Salmonella Infections

Salmonellosis includes several syndromes (gastroenteritis, enteric fevers, septicemia, focal infections, and an asymptomatic carrier state) . Particular serovars show a strong propensity to produce a particular syndrome (*S typhi*, *S paratyphi-A*, and *S schottmuelleri* produce enteric fever; *S choleraesuis* produces septicemia or focal infections; *S typhimurium* and *S enteritidis* produce gastroenteritis); however, on occasion, any serotype can produce any of the syndromes. In general, more serious infections occur in infants, in adults over the age of 50, and in subjects with debilitating illnesses.

Most non-typhoidal salmonellae enter the body when contaminated food is ingested . Person-to-person spread of salmonellae also occurs. To be fully pathogenic, salmonellae must possess a variety of attributes called virulence factors. These include (1) the ability to invade cells, (2) a complete lipopolysaccharide coat, (3) the ability to replicate intracellularly, and (4) possibly the elaboration of toxin(s). After ingestion, the organisms colonize the ileum and colon, invade the intestinal epithelium, and proliferate within the epithelium and lymphoid follicles. The mechanism by which salmonellae invade the epithelium is partially understood and involves an initial binding to specific receptors on the epithelial cell surface followed by invasion. Invasion occurs by the organism inducing the enterocyte membrane to undergo “ruffling” and thereby to stimulate pinocytosis of the organisms. Invasion is dependent on rearrangement of the cell cytoskeleton and probably involves increases in cellular inositol phosphate and calcium. Attachment and invasion are under distinct genetic control and involve multiple genes in both chromosomes and plasmids.

After invading the epithelium, the organisms multiply intracellularly and then spread to mesenteric lymph nodes and throughout the body via the systemic

circulation; they are taken up by the reticuloendothelial cells. The reticuloendothelial system confines and controls spread of the organism. However, depending on the serotype and the effectiveness of the host defenses against that serotype, some organisms may infect the liver, spleen, gallbladder, bones, meninges, and other organs. Fortunately, most serovars are killed promptly in extraintestinal sites, and the most common human *Salmonella* infection, gastroenteritis, remains confined to the intestine.

After invading the intestine, most salmonellae induce an acute inflammatory response, which can cause ulceration. They may elaborate cytotoxins that inhibit protein synthesis. Whether these cytotoxins contribute to the inflammatory response or to ulceration is not known. However, invasion of the mucosa causes the epithelial cells to synthesize and release various proinflammatory cytokines, including: IL-1, IL-6, IL-8, TNF-2, IFN-U, MCP-1, and GM-CSF. These evoke an acute inflammatory response and may also be responsible for damage to the intestine. Because of the intestinal inflammatory reaction, symptoms of inflammation such as fever, chills, abdominal pain, leukocytosis, and diarrhea are common. The stools may contain polymorphonuclear leukocytes, blood, and mucus.

Much is now known about the mechanisms of *Salmonella* gastroenteritis and diarrhea. Only strains that penetrate the intestinal mucosa are associated with the appearance of an acute inflammatory reaction and diarrhea,the diarrhea is due to secretion of fluid and electrolytes by the small and large intestines. The mechanisms of secretion are unclear, but the secretion is not merely a manifestation of tissue destruction and ulceration. *Salmonella* penetrate the intestinal epithelial cells but, unlike *Shigella* and invasive *E. coli*, do not escape the phagosome. Thus, the extent of intercellular spread and ulceration of the epithelium is minimal. *Salmonella* escape from the basal side of epithelial cells into the lamina propria. Systemic

spread of the organisms can occur, giving rise to enteric fever. Invasion of the intestinal mucosa is followed by activation of mucosal adenylate cyclase; the resultant increase in cyclic AMP induces secretion. The mechanism by which adenylate cyclase is stimulated is not understood; it may involve local production of prostaglandins or other components of the inflammatory reaction. In addition, *Salmonella* strains elaborate one or more enterotoxin-like substances which may stimulate intestinal secretion. However, the precise role of these toxins in the pathogenesis of *Salmonella* enterocolitis and diarrhea has not been established.

The pathogenesis of salmonellosis is complex. Several virulence genes are responsible for the severity of disease observed with certain species. Nontyphoidal isolates are rarely invasive because most do not extend past the lamina propria or the intestinal lymphatic system. However, interactions with host cells in the intestines may lead to a release of proinflammatory cytokines that result in the recruitment of neutrophils to the area, resulting in gastroenteritis. Some genes appear to play a role in the survival of bacteria within the liver and spleen and promote the replication within macrophages. Salmonella Typhi is known to adhere to epithelial cells over the lymphatic Peyer patches, allowing for penetration through the intestinal mucosa. Engulfment by macrophages and translocation into draining lymph nodes results in bacteremia and subsequent dissemination. The organism survives within the host cells in a Salmonella-containing vacuole, assuring its ability to replicate, survive, and invade and resulting in the multiplication and survival of bacteria within the liver, spleen, and bone marrow. After an incubation period of 7 to 14 days, bacteremia occurs and symptoms emerge. Salmonella Typhi can be found in the gallstones of individuals who live in endemic regions. Its presence correlates with fecal shedding, and these people are known to infect others.