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Department of Biology

Lectures of Pathogenic Bacteria

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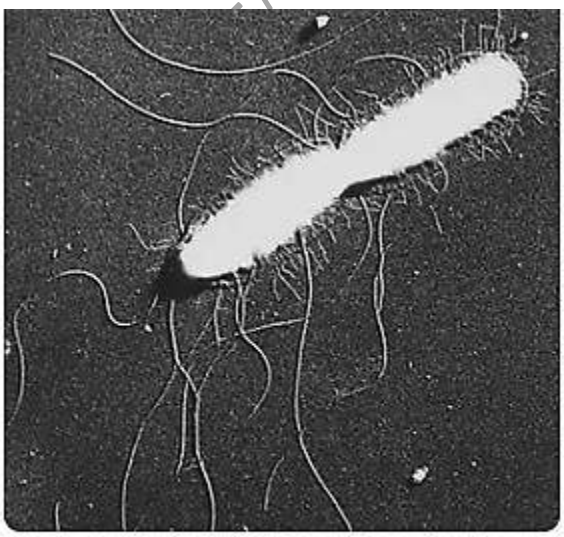
Salmonella

is a genus of rod-shaped, (bacillus) gram-negative bacteria of the family Enterobacteriaceae. The two known species of Salmonella are Salmonella enterica and Salmonella bongori. S. enterica is the type species and is further divided into six subspecies that include over 2,650 serotypes. Salmonella was named after Daniel Elmer Salmon (1850–1914), an American veterinary surgeon.

Salmonella species are non-spore-forming, predominantly motile enterobacteria with cell diameters between about 0.7 and 1.5 µm, lengths from 2 to 5 µm, and peritrichous flagella (all around the cell body, allowing them to move). They are chemotrophs, obtaining their energy from oxidation and reduction reactions, using organic sources. They are also facultative anaerobes, capable of generating adenosine triphosphate with oxygen ("aerobically") when it is available, or using other electron acceptors or fermentation ("anaerobically") when oxygen is not available.



Salmonella Electron micrograph of a metal-shadowed whole cell of *Salmonella typhi*, showing flagella and shorter straight.....(more)

Salmonella species are intracellular pathogens of which certain serotypes cause illness such as salmonellosis. Most infections are due to the ingestion of food contaminated by feces. Typhoidal Salmonella serotypes can only be transferred between humans and can cause foodborne illness as well as typhoid and paratyphoid fever. Typhoid fever is caused by typhoidal Salmonella invading the bloodstream, as well as spreading throughout the body, invading organs, and secreting endotoxins (the septic form). This can lead to life-threatening hypovolemic shock and septic shock, and requires intensive care, including antibiotics.

Nontyphoidal Salmonella serotypes are zoonotic and can be transferred from animals and between humans. They usually invade only the gastrointestinal tract and cause salmonellosis, the symptoms of which can be resolved without antibiotics. However, in sub-Saharan Africa, nontyphoidal Salmonella can be invasive and cause paratyphoid fever, which requires immediate antibiotic treatment.

Taxonomy

The genus Salmonella is part of the family of Enterobacteriaceae. Its taxonomy has been revised and has the potential to confuse. The genus comprises two species, S. bongori and S. enterica, the latter of which is divided into six subspecies: S. e. enterica, S. e. salamae, S. e. arizonae, S. e. diarizonae, S. e. houtenae, and S. e. indica. The taxonomic group contains more than 2500 serotypes (also serovars) defined on the basis of the somatic O (lipopolysaccharide) and flagellar H antigens (the Kauffman–White classification). The full name of a serotype is given as, for example, Salmonella enterica subsp. enterica serotype Typhimurium, but can be abbreviated to Salmonella Typhimurium. Further differentiation of strains to assist clinical and epidemiological investigation may be achieved by antibiotic sensitivity testing and by other molecular biology techniques such as pulsed-field gel electrophoresis, multilocus sequence typing, and, increasingly, whole genome sequencing. Historically, salmonellae have been clinically categorized as invasive (typhoidal) or

non-invasive (nontyphoidal salmonellae) based on host preference and disease manifestations in humans.

Colonial characteristics:

On blood agar: Salmonellae are grey/white, non-hemolytic, non-swarming colonies that range from 2 to 3 mm in diameter after 24 hours of incubation. On MacConkey: colourless colonies between 2 to 3 mm in diameter after 24 hours of incubation. On XLD: red-pink colonies from 2-3 mm in diameter at 24 hours, usually with black centres

Salmonella on XLD.

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Serotyping

Serotyping is done by mixing cells with antibodies for a particular antigen. It can give some idea about risk.Serotyping can assist in identifying the source of contamination by matching serotypes in people with serotypes in the suspected source of infection.Appropriate prophylactic treatment can be identified from the known antibiotic resistance of the serotype.

Newer methods of "serotyping" include xMAP and real-time PCR, two methods based on DNA sequences instead of antibody reactions. These methods can be potentially faster, thanks to advances in sequencing technology. These "molecular serotyping" systems actually perform genotyping of the genes that determine surface antigens.

Species of Salmonella

Salmonella typhi causes typhoid fever; paratyphoid fever is caused by S. paratyphi, S. schottmuelleri, and S. hirschfeldii, which are considered variants of S. enteritidis.

S. choleraesuis, from swine, can cause severe blood poisoning in humans; *S. gallinarum* causes fowl typhoid; and *S. arizonae* has been isolated from reptiles in the southwestern United States.

Refrigeration prevents bacterial reproduction but does not kill these microorganisms. As a result, many Salmonella can develop in foods, which, when ingested, can result in gastroenteritis.

Pathogenicity

Salmonella species are facultative intracellular pathogens.Salmonella can invade different cell types, including epithelial cells, M cells, macrophages, and dendritic cells. As facultative anaerobic organism, Salmonella uses oxygen to make adenosine triphosphate (ATP) in aerobic environments (i.e., when oxygen is

available). However, in anaerobic environments (i.e., when oxygen is not available) Salmonella produces ATP by fermentation — that is, by substituting, instead of oxygen, at least one of four electron acceptors at the end of the electron transport chain: sulfate, nitrate, sulfur, or fumarate (all of which are less efficient than oxygen).

Most infections are due to ingestion of food contaminated by animal feces, or by human feces (for example, from the hands of a food-service worker at a commercial eatery). Salmonella serotypes can be divided into two main groups— typhoidal and nontyphoidal. Typhoidal serotypes include Salmonella Typhi and Salmonella Paratyphi A, which are adapted to humans and do not occur in other animals. Nontyphoidal serotypes are more common, and usually cause self-limiting gastrointestinal disease. They can infect a range of animals, and are zoonotic, meaning they can be transferred between humans and other animals.

Salmonella pathogenicity and host interaction has been studied extensively since the 2010s. Most of the important virulent genes of Salmonella are encoded in five pathogenicity islands — the so-called Salmonella pathogenicity islands (SPIs). These are chromosomal encoded and make a significant contribution to bacterial-host interaction. More traits, like plasmids, flagella or biofilm-related proteins, can contribute in the infection. SPIs are regulated by complex and fine-tuned regulatory networks that allow the gene expression only in the presence of the right environmental stresses.

Typhoid Fever(Enteric Fever)

Typhoid fever (enteric fever) is a systemic disease caused by the gram-negative bacterium *Salmonella enterica* serotype Typhi (*S.* Typhi). Symptoms are high fever, prostration, abdominal pain, and a rose-colored rash. Diagnosis is clinical and confirmed by culture. Treatment is with ceftriaxone, a fluoroquinolone, or azithromycin.

Transmission

Humans are the only natural host and reservoir. Typhoid bacilli are shed in stool of asymptomatic carriers or in stool or urine of people with active disease. The

infection is transmitted by ingestion of food or water contaminated with feces. Inadequate hygiene after defecation may spread S. Typhi to community food or water supplies. In endemic areas where sanitary measures are generally inadequate, S. Typhi is transmitted more frequently by water than by food. In areas where sanitary measures are generally adequate, transmission is chiefly by food that has been contaminated during preparation by healthy carriers. Flies may spread the organism from feces to food.

Occasional transmission by direct contact (fecal-oral route) may occur in children during play and in adults during sexual practices. Rarely, hospital personnel who have not taken adequate enteric precautions have acquired the disease when changing soiled sheets and blankets.

Symptoms and Signs of Typhoid Fever

For typhoid fever, the incubation period (usually 8 to 14 days) is inversely related to the number of organisms ingested. Onset is usually gradual, with fever, headache, arthralgia, pharyngitis, constipation, anorexia, and abdominal pain and tenderness. Less common symptoms include dysuria, nonproductive cough, and epistaxis.

Without treatment, the temperature rises in steps over 2 to 3 days, remains elevated (usually 39.4 to 40° C) for another 10 to 14 days, begins to fall gradually at the end of the third week, and reaches normal levels during the fourth week. Prolonged fever is often accompanied by relative bradycardia and prostration. Central nervous system symptoms such as delirium, stupor, or coma occur in severe cases. In uncomplicated cases, 5 to 30% of patients may have discrete, pink, blanching lesions (rose spots) in crops on the chest and abdomen during the second week and resolve in 2 to 5 days.

Splenomegaly, leukopenia, anemia, liver function abnormalities, proteinuria, and a mild consumption coagulopathy are common. Acute cholecystitis and hepatitis may occur.

Diagnosis of Typhoid Fever

Cultures

Typhoid fever should be considered in patients with fever in or those returning from endemic areas, particularly if fever has lasted more than 3 days or there is diarrhea, abdominal pain, or constipation.

Cultures of blood, stool, and urine should be obtained. Because drug resistance is common, standard susceptibility testing is essential. The nalidixic acid susceptibility screening test is not recommended because it does not reliably predict susceptibility to ciprofloxacin. Blood cultures are usually positive only during the first 2 weeks of illness and are not highly sensitive, but stool cultures are usually positive during the third to fifth weeks. If these cultures are negative and typhoid fever is strongly suspected, culture from a bone marrow biopsy specimen (which is highly sensitive) may reveal the organism.

Serological test

Typhoid bacilli contain antigens O and H that stimulate the host to form corresponding antibodies. A 4-fold rise in O and H antibody titers in paired specimens obtained 2 weeks apart suggests S. Typhi infection (Widal test). However, this test is only moderately (70%) sensitive and lacks specificity ; many

nontyphoidal Salmonella strains cross-react, and liver cirrhosis causes false-positives.

Prevention of Typhoid Fever

1-Drinking water should be purified, and sewage should be disposed of effectively.

2-Chronic carriers should avoid handling food and should not provide care for patients or young children until they are proved free of the organism; adequate patient isolation precautions should be implemented. Special attention to enteric precautions is important.

3-Travelers in endemic areas should avoid ingesting raw leafy vegetables, other foods stored or served at room temperature, and untreated water (including ice cubes). Unless water is known to be safe, it should be boiled or chlorinated before drinking.

Vaccination

A live-attenuated oral typhoid vaccine is available (Ty21a strain); it is used for travelers to endemic regions and is about 40 to 80% effective . It may also be considered for household or other close contacts of carriers.

The Ty21a typhoid vaccine is given orally every other day for a total of 4 doses, which should be completed ≥ 1 week before travel. A booster is required after 5 years for people who remain at risk. The vaccine should be delayed for > 72 hours after patients have taken any antibiotic and should not be used with the antimalarial mefloquine. Because the vaccine contains living S. Typhi organisms, it is contraindicated in patients who are immunosuppressed. In the United States, the Ty21a vaccine is not used in children < 6 years.

An alternative is the single-dose, IM Vi capsular polysaccharide typhoid vaccine (ViCPS), given ≥ 2 weeks before travel. This vaccine is 50 to 80% effective and is well-tolerated (1), but it is not used in children < 2 years. For people who remain at risk, a booster is required after 2 years.