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## 2 Shigellosis

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Shigellosis is an infectious disease caused by Shigellae, which are bacilli with capacity to invade the mucosa of the colon and less frequently the ileum. The disease occurs sporadically and in epidemics with mild to severe clinical manifestations. The principal symptoms in severe cases (bacillary dysentery) are abdominal cramps, fever, tenesmus, and diarrhoea. Toxicosis and dehydration are common in young children. Asymptomatic infections (healthy carriers) are rare; convalescent carriers are common, particularly in children with growth retardation or protein-energy malnutrition (Mata et al., 1966).

### Pathogenicity

All shigellae are capable of inducing diarrhoea but certain *Sh. flexneri* and *Sh. dysenteriae* are more pathogenic. Mechanisms responsible for the disease are not clear. The endotoxin of these bacteria elicits a physiological response in man and animals indistinguishable from that evoked by other Gram-negative bacteria. When inoculated into modified animals, the resulting disease resembles the dysentery of man. Labrec et al. (1964) showed that virulent *Shigella* strains penetrate the lamina propria with production of diarrhoea or dysentery; this does not occur with the nonpathogenic variants. Multiplication of the organisms in the lamina propria is associated with synthesis of significant amounts of endotoxin.

*Shigella* dysentery primarily is a disease of humans, but dogs and primates can be attacked.

### Geographical distribution

Shigellae have a world-wide occurrence. There have been no major changes reported in distribution of strains since the report of Young (1947) who emphasized localization of *Sh. flexneri* 1 and 4 in the USA and India, while serotypes 2 and 3 are more cosmopolitan. *Sh. sonnei* is most frequent in North America and Eastern Europe. Felsenfeld (1965) suggests that this distribution of *Sh. sonnei* may be due to the greater resistance of this species to antibacterial treatment. In recent times the Shiga bacillus (*Sh. dysenteriae* 1) has emerged again as an important serotype, predominating over other serotypes during large outbreaks in Central America (Gangarosa et al., 1971; Mata et al., 1970).

Environmental factors largely determine distribution of these organisms. Deficient sanitary conditions, poor housing and overcrowding, together with improper disposal of wastes, are contributing factors. Lack of a sufficient and safe water supply appears to be the most important determinant in rural areas.

### Pathology

The pathological features of shigellosis vary considerably, depending upon the age of the child, nutritional status, intercurrent infection, duration of the disease, and whether the child is breast-fed or receives artificial feeding. In severely ill infants dying of dehydration and shock, lesions may bear little correlation with severity of clinical manifestations. Stowens (1957) seldom found ulceration in infant shigellosis, and in fulminating cases with death occurring within 48-72 hours, usually there was little more than diffuse hyperaemia of the mucosa, with or without oedema. However, a WHO Expert Committee (1964) described mucosal ulceration as common. Lesions predominate in the proximal and distal colon, but

they may be found in the terminal ileum and in the large intestine as well. The evolution lesions includes an increase in inflammation, oedema of the submucosa and muscularis, and cellular infiltration with polymorphonuclear leucocytes. At this stage considerable haemorrhage may occur. In cases of long duration, hypertrophy of the lymphoid tissue is a constant finding. Development of pseudo-diphtheritic membranes or passage of tubular casts have occasionally been observed in chronic or relapsing cases. Degenerative or toxic changes have been observed in the liver, spleen, and kidneys. The fatty degeneration described in the liver in chronic cases may be due to starvation. Pathologic changes in Shiga dysentery tend to be more pronounced and varied. The advanced colonic lesion shows varying degrees of coagulation necrosis of the mucosa and sometimes the submucosa. Toxic megacolon is found in 5% of autopsy cases. Intravascular coagulation phenomena are found in 24% of cases in a variety of organs, particularly in kidneys, adrenals, pancreas, and liver (Mata and Castro, 1974).

### Clinical manifestations

There is a great variation in the clinical picture of shigellosis. Symptoms may be virtually absent and recognizable only by isolation of the organism; fever, profuse diarrhoea, vomiting, and inflammation characterize the dysentery form; the latter often leads to death. Studies in Egyptian and Guatemalan villages revealed that shigellae are highly endemic (Higgins et al., 1955; Gordon et al., 1962), although they could not be recovered from a high percentage of children with diarrhoeal symptoms. The attack rate in infants less than 6 months of age was lower than for older infants and young children (Mata et al. 1969). Breast feeding is customary in such regions and the nursing infant has good nutrition and a greater resistance to intestinal infection (Mata and Urrutia, 1971). He is endowed with passive maternal resistance and possesses a series of immune mechanisms derived from breast milk (Wyatt et al., 1972; Hanson et al., 1975). With the introduction of supplemental foods prepared under unhygienic conditions, the risk of exposure increases as the nutritional status deteriorates (Gordon et al., 1963). The course of *Shigella* infection in kwashiorkor and other nutritional deficiencies, or with concurrent diseases, is usually more severe. Heavy infection with parasites, and multiple and mixed infections with *Salmonella*, enteropathogenic *E. coli*, and viruses are more common in the tropics (Young et al., 1962; Mata et al., 1967). In such cases it is difficult to assess the contribution of the shigellae to the symptomatology observed.

The average incubation period is 2 to 5 days, with extremes of 1 to 7 days. Some believe that children seldom experience a prodromal phase with marked and sudden diarrhoea and vomiting. Several authors (Hardy, 1954) showed that slight fever, abdominal discomfort, and nausea may precede diarrhoeal symptoms by 12 hours or more. Convulsions or central nervous manifestations may announce an attack in the very young.

Dysentery is a syndrome of watery and foul diarrhoea evolving rapidly into an acute, painful, and sometimes fulminating disease with passage of many stools of small size containing blood, mucus, and pus. Cramps and tenesmus are characteristic and may or may not be accompanied by prostration. Vomiting is observed in as many as a third of the cases. Rectal prolapse is observed sometimes. Fever is often found with general toxic manifestations. Attacks are self-limited and of short evolution.

Acute dysentery particularly due to the Shiga bacillus is usually preceded by vomiting, abdominal colic, and an increasingly frequent urge to defecate. Stools of decreasing amounts are passed more and more often until bloody mucus and pus may be all that is evacuated. It is in this stage of the disease in children that dehydration, loss of electrolytes, and toxicosis assume great importance. Fever and prostration are almost always

present. Cramps, tenesmus, and straining also usually occur. The duration of symptoms is dependent upon the severity of the disease and the success of therapy. In a small percentage of cases chronic recurrent diarrhoea with bouts of acute dysentery alternates with periods of apparent health. Such a prolonged illness in children who continue to excrete Shiga bacilli in their stools is accompanied by chronic malnutrition (Mata *et al.*, 1966).

Fulminating dysentery develops as a severe diarrhoea accompanied by vomiting and a sharp rise in temperature. The infant becomes very dehydrated and goes into shock. Convulsions may be frequent in some areas, but in Central America these are not an important feature of the disease. The course is serious and response to therapy may be poor. Fulminating dysentery is not frequent, except under special conditions, for instance, during the regional epidemic of Shiga dysentery in 1969-72 (Mata and Castro, 1974).

Choleraiform dysentery is also a fulminating form which is characterized by profuse diarrhoea, subnormal temperature, and exhaustion and collapse. The outcome of this form is almost always fatal.

In chronic bacillary dysentery, symptoms may subside but do not disappear completely for a considerable period during which an attack may recur. In other cases remissions of symptoms are interspersed with repeated attacks. Extensive ulcer formation may result in scars and strictures. However, intestinal perforation is rare. There is considerable interference with digestion and absorption, and in an infant already weakened by malnutrition, prognosis is bad unless supportive therapy is provided.

Some children experience little or no diarrhoea, but have marked toxic systemic manifestations. Japanese observers differentiated between frank bacillary dysentery and *ekiri*. Sakamoto *et al.* (1956) described the two cardinal characteristics of *ekiri* as central nervous symptoms (particularly convulsions, and sensory disturbances) and circulatory alterations (especially cyanosis, vomiting, and duodenal haemorrhage). The severe form of *ekiri* is almost 100% fatal within 48 hours. The condition is now much less common in Japan.

Shigellosis simulates other diseases only in rare instances. Severe atypical forms of the disease may resemble pneumonia, agranulocytosis, meningitis, or appendicitis.

### Laboratory diagnosis

A definitive diagnosis can be made by the recovery of shigellae from the stool, or by demonstration of a high titre of passive haemagglutinating antibody (Neter *et al.*, 1957; Young *et al.*, 1960; Haltalin *et al.*, 1966; Lee *et al.*, 1966; Cáceres and Mata, 1974). Blood cultures are not recommended because septicaemia seldom occurs. Stool examination for other possible aetiological agents should be made because of the frequency of multiple infections among children (Young *et al.*, 1962).

Rectal swabs or faecal samples are collected and streaked as soon as possible on primary plating media. Care should be exercised that swabs are not allowed to dry, or the stool allowed to stand, because die-off rates for shigellae generally are high. When the faecal specimen cannot be cultured within a short time, a 30% buffered glycerol-saline should be used as a preservative. If possible, flecks of bloody mucus should be selected for inoculation as they are most apt to contain large numbers of shigellae. Because some strains of shigellae are sensitive to inhibitory agents, it is best to use one or more mildly selective media such as Levine's eosin methylene blue agar, MacConkey agar, or xylose lysine desoxycholate citrate agar, as well as more selective media such as Salmonella-Shigella agar or desoxycholate citrate agar. Tergitol 7 with triphenyl tetrazolium chloride has become popular in recent times and is optimal for isolation of the Shiga bacillus (Mata

*et al.*, 1970). *Shigella* colonies can be picked for biochemical and serological tests (Edwards and Ewing, 1962). Polyvalent antisera are used to establish the group and serotype of *Shigella*.

Agglutination tests performed on the patient's serum are frequently misleading. Haemagglutination tests, however, provide a much more reliable means of antibody detection (Neter *et al.*, 1957; Young *et al.*, 1960). Haemagglutination uses formalinized red cells sensitized with 'O' polysaccharide antigens of several of the most prevalent shigellae. Acute and convalescent sera are tested for rises in antibody titre. Results obtained on a single serum are not meaningful unless the titre is significantly elevated. Any titre above 1:40 is important in assessing the epidemiology of a particular serotype, more specifically of those to which the test is specific, namely, *Sh. dysenteriae* 1, *Sh. dysenteriae* 2, *Sh. flexneri* 4 and 6, and *Sh. sonnei* (Cáceres and Mata, 1974).

Microscopic examination of the stool specimen in bacillary dysentery may be informative because it contains large numbers of leucocytes and mucus. Red blood cells, if present, tend to clump. Large amounts of mucus are a constant finding in children, and blood is present less frequently. After administration of broad-spectrum antibiotics large numbers of yeasts, in the absence of other flora, can be seen.

In cases of dehydration or shock, levels of serum sodium, potassium, and CO<sub>2</sub> combining power may be significantly altered. Leucocytosis may or may not be present during the early stages of acute shigellosis, but often occurs when secondary infection is involved. However, severe leucocytosis is a common finding in patients with Shiga dysentery; leucocyte counts as high as 50 000 have been reported (Basagoitia, 1974).

### Differential diagnosis

The diagnosis of shigellosis can be made with certainty only by culturing shigellae from the stool. Various other diseases capable of producing dysentery can be ruled out by adequate parasitological and bacteriological examinations, which will also reveal the cases of mixed infection. Among the parasitic diseases, giardiasis, balantidiasis, amoebiasis, strongyloidiasis, and schistosomiasis can be recognized by microscopic examination of the stool, and malaria by identification of the blood parasites.

Diarrhoea caused by salmonellae or enteropathogenic *E. coli* can be differentiated by proper bacteriologic techniques.

Coccal food poisoning may occasionally be mistaken for shigellosis, from which it usually differs in so far as outbreaks are small, vomiting is more prominent and stool cultures are negative. Food poisoning can occasionally be caused by *Shigella* spp. (Felsenfeld and Young, 1951) and attempts should be made to isolate the organisms from contaminated food and from the patients.

Convulsions, stupor, severe headaches, violent vomiting, and rigidity of the neck are sometimes encountered in infants and young children, and may be confused with an attack of meningitis. Such cases of shigellosis yield a negative spinal fluid culture and the fluid generally has a normal cytology.

The presenting symptoms of acute intussusception on occasion are diarrhoea and vomiting, but the considerable quantity of blood present in the stool in most of these instances should suggest the proper diagnosis, confirmed by palpation of the typical mass.

### Treatment

Therapy must be varied according to the severity of the disease and should be symptomatic and specific. Symptomatic treatment deals with dehydration, 'intoxication', and possible shock. Of primary importance is the restoration of proper fluid and electrolyte

balance. The drugs frequently employed for relief of diarrhoeal symptoms in older children and adults are not indicated in infant cases. Purgatives are definitely contraindicated. Tincture of opium makes the child less irritable, but does not stop diarrhoea, and is not recommended, except in cases of intense pain.

Various feeding regimens may be advocated. Foods are usually withheld during the first 12 hours of disease, though some clinicians recommend the use of small feedings of glucose solution; milk feedings are resumed gradually, diluted initially. Breast feeding, if interrupted, should be recommenced as soon as possible. Solid foods are not given in the first 6 to 12 hours.

Most cases of shigellosis subside with symptomatic treatment, adequate handling of the diet, and proper care (moral support from mother and attendants). Rehydration definitely plays a significant role.<sup>1</sup> If mucosal involvement is significant and toxicosis, exhaustion, and other serious manifestations are developing or have become established, antimicrobials should be instituted without hesitation. Such is the case in explosive *Shigella* diarrhoeas and dysenteries, particularly the varieties caused by *Sh. dysenteriae* 1 and certain *flexneri* serotypes. Sulphonamides, chlortetracycline, and chloramphenicol are frequently recommended. In the last decade a significant proportion of *Shigella* organisms have become resistant to these drugs, often through acquisition of episomes by conjugation. Ampicillin has been found to be excellent (Haltalin *et al.*, 1967) and nalidixic acid, and more recently trimethoprim-sulphamethoxazole have been found excellent for severe shigellosis, particularly for the Shiga variety (Mata *et al.*, 1971). The nutritional status and age of the child must be carefully considered when deciding on the type of drug and its dosage. Testing for sensitivity to antibiotics is of paramount importance since *Shigella* resistance to some of these drugs (for instance nalidixic acid, and ampicillin) has been reported.

### Prognosis

The prognosis for infants and young children has improved since the advent of specific drug and antibiotic therapy, and of better methods for rehydration and restoration of electrolyte balance. Prior to their use, fatality rates of 30-40% in infants under 1 year were common. At present, only fulminating cases with acute sudden onsets, with headaches, convulsions, irritability, and/or shock, are fatal. Proper treatment lowers the fatality rate of Shiga dysentery to less than 1%.

The well-nourished child over 1 year of age is able to withstand an attack of acute bacillary dysentery. However, after the weaning period, such an attack may constitute a hazard to the pre-school child, at risk of increasing malnutrition and exposure to infection in areas of poor hygiene.

### Prevention

Shigellosis must be regarded as a disease of societies living under inadequate conditions of hygiene. It occurs as a result of direct or indirect faecal ingestion. It is rarely transmitted by water, milk, or insects. Thus, the human host is the chief source of infection. Human to human transfer is common in mental institutions, prisons, and refugee camps, and where crowding and low sanitation are present. Sub-clinical cases or true carriers are as potentially dangerous as are clinical cases. The importance of easy availability of water for

<sup>1</sup> Rehydration is extremely important, particularly to replenish water and electrolytes lost primarily during the cholera-like phase of shigellosis. The fluid to be employed for rehydration is the same recommended for cholera patients (see section 5 of this chapter). Rehydration should be by cup, or spoon, or by nasogastric tube if necessary. Intravenous rehydration is justified only for severe cases.

washing purposes was pointed out by Stewart *et al.* (1955) who found the highest infection rates where water was least available. In areas with dense fly populations, a notable parallelism in seasonal incidence of diarrhoea and flies has been noted. Outbreaks of food-borne shigellosis do occur. They are relatively prominent in industrial societies where person-to-person spread is rare due to the significant improvement in sanitation.

Chemoprophylaxis with sulphonamides and antibiotics is of no value and should not be encouraged on ethical grounds (Rosenberg *et al.*, 1974). Its use would favour bacterial acquisition of R factors responsible for antibiotic resistance, and other pathogenic properties. Vaccines have thus far only limited application (DuPont *et al.*, 1974) as in many areas many *Shigella* serotypes are found at any one time. Colostrum and breast milk provide a powerful resistance against *Shigella* infection through the secreted IgA, high content of lysozyme, and the inhibitory influence of the Gram positive lactobacillary flora maintained by breast milk.

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### 3 **Salmonellosis**

#### *P. E. Soysa*

The term salmonellosis is not intended to cover typhoid and paratyphoid infections. Salmonellosis is a global problem though differences in incidence appear to exist between countries, depending in part on the interest in case finding and on laboratory techniques employed. There has been a progressive rise in the frequency of *Salmonella* infections in recent years. This trend has been linked with international traffic in animals and food-stuffs, with industrial food production methods, with large scale intensive stock breeding, and with communal restaurants, all of which are conducive to the introduction of new serotypes and the spread of *Salmonella*. On the other hand in Sri Lanka, the incidence is declining steadily. An early combined study by the Department of Paediatrics and the Medical Research Institute in 1951 revealed that 32.2% of the so-called non-specific diarrhoeas were due to *Salmonella*. More recent annual statistics from the Medical Research Institute are as follows: 13.3% of all stool cultures were positive for *Salmonella* in 1970; 9% in 1971; and 7.8% in 1972. The only dairy products presently imported are butter and powdered infant milk foods. No meats or fish are imported now. This could be one of the reasons for the reduction in incidence.

#### **Serotypes and transmission of infection**

Though the host range for *Salmonella* includes many wild animals, the threat to man arises from his predilection for domestic animals, such as chicken, ducks, geese, turkeys, pigs, and cattle.

The main transmission of bovine salmonellosis is by direct contact with infected cattle, contaminated milk and dairy products (also ice-cream), meat (particularly processed minced meat), and river water. Shellfish, eggs and egg products (including mayonnaise and cakes), and sausages together with communal feeding habits in the modern world are responsible for recent outbreaks. Epidemics also attack crowds on the move as in the case of wars and pilgrimages. This is also true of animals transported to markets and abattoirs, due to bad hygiene and poor environment during transport.

Animals play an epidemiological role in the spread of salmonellosis. *S. typhimurium* accounts for over 70% of isolations in many parts of Europe. Dogs, cats, rats, and wild mammals (hares, wild boars, foxes, etc.) are infected by serotypes most commonly found in man such as *S. typhimurium* and *S. enteritidis*. Pet caged birds and pet tortoises are important sources of infection. Some serotypes that easily adapt to man are regularly associated with the same product or the same animal: *S. infantis*, *S. derby*, and *S. panama* with pigs, pork products, and sausages; *S. dublin* with beef and veal; *S. infantis*, *S. enteritidis*, *S. agona*, and *S. thompson* with chickens; and *S. saint paul* with turkeys.

Hospital outbreaks often occur in children's wards and psychiatric wards. In Sri Lanka in 1972, cross-infection in a children's ward of a General Hospital accounted for a high incidence of *S. san diego* and *S. thompson*.