by Jordan during an outbreak among American troops in Panama Canal [5]. Hormaeche and Peluffo in 1936 were reported the isolation of *S. montevideo* from a monkey in Uruguay [7]. In 1939, a Gram-negative bacterium was isolated from a lizard carcass in Arizona and tentatively identified as *S. var arizona* [10]. *S. melagridis* was described by Bruner and Edwards in 1940 [7].

### Definition of the genus Salmonella

Salmonella is straight, non-spore forming rods, medium-sized, measuring about (0.7 - 1.5 × 2.0 - 5.0 Mm), Gram-negative, non-capsulated, nonacid fast, but cells can be stained readily with common dyes, such as methylene blue or carbol-fuchsin [8,10]. They are facultatively anaerobic, can grow well under both aerobic and anaerobic conditions. They are chemoorganophilic, having both a respiratory and fermentative type of metabolism [11]. Salmonella bacteria are using peritrichous flagella for their movement (Figure 1) (except *S. pullorum* and *S. gallinarum*). Some Salmonella possess fimbriae [12].

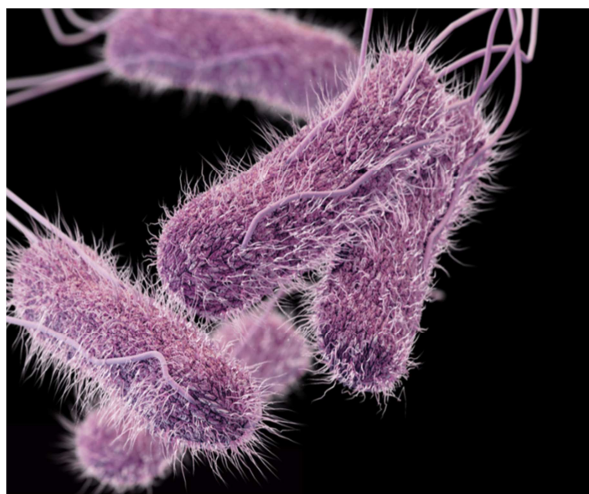


Figure 1. Salmonella bacteria with peritrichous flagella.

The optimum temperature to support their growth is 37° C, but some growth observed generally over arrange of about 5 - 47° C, and are killed at 60° C within 10 minutes [8,13]. They can grow within a pH range of approximately 4.0 - 9.0, with an optimum pH around 7.0, although some cellular characteristics such as flagella and fimbria may not be expressed under extreme pH conditions and can grow in water activity (Aw) about 0.93 - 0.98, can tolerate NaCl 8% [12,14].

Generally, they ferment carbohydrates with the production of acid with or without gas. Typically, glucose, mannitol, arabinose, maltose, dulcitol, sorbitol, mucate, trehalose, xylose, mannose, and rhamnose are fermented, but not lactose, sucrose, raffinose, salicin or adonitol [15, 16]. Salmonella decarboxylate the amino acid lysine, ornithine, and arginine, but not glutamic acid. *S. typhi* is exceptional in lacking ornithine decarboxylase, however, *S. paratyphi* is lacking lysine decarboxylase enzyme [8].

Genus Salmonella is negative for oxidase, urease, Beta-galactosidase, phenylalanine deaminase, DNAase, ONPG test, Indole, and Voges- Proskauer test [17]. But they reduce nitrates to nitrites and positive for catalase, methyl red, and produce hydrogen sulfide (H<sub>2</sub>S) in ferrous chloride- gelatin medium, except *S. paratyphi A*, *S. cholerasui*, *S. typhi suis*, and *S. sendai*. They cannot produce acetyl methyl-carbinol, and not utilize gluconate, neither liquefying gelatin [18]. Salmonella bacteria can grow on KCN and however, their utilization for malonate and citrate are variable [15].

In contrast to other enteric bacteria, the growth of Salmonella is not inhibited by certain chemicals, such as brilliant green, sodium tetrathionate, sodium deoxycholate. Therefore these compounds are used in selective media to isolate Salmonella [19]. They survive freezing in water for long periods and can survive for several months in micro-environments such as fecal materials, moist soil and stream sediments [20, 21].

## Classification of the Salmonella species

The classification of Salmonella has been controversial for many years, now its taxonomic classification depends on the Kauffman – White scheme (1934) in which typing is primarily performed using serological identification of somatic (O), flagella (H) and capsular (K) or (Vi) antigens [13,21]. According to most recent nomenclature, the genus Salmonella consists of two major species [22, 23]:

### 1- *Salmonella enterica*

Depending on the differences in biochemical reactions, antigenic nature, host adaptations, geographic distribution and DNA-relatedness, this species is further subdivided into 5 subspecies [24, 25]:

**Subspecies I:** *S. enterica subspecies enterica*: It includes the greatest majority of Salmonella serotypes contain about 1435 serovars which commonly cause disease in man and warm-blooded animals [26, 27].

**Subspecies II:** *S. enterica subspecies salamae*: Contains about 485 serovars and cause disease in cold-blooded animals, while human infections with this Salmonella serotypes have rarely been documented [25].

**Subspecies III:** Consists of 94 serovars, mainly exists in reptile and birds. Based on DNA hybridization techniques this group has been further subdivided into:

**Subspecies III a:** *S. enterica subspecies arizonae*.

**Subspecies III b:** *S. enterica subspecies diarizonae*: Consists of 321 serovars, this subdivision correlates with differences in the flagellar antigen and the speed of lactose fermentation [25, 28].

**Subspecies IV:** *S. enterica subspecies houtenae*: Consists of 96 serovars [28].

**Subspecies V:** *S. enterica subspecies indica*: Consists of 11 serovars [11, 22].

### 2- *S. bongori*

It occurs more commonly in cold-blooded animals and in the environment. Seventeen serovars have been identified and the symbol V is used to differentiate them from serovars of *S. enterica subspecies enterica* [9, 14].

Regarding the pathogenicity of Salmonella, serovars of subspecies I are highly pathogenic, whilst serovars in other subspecies and *S. bongori* are relatively less pathogenic to animals and humans [14, 29]. Based on biochemical characteristics, Salmonella is grouped into three species [25]:

1. *S. choleraesuis*: Have only one serovar, and affects swine.
2. *S. typhi*: Have only one serovar, and affects mainly human.
3. *S. enteritidis*: Contain about 2000 serovars, each of which is given a species name and includes all the serovars infecting animals and human nowadays.

Salmonella can also be divided according to their host predilection into 3 groups [12]:

1- Salmonella which primarily adapted to man: includes *S. typhi* and *S. paratyphi*.

2- Salmonella which primarily adapted to a particular animal host includes: *S. choleraesuis* and serovars of *S. enteritidis* like *S. pullorum*, *S. gallinarum*, and *S. dublin*.

3- Salmonella which has not been adapted to a particular host: includes over 2000 serovars of *S. enteritidis* that affect man and other animals. New serotypes are continually identified and added to the many serotypes already classified [29].

## Sources of Salmonella

### 1. Human

a- The intestinal tract of man (sick, convalescent and sub-clinical carriers) is the primary source of Salmonella, from which the organism shed and may enter water leading to contamination of poultry products and other foods when such water is used [14, 18].

b- Peoples on a poultry farm and animal farms can carry Salmonella mechanically on contaminated footwear, clothing and hands, thus can transmit infection from poultry to cattle, sheep, pigs, dogs, cats, horses on the same farm and vice versa [30, 31].

## **2. Animal**

Some serotypes are confined to a particular animal reservoir, but many are capable of crossing between species to cause disease in man, by direct contact and via food (zoonosis) [14]. Animal fecal materials are of greater importance than human and it may be noted that animal hides and poultry products may become contaminated from this source [21]. Contaminated feed especially those contain bone meal, fish meal and meat meal considered to be possible sources of Salmonellosis in farm animals [32,33].

Animal dyes like carmine that are used in drugs, foods, and cosmetics are also considered as a source of infection [19]. Food animals (especially poultry) which are reared intensively remain a major source of Salmonella in various countries. Although most Salmonella infections in animals are symptomless, the majority of infected animals become subclinical carriers [34]. The most common animal reservoirs are chickens, turkeys, guinea fowl, pheasants, quails, sparrows, parrots [21], ducks, geese, canaries, bull-finches, ring doves, pigeons, pea-fowls, and grouse [35]. Salmonella can also be found in fish, terrapins, frogs, house pets (turtles, dogs, and cats) [30], rodents, reptiles (Snakes and lizards are commonly infected sometimes with several serotypes) [32], shellfish from innate water [19], cattle, sheep, goats, pigs, horses [25], chinchillas, minks, chimpanzees, rabbits, and guinea pigs [36]. However, Salmonella occurs infrequently in ratites including ostrich, emu, rhea, cassowary, and kiwi, while dozens of other domestic and wild animals are also harboring these organisms [13].

## **Food**

Foods from animal origin especially from poultry is an important source of human Salmonella infections, especially those which may become contaminated during handling by an ill patient or carrier persons [37]. Raw and under cooked poultry, beef and pork meat, meat products (burger, luncheon, hash, and sausage) [38], milk (fresh, raw, fermented, unpasteurized, inadequate pasteurized, recontaminated pasteurized or improper handling) [39], dairy products (ice cream, cheese, butter, yoghurt, and custard) [40], eggs (liquid, dried, frozen, cracked, damaged or immature cuticles, dirty, soiled, under cooked, contaminated during processing, and floor eggs), egg-derived constituents (cake mixes, cookie doughs, backed goods and Alaska, eggnog, and mayonnaise) [41], dinner rolls, corn bread mixers, coconut meal, salad dressing and many other foods such as carrot which considered as one of the most commonly implicated vehicle of Salmonella infection [42,43].

## **Environment**

Salmonella that shed in feces can contaminate pasture, vegetables, soil, foods, and water. However, they can survive for 9 months or more in the environment in sites such as moist soil, water, fecal particles especially animal feces, blood-and-bone and fish meals. Contamination in the environment can serve to act as a source of infection to other animals and man [14, 21].

## **Transmission routes of Salmonella**

### **1. Human**

A- Non-Typhoidal Salmonella may be transmitted to human via contaminated food or water, animal contact (most frequently pets or farm animals) or from a contaminated environment, because it is zoonosis and has an enormous animal reservoir [44-46].

b- Typhoidal Salmonella and other enteric fevers primarily transmitted to human via person-to-person spread because these organisms lack a significant animal reservoir. Contamination with human feces is the major mode of spread, and the usual vehicle is contaminated water [19, 47].

## **2. Poultry**

### **a. Vertical transmission**

Means transmission of Salmonella from infected breeder flocks to their progeny via the egg (Ovarian transmission) and even to chicks hatched from eggs laid by infected progeny which leading to lateral spreading of the organism in hatcheries, brooding and rearing units. Salmonella on eggshell is able to penetrate the shell during incubation and causes vertical transmission of the bacteria [9].

### **b. Horizontal transmission**

Salmonella can also spread horizontally within and between flocks. It is mediated by mechanisms including direct bird-to-bird contact, ingestion of contaminated feces, litter, food-stuff, water, or personnel, equipment and environment [8]. Transmission may also occur within a flock as a result of pecking in contaminated soil or litter, cannibalism of infected birds, wounds on the skin, or through eating infected eggs.

The egg has been positively identified as the chief vehicle of transmission and an important cause of both sporadic cases and outbreaks [37]. Eggs mainly become contaminated as it passes through the cloacae, in which Salmonella in feces attach themselves to the warm-wet surface of the shell and may draw inside as it cools [8].

Biological vectors, wild birds, dogs, cats, mice, rats, rodents, roaches or their droppings, human and their feces has sometimes been identified as risk factor for commercial poultry contamination because of the dissemination and amplification of Salmonella in poultry flocks [48]. Generally, transmission is usually by the feco-oral route, but infection via mucous membrane of the conjunctivae or upper respiratory tract have rarely been reported [49].

### **Pathogenesis of Salmonella**

Pathogenesis of Salmonella is a multi-factorial phenomenon and varies with the serovars, dose, age and immune status of the host, as the infection is almost always acquired by ingestion of microorganisms, usually as contamination of food or water [17]. The disease is sometimes endemic in farms, in stables and clinics, its incidence often high, but the occurrence of clinical infection is low. Stresses resulting from transportation, overcrowding, pregnancy, parturition, water deprivation, oral antimicrobial therapy, surgery, depressed immunity systemic viral and chronic diseases may precipitate clinical disease in both animals and man [25, 50].

The virulence factors involved in Salmonella infections are numerous and complex, which include [25, 49, and 51]:

1. The ability to invade cells (contributing agents like surface polysaccharide O antigen, flagellar H antigen, and fimbriae).
2. A complete lipopolysaccharide coat.
3. The ability to replicate intracellularly.
4. Elaboration of at least three toxins:
  - a. Endotoxin: It is a lipopolysaccharide of the wall of the bacteria, which can produce fever when released into the bloodstream of the infected individual.
  - b. Enterotoxin: It reduces a secretory response by epithelial cells that result in fluid accumulation in the intestinal lumen while it is thought that this toxin may not play a major role in diarrhea seen in Salmonella food poisoning.
  - c. Cytotoxin: Cause iron chelating structural damage to intestinal epithelial cells by inhibiting protein synthesis.
5. Iron chelating proteins (siderophores and enterobactin of the bacteria) provide iron from the iron-binding proteins of the host necessary for bacterial growth.

6. Several other virulence factors are known to contribute to the establishment of disease like adhesion pilli, production of colicin and porins, ability to resist the lethal effects of serum complement and large plasmids (30- 60 mega daltons).

After ingestion of non-typhoid Salmonella, it colonize the mucosa of caecum, ileum and colon (sometimes bacilli enter through the pharyngeal mucosa, attach to the epithelial cells of the intestinal villi, induce their own intake in to the cells by process of endocytosis, pass through the cells (transcytosis) and within 24 hours are found in the lamina propria and sub mucosa [52], where they are rapidly phagocytosed by polymorphs and macrophages, if immune status of the host is diminished, it disseminate and multiply within phagocytic cells (mostly macrophages) within phagosomes [53].

Production of cytotoxic and enterotoxin by the organism likely contribute to gut damage and provocation of the inflammatory response, then the intestinal mucosa releases prostaglandin in which activates adenylate cyclase and the resulting increases in cyclic Adenosine Monophosphate (cAMP) induces secretion of water, bicarbonate, and chloride that may result in marked fluid increase in the intestinal lumen and diarrhea, can also cause ulceration and destruction of the mucosa [44]. Feces may contain blood, mucus, and neutrophils, however, intestinal infections may lead to bacteremia, or septicemia, with death or the infection, may remain localized in the internal organs [25, 54].

In contrast, *S. typhi* enter the gastrointestinal tract, invade the local lymphatic tissue, pass via the bloodstream to various organs, and multiply in the liver, gallbladder, inflammation of the intestine can be so intense manifested by lymphoid hyperplasia (as in Peyer's patches) that it causes local necrosis of the tissue, leading to ulceration and perforation of the intestine and hemorrhage [19].

## Conclusion

We are concluding that, all Salmonella species are very dangerous to both human and animals, and Salmonellosis is one of the most common zoonotic disease and public health hazard that still available in some community especially in poor countries and among non-well hygenic peoples. Poultry and their products are considered as the main cause of contaminants and spreading of the disease. Thus, it is essential that efforts be directed toward their elimination from eviscerate poultry, hence, decontamination measures should be implemented during processing through regular cleaning and sanitizing of the processing plant and its equipment to prevent contamination of the environment and poultry meat. Effort must be made to prevent the transmission of Salmonella from carriers to poultry meat. Also carriers must not be allowed to work as food handlers and should observe strict hygienic precautions. Poultry meat and giblets must be thoroughly cooked to destroy salmonella contaminants and if not eaten immediately after preparation, it must be stored at temperature which will prevent multiplication of chance survivors or cross contamination.

## Conflict of Interest

There is no conflict of interest to this review article.

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