

# EPIDEMIOLOGIC, PATHOGENIC AND EVOLUTIVE ASPECTS IN SHIGELLA AND SALMONELLA ENTEROCOLITIS

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**Abstract:** *Shigella* is a nonmotile, gram-negative, aerobic, bacterium. There are four species of *Shigella* which determine shigellosis: *dysenteriae*, *flexneri*, *sonnei* and *boydii*. *Shigella* infection has a global distribution. *Shigella* produces shiga toxin with neurotoxic, enterotoxic and cytotoxic effects. It can also produce enterotoxins, determining various clinical manifestations, from acute, non – bloody diarrhoea to bacillary dysentery. In evolution, complications, such as: seizures, arthritis or hemolytic – uremic syndrome may occur. *Salmonella* is a gram-negative, nonmotile, aerobic bacillus belonging to the *Enterobacteriaceae* family. There are two *Salmonella* species: *enterica* and *bongori*. It is one of the most important pathogens involved in bacterial acute diarrhoea in children. *Salmonella* can invade the enterocytes. In evolution, complications like: severe acute dehydration or extradigestive infections, such as: arthritis and meningitis may also occur.

**Keywords:** *Shigella*, *Salmonella*, diarrhoea, complications, child.

**Rezumat:** *Shigella* este un bacil aerob, gram negativ, imobil. Patru specii de *Shigella* determină shigeloză: *dysenteriae*, *flexneri*, *sonnei* și *boydii*. Infecția cu *Shigella* are o distribuție globală. Germenele produce toxina shiga cu efecte neurotoxice, citotoxice și enterotoxice. Poate produce și enterotoxină, așa încât determină un spectru variat de manifestări clinice, mergând de la dizenterie până la diaree apoasă. Ca și complicații pot fi menționate: convulsiile (mai ales la copiii mici), artrită și sindrom hemolitic-uremic. *Salmonella* este un bacil mobil, aerob, gram negativ din familia *Enterobacteriaceae*. Sunt recunoscute două specii distincte de *Salmonella*: *enterica* și *bongori*. Reprezintă unul dintre cei mai frecvenți germeni cauzali ai diareei bacteriene la copil. Poate invadea enterocitele și colonocitele, prin aderență specifică la celulele M din plăcile Peyer. Produce variate manifestări clinice, mergând de la diaree sanguinolentă până la diaree apoasă. Ca și complicații poate determina bacteriemie sau infecții localizate extradigestiv (osteomielită, meningită, artrită supurată) și sindrom acut de deshidratare.

**Cuvinte cheie:** *Shigella*, *Salmonella*, diaree, complicații, copil.

## **Shigella enterocolitis.**

*Shigella* is a gram-negative, nonmotile, aerobic, lactosonegative bacillus, closely related to *Escherichia* genus. Four species of *Shigella* determine shigellosis: *dysenteriae* (serogrup A), *flexneri* (serogrup B), *sonnei* (serogrup D) and *boydii* (serogrup C). *Shigella dysenteriae* presents 13 serotypes, *flexneri* 6 serotypes and 15 subserotypes, *boydii* 18 serotypes, and *sonnei* one serotype. (2)

**Epidemiology.** *Shigella* infection has a global distribution and it most frequently occurs in the warm season of the temperate climate and in the rainy season of the tropical climate. It equally affects both genders and although it may occur at any age, it is most frequently encountered in children between 2 and 3 years old. The infection in the first months of life is rare, due to the absence of the receptors for shiga toxin at this early age. The asymptomatic infection occurs commonly in adults and in the children within the endemic area. Certain studies treat *Shigella* as the second cause of bacterial diarrhoea in the children between 6 months and 10 years old, in terms of frequency and, as the first cause of enterocolitis outbreaks in the care centres (1).

In most of the cases, *Shigella* is transmitted faecally- orally, the interpersonal contact being the most frequent transmission way. It may also be transmitted by food and contaminated water within the area with precarious hygienic sanitary standard. In the industrialized countries, *S. sonnei* is the most frequent cause of bacillary dysentery and, in the developing countries, the most frequent cause of dysentery is represented by *S. flexneri*. *S. dysenteriae* serotype 1 tends to occur during the large epidemics and is being endemic in Asia and Africa. The incidence of 10-20% of the cases of diarrhoea is similar in the statistics of different countries (3).

**Pathogeny.** *Shigella* is extremely virulent, a number of 10 microorganismes is sufficient in order to start the disease in adults. The infected patients may excrete  $10^5$ - $10^8$  germs/g of faeces. The main virulence factor of *Shigella* is the capacity of invading the intestinal mucosa. This characteristic is encoded by a plasmid with large molecular weight (120-140 megadaltons), necessary for the synthesis of certain bacterial polypeptides involved in the invasion of the host cell. Besides the virulence factors encoded by plasmids, there are virulence factors

chromosomally coded (lyposaccharides for all types of *Shigella*; the synthesis of shiga toxin by *Shigella dysenteriae* type 1, especially). The stage of aqueous diarrhoea within dysenteriae is caused by the production of enterotoxins. (6).

Initially, the bacterium enters into contact with the epithelium of the intestinal mucosa, it induces changes of cytoskeleton and subsequently, it is phagocytated. The enzymes secretion follows, which damages the lysosomal membrane, the germ being released in the cytoplasm of the host cell. The bacterium moves rapidly intracytoplasmically, in association with a "comet tail" made up by actin filaments of the host cell. When it reaches the *Shigella* cell edge, it is capable to enter the neighbouring cell, this way the infection spreads from cell to cell (6).

Shiga toxin is produced by all types of *Shigella*, and in the largest quantities, by *Shigella dysenteriae* serotype 1. It has neurotoxic, cytotoxic and enterotoxic effects. It is made up by an active subunit A, by 32 kilodaltons, surrounded by 5 B subunits, each having the molecular weight of 77 kilodaltons. The B subunits serve a link between the toxin and the specific enterocytary receptors, the toxin is subsequently introduced intracellularly by endocytosis.

Intracellularly, the A subunit is shorten by proteolysis, being capable to link the 60S ribosomes, or to determine the inhibition of the proteic synthesis and finally, the death of the host cell. These processes represent the cytotoxic effect of this toxin, manifested mainly at the level of the distal colon. The enterotoxic effects appear mainly in ileum, contributing to the occurrence of the initial stage of aqueous diarrhoea within dysentery (1).

**Clinical evolution.** The patients infected with *Shingella* may present an easy form, self-limited by aqueous diarrhoea. The classic clinical picture of this infection is represented by the bacillary dysentery (3). After an incubation period of about 12 hours, the disease starts with fever, alteration of the health general state, aqueous diarrhoea and colic, abdominal pain. From the second day of disease, the blood and the mucus may be observed in the stool, and the tenesmus becomes an important symptom of the affection. In this stage of disease, in more than 50% of the patients, the volume of the stools is reduced, these become mucosanguinolent. Bacteriemia occurs rarely and from the point of view of the complications, the following may be observed: convulsions (especially in the little children), arthritis, purulent keratitis and uremic-hemolytic syndrome.

The non-suppurative arthritis is the most common extradigestive complication of dysentery. The patients carrying the histocompatibility antigen HLA-B27 are especially predisposed to this complication. The convulsions occur at the beginning of dysentery were attributed to the neurotoxic effects of Shinga toxic; today, they are considered as febrile convulsions, without having a direct relation with the Shiga toxin effects (6).

### **Salmonella Enterocolitis.**

*Salmonella* represents one of the most frequent causal germs of the bacterial diarrhoea in children, both in the Unites States and in the developing countries. The incidence of salmonella enterocolitis is increasing (3, 6) *Salmonella* is a gram-negative motile, aerobic bacillus, belonging to the Enterobacteriaceae family. Two distinct species of *Salmonella* are known: enterica and *S. bongori*. *Salmonella enterica* is further divided into 1700 serotypes. The other species has only one serotype (5). The infection with *Salmonella* may bring about more clinic syndromes: acute enterocolitis, extraintestinal infections, bacteriemia, asymptomatic carrier status and enteric fever (including the typhoid fever). Each of these entities may be determined by any of the known species of *Salmonella*. (3, 6).

**Epidemiology.** *Salmonella* causes almost 1-5 million of cases of acute enterocolitis in children, in the Unites States. (4). The maximum risk of disease is presented in infants and the incidence of the symptomatic infection is reduced in the children over 6 years old. Netific *Salmonella* is transmitted through water and contaminated food (meat, eggs, dairy products, most frequently). Eggs are frequently contaminated with *Salmonella*, the number of bacteria being most of the times inferior to the necessary one, in order to produce the infection. Food may become contaminated due to those who manipulate it and the farm animals are also frequently contaminated, usually being asymptomatic. *Salmonella* tends to colonize the domestic animals, and the infection by interpersonal contact may occur especially in the cases, which intersect the infants. (3)

**Pathogeny.** An inoculum of  $10^3$  microorganisms is sufficient in order to produce the affection. The patients with altered defence mechanisms are predisposed to develop symptomatic forms of the infection. This was proved in the patients with aclorhidria or with reduced level of gastric secretion. The patients suffering from lymphoproliferative diseases and hemolytic affections (especially, sicklemlia) are more likely to present sever manifestations of the disease and complications of the infection with *Salmonella*. This increased susceptibility for the severe forms of disease in the patients of the above-mentioned categories are explained by functional defects of macrophages and by the defective activity of the complement. After having surpassed the defence mechanisms of the host, *Salmonella* produces enterocolitis through a process, which affects the terminal ileum and the proximal portion of the colon. After the multiplication within the intestinal lumen, the bacterium will invade the enterocytes and colonocytes, through an adherence specific to the M cells from the Peyer plates and then, through internalization by mediate receptor endocytosis. The genes governing the invasion of the host cell are closely related to those of *Shigella*. It is followed by the intracellular proliferation of the germs and by the invasion of lamina propria. The majority of the infections with *Salmonella* do not end with the penetration of lamina propria and with its dissemination in the regional

lymphatic ganglions and the systemic circulation, determining the appearance of the bacteriemia. This process occurs mainly in the case of *S. serotype* Dublin and *Choleraesuis*. The majority of *Salmonella* serotypes are capable of synthesising a thermolabile enterotoxins similar to the choleric one, which, together with prostaglandins locally produced in large quantity, due to the mucosa inflammation, determine the water efflux and electrolytes within the intestinal lumen. (1, 3, 6)

**Clinic evolution.** The acute enterocolitis is the most frequent manifestation of the infection with *Salmonella*. After an incubation period of 12-72 hours, the disease starts with nausea, vomiting, colic, abdominal pain, initially at the level of navel, then at the level of the right hypocondrium, followed by aqueous diarrhoea in an easy form, then more severe, sometimes with diarrhoea with mucus and blood. Moderate fever (38,5 °C) occurs in almost 70% of the patients. Some of the children may present severe forms of the disease, with high fever, convulsions, meningism and abdominal distension. The manifestations could be observed in the majority of patients within 2-7 days. The severe forms of aqueous diarrhoea may become complicated, turning into acute syndromes of dehydration. If *Salmonella* enters the sanguine torrent, it may cause bacteriemia or extradigestive infections (osteomyelitis, meningitis, suppurate arthritis). Arthritis occurs more frequently in the children with the histocompatibility antigen HLA-B27. Meningitis occurs 100 times more frequently than bacteriemia, especially in infants. Regarding the patients infected with HIV, the salmonella meningitis causes a rate of mortality of more than 50% (1). There is a series of conditions which increase the risk of bacteriemia with *Salmonella*, during the episodes of acute enterocolitis, such as: newborn babies and infants under 3 months old, immunodeficiencies, chronic granulomatous diseases, AIDS, malign affections, especially leukaemia and lymphomas, the therapy with immunosuppressors and corticoids, hemolytic anemia, malaria, collagen vascular diseases, intestinal inflammatory diseases, gastrectomy and gastroenterostomy and the use of anti-acid drugs, alteration of the intestinal motility, schizostomiasis, malnutrition. (3, 6).

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