Salmonella – description, pathogenesis, symptoms

Salmonella is a gram-negative bacillus that causes inflammation of the GI tract and in some cases, if the immune response is not sufficiently powerful and treatment is not administered, can become systemic and cause even more serious conditions throughout the body. After ingestion, these bacteria cause infection by invading the epithelial cells of the small intestine and macrophages. Though there are more than two thousand different subspecies of Salmonella, few of them are able to cause serious conditions in humans—for most, the disease resolves itself in a matter of days. Those who are most affected by Salmonella infection are infants, the elderly, and people with compromised immune systems. Some of the main conditions caused by Salmonella are gastroenteritis, enteric fever, and bacteremia, while the general symptoms of salmonella include vomiting, nausea, diarrhea, and abdominal pain. While there are typically few to no long-term effects as a result of a Salmonella infection, more serious complications may arise.

The mention of the latest salmonella outbreak is often enough to make anyone’s stomach turn—people in the US and other countries have long maintained a strong aversion to, and even anxiety towards, the very idea of salmonella entering the food supply. It is this fear that drives the government and the agricultural industry, which are also prey to the overwhelming dread of the salmonella contamination, to take extreme measures to prevent the slightest risk of salmonella contamination and that continually puts the public on edge—but despite this widespread apprehension, much of the public remains ignorant of what salmonella really is. For many, it is but an ominous name, nothing more than an impending threat held at bay on by the powers of modern technology. Little is known about salmonella’s growing resistance, what it causes, or how it actually affects the body. A bacterial disease of growing importance to the populace,
salmonella is a specialized invader of the gastrointestinal system that can cause a variety of painful conditions of varying severity.

The bacteria known as Salmonellae are gram-negative, rod-shaped bacilli that belong to the family Enterobacteriacea—they are typically anaerobic, unable to form spores, and motile, or able to move around spontaneously. An important characteristic of the Salmonella bacteria is that they are able to grow and multiply outside living host organisms, thus having greater survival chances than otherwise (Gray and Fedorka-Cray 56).

The bacteria can have a combination of three antigens: the O antigen, H antigen, and Vi antigen. The O antigen is located in the cell wall of the bacterium, and each salmonella bacillus may possess 2 or more O antigens on its surface. Also, the H antigen is a flagellar antigen that can be destroyed by heat and enables the motility of the Salmonella bacterium (Slack and Snyder 295). The last antigen is known as the Vi antigen because this antigen is related the virulence of the bacterium. As a capsular antigen, its presence enhances the virulence of the bacterium that has it—of all the subspecies of Salmonella, only two, Salmonella enterica serovar (S.) typhi and S. choleraesuis, have the Vi antigen (296).

Depending on whether the type of Salmonella has one of two antigens, the bacteria are either monophasic or diphasic, since the bacteria only produce one antigen at a time, each in a certain phase. Those that have only one set of antigens are monophasic—i.e. they have only one phase of antigen production—while those that have two sets of antigens are diphasic—i.e. they have to have two phases of production, one for each set of antigens (295).
An increasingly common characteristic of Salmonella strains that may soon develop into an issue of great importance is its growing resistance to the antibiotics that have been used to combat it. Rather than a temporary adaptation, which would not be too serious, some strains of Salmonella have developed multi-drug resistance (MDR) as a part of their fundamental genetics, thus having become permanently resistant to the drugs. MDR Salmonella is so far known to be resistant to fluoroquinolones and third-generation cephalosporins (World Health Organization 10-14).

Overall, Salmonella generally has four disease patterns: gastroenteritis, enteric fever (also known as Typhoid Fever), bacteremia with or without intestinal infection, and an asymptomatic carrier state common to humans and other animals (Gray and Fedorka-Cray 57).

There are numerous types, or serotypes, of the Salmonella bacteria, each causing different types of medical conditions (Gray and Fedorka-Cray 57). As of 2004, there had been a total of 2501 different Salmonella serotypes identified (World Health Organization 4). The bacilli vary by whether or not they have capsular antigens (Vi antigens), flagellar antigens (H antigens), or envelope antigens (O antigens), and also by their different reactions to various antisera (Gray and Fedorka-Cray 57).

Overall, each type of Salmonella is distinguished by a specific protein coating called a serovar (hence ‘serotype’), but there are two main accepted methods of classifying the different types of Salmonella among scientists. The first method dictates that the diverse species are all to be considered serovars of two main types, S. enterica and S. bongori, whereas the second method of classification has the species be designated
according to the names of the serovars, such as S. typhimurium, S. enteritidis, S. typhi, etc (MedicineNet 1-2).

Most serotypes of Salmonella are not host-specific—in other words, the bacteria infect most animals (including humans) and can be easily transferred from one to another. Only a few have a limited host-spectrum, thus able to infect only certain organisms (World Health Organization 4). S. enteritidis is one serotypes that has very little host preference—though it is found in animals, it can easily transfer to humans and can survive in most living hosts (Slack and Snyder 295). The two serotypes that most commonly infect humans in the United States have been found to be S. typhimurium and s. enteritidis (Centers for Disease Control and Prevention 2).

With respect to host-specific serotypes, S. typhi and S. paratyphi infect only humans, S. pullorum infects avian species, S. dublin infects cattle, and S. choleraesuis infects pigs. The latter three types of salmonella rarely ever infect humans, but if and when they do, they are extremely dangerous, invasive, and have high rates of mortality in humans. The most common serotypes that infect humans each year are S. enteritidis, S. typhimurium, and S. heidelberg (Gray and Fedorka-Cray 57).

Three common conditions caused by Salmonella are gastroenteritis, enteric fever, and bacteremia (MayoClinic 3-5). S. typhimurium, S. enteritidis, and S. Newport are serotypes associated with human and animal gastroenteritis, S. typhi and the paratyphoid species are associated with human enteric fever, and S. choleraesuis is associated with bacteremia in pigs (Gray and Fedorka-Cray 57). S. choleraesuis is found mostly among animals other than humans, yet it is not as deadly in animal hosts as it is in human hosts (Slack and Snyder 294; Gray and Fedorka-Cray 58).
In order to cause disease, the Salmonella bacteria, in general, are first ingested and then travel through the digestive system to reach the small intestine. Within the small intestine, they generate an inflammation of the intestinal cells that leads to the gastroenteritis that is typical of salmonella (Slack and Snyder 297).

In the case of S. typhimurium, the bacteria attack the small intestine by changing the natural architecture of the surfaces of the intestinal cells. Adhesins on the surface of each bacterium bind to receptor sites on the membrane of the intestinal cells, locally stimulating the formation of membrane ‘ruffles’. The ‘ruffling’ enables S. typhimurium to be engulfed through induced pinocytosis, a form of endocytosis, and once a single site of entrance has been established, many bacteria can enter the cell (Gray and Fedorka-Cray 59).

Certain species of salmonella are virulent enough to be able to penetrate the intestinal walls, and if they accomplish this, they can then enter the lymphatic system and cause widespread infections in many of the major organs (Slack and Snyder 300). In order to do this, the bacteria have to pass through the lacteals of the small intestine—i.e. the capillaries through which fatty acids are transported into the lymphatic system—and be taken to the lymph nodes, from which they can gain entrance into the blood stream. In this way, septicemia can occur and Salmonella is spread to secondary sites throughout the body—in addition, the bacilli will invade the mucous membranes of the GI tract, causing ulceration, gut wall perforation, hemorrhage, and/or ischemia (297).

One way in which Salmonella bacteria are transported to various tissues is by hijacking members of the body’s defense system: the macrophages. After passing through the intestinal epithelium, the bacilli encounter macrophages—however, they invade these
macrophages by using the membrane ruffling technique to stimulate phagocytosis and are able to survive within and be carried by the macrophages (Gray and Fedorka-Cray 61). The survival of the bacteria within the macrophages is probably due to the presence of the O antigen and/or the Vi antigen (Slack and Snyder 300). It is necessary for Salmonella to live within the macrophages for a number of reasons: first of all, the bacilli are able to avoid being destroyed by neutrophils, which are more effective leukocytes employed by the body. Also, staying in macrophages allows the Salmonella bacteria to enter and invade the reticuloendothelial system (REM), where they stay in the liver and spleen. Lastly, the ability to disseminate throughout the bloodstream is key to long-term colonization by the bacteria (Gray and Fedorka-Cray 61).

S. typhimurium is one serotype that well demonstrates the numerous adaptations that Salmonellae have developed in order to survive within animals. It employs two acid-tolerance response systems: in addition to passing through and surviving gastric acid, the bacilli must also be able to survive bile. In the presence of high bile concentrations, it does not try to invade cells, but once it experiences a decrease in bile concentration, it is stimulated to express genes for the invasion of epithelial cells in the distal ileum, or the latter end of the small intestine (Gray and Fedorka-Cray 62).

Salmonella bacteria produce two toxins: an endotoxin and an enterotoxin, which is a factor associated with the cell wall that can cause diarrhea in mice (Slack and Snyder 296). The production of enterotoxin is related to the incidence of gastroenteritis (299).

The survival of Salmonella within people is highly dependent on a number of factors: one such factor is the acidity of the stomach. If the salmonella is to survive the high concentrations of stomach acids, it is better if the bacilli are ingested together with
food—which would buffer the acid—or water—which would dilute the acid. Also, any surgical procedures that affect stomach acidity also make people more susceptible to Salmonella infection, as do such diseases as liver cirrhosis, lupus, sickle cell anemia, and malaria (299).

Other factors are the virulence of the bacilli, the diminished resistance of the host, and the number of bacteria ingested (299). The infectious dose of Salmonella necessary to cause illness in humans is usually quite high—in one study conducted on human volunteers, it took 10,000 or more bacilli to cause disease in 25% of the subjects. However, the dosage required was noticeably decreased for those subjects who had taken antacid prior to the ingestion of the bacilli (Gray and Fedorka-Cray 58). Treatment with antibiotics that change the natural oral flora can also reduce the number of bacilli that must be ingested (Slack and Snyder 299).

In the case of animals other than humans, higher doses are typically necessary. For example, a study showed that doses ranged from 1,000,000 to 1,000,000,000 in order to cause just clinical disease in animals—in order to cause death, even greater amounts of salmonella would need to be ingested (Gray and Fedorka-Cray 58).

So far, there is apparently no human immunity to Salmonella—it has been seen that even individuals that have high levels of O, H, and Vi antibodies still can contract Salmonella infections (Slack and Snyder 300).

Symptoms of a salmonella infections are usually apparent 24 to 36 hours after ingestion, which as been seen to be the primary time for any clinical disease to appear for both animals and people. Subsequent diarrhea last for 1 to 4 days, but the disease usually resolves within a week (Gray and Fedorka-Cray 58). Specifically, the onset of abdominal
cramps is around 12 to 72 hours after the infection, while the overall disease may last from 4 to 7 days (Centers for Disease Control and Prevention).

Gastroenteritis is the most common result of a salmonella infection: in this case, the initial symptoms may be nausea and vomiting. Afterwards, symptoms such as abdominal pain, mild to severe diarrhea, temperatures ranging from 100.4 to 102.2°F (38 to 39 °C), and bloody stools appear, though the leukocyte count in such individuals is generally found to be normal (Slack and Snyder 298; MayoClinic 3). For most cases of gastroenteritis, the incubation period can be several hours to two days (MayoClinic 3).

The symptoms for S. typhi, which is the cause of enteric fever, are a gradually increasing fever, a non-productive cough, frontal headaches, constipation, and occasionally diarrhea. In addition, raised rose spots—maculopapular lesions—appear on the trunk of the body, and often delirium also occurs. The incubation period for S. typhi is 7 to 14 days, severe illness appears after 2 to 3 weeks, and recovery may take a month of more in total (Slack and Snyder 297). Other possible symptoms include a slowing of the heartbeat (bradycardia), sleep and/or liver enlargement, a sore throat, fevers of up to 104°F (40°C), sweating, and GI inflammation (MayoClinic 4; MedicineNet 5). Paratyphoid has similar symptoms to those of typhoid, but generally these symptoms are not as severe (MedicineNet 6).

Bacteriemia mostly occurs in immunologically weak people, such as infants and the elderly, and has a number of complications including meningitis—the infection of the brain and spinal cord tissues—and sepsis—an infection within the bloodstream. Sometimes there are few symptoms that come with bacteremia, but there can be fever (MayoClinic 5).
Septicemia is characterized by chills, anorexia, weight loss, serious anemia, prolonged bacteremia, prolonged and intermittent symptoms as a result of fever, enlargement of the liver or spleen, and, in non-complicated septicemia, normal leukocyte count (Slack and Snyder 298).

In cattle, S. typhimurium causes diarrhea, fever, loss of appetite, and decreased body weight. Adults show symptoms earlier than juveniles, but more calves actually display symptoms and die from S. typhimurium (Gray and Fedorka-Cray 58). Cattle can be healthy carriers of the bacteria for up to 18 months (59).

In cats, S. typhimurium is the cause of severe gastroenteritis, the symptoms of which include bloody diarrhea, vomiting, fever, anorexia, dehydration, and depression. The disease usually lasts for 4 to 10 days, and the cats can silently shed Salmonella for about 10 days after recovery (59).

There are few long-term effects of gastroenteritis, though it can cause serious dehydration and/or electrolyte loss. Recovery, with or without treatment, generally occurs about 5 days after the onset of clinical disease (Slack and Snyder 299).

Possible complications that come as a result of an infection with S. typhi are thrombophlebitis, cerebral thrombosis, cholecystitis, encephalopathy, pneumonia, infection of bone and/or bone marrow (osteomyelitis), meningitis, and the inflammation of lining of the heart or valves (endocarditis) (298).

For those who develop severe diarrhea, there are generally no permanent effects, but it may take a number of months before bowel habits return to normal. Some people who contract some form of salmonella may develop what is called Reiter’s Syndrome, which consists of eye irritations, joint pain, and painful urination. This unpleasant
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	syndrome may last from months to even years, and in some cases it leads to chronic arthritis, which is not easily treatable (Centers for Disease Control and Prevention 5).

Despite the enormous fear surrounding salmonella, this disease has not yet reached the frightening proportions that many would be lead to believe—for the time being, it is still largely under control as a result of sanitary preparation and growing of food and effective inspection systems. Nevertheless, we are by no means clear of Salmonella—the bacteria are gradually gaining resistance to antibiotics, and as time passes, they shall increasingly plague human society. It has not been vanquished, and as the issue of salmonella outbreaks becomes more of an issue, it is not preferable but necessary that this bacterium be understood. On the whole, salmonella is becoming more adapted to surviving in the human body and merits the attention of the public as a contemporary issue in the medical field.
Works Cited


