

SHIGELLOSIS

Shigellosis, or 'bacillary dysentery', is an intestinal infection that is a major public health problem in many developing countries, where it causes about 5 to 10 per cent of childhood diarrhoea. This special *DD* insert provides an overview of shigellosis, including cause, effect and treatment.

Shigellosis is characterised by the frequent and painful passage of stools that consist largely of blood, mucus and pus, accompanied by fever and stomach cramps. In some developing countries more people die from shigellosis than from watery diarrhoea. As many as 25 per cent of all diarrhoea related deaths can be associated with *Shigella*.



Blood and mucus in the stool are signs of shigellosis.

What causes shigellosis?

The symptoms of shigellosis result from infection with the *Shigella* bacterium. Two of the four species of *Shigella* are common in developing countries. *Shigella flexneri* is endemic (present at all times) in most communities. *Shigella dysenteriae* type 1 often occurs in an epidemic pattern; the organism can be absent for a number of years, only to reappear and infect a large proportion of the population. These two species of *Shigella* generally produce the most severe illness. In developed countries *Shigella sonnei* is the most common and is the least virulent *Shigella* bacterium. *Shigella boydii* causes disease of intermediate severity and is least common of the four, except in the Indian sub-continent.

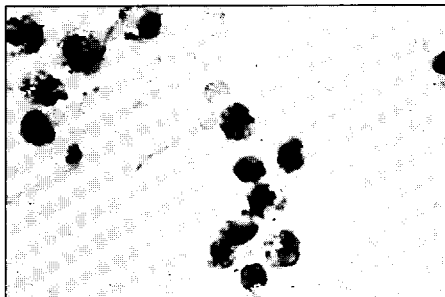
Who gets shigellosis, and how common is it?

Shigellosis is found throughout the world, mostly in children aged under five. Rates of *Shigella* infection are highest where sanitation is poor. They are also in-

fluenced by nutritional status, and environmental factors affecting transmission such as rainfall and temperature. *Shigella* infections can occur throughout the year, but in most communities the incidence is highest when the weather is hot and dry. This may be because the scarcity of water limits handwashing and other hygiene measures that reduce transfer of the very small number of bacteria needed to cause infection.

Health workers are usually aware of the number of shigellosis cases, because symptoms are severe, and therefore children with *Shigella* infections are more likely to be brought to hospitals or clinics. Case fatality rates, even in hospitalised cases of dysentery, are six to eight times greater than for watery diarrhoea. Dysentery is associated with persistent diarrhoea. In rural north India, for example, nearly a third of all persistent diarrhoeal episodes are dysenteric.

During disease epidemics caused by *Shigella dysenteriae* type 1, as many as one in ten people in affected communities will become infected, and as many as 10 to 15 per cent of these will die. At the Diarrhoea Treatment Centre of the International Centre for Diarrhoeal Disease Research in Bangladesh (ICDDR,B), over 700 patients a year with shigellosis are admitted to an in-patient unit. Ten per cent of these patients die while in hospital. Although these are patients with the most severe illness, their high mortality rate shows the difficulties in treating patients with shigellosis, especially when they come for care



A microscopic view of bloody diarrhoea, showing red and white blood cells (from the ulcerated intestinal wall).



Inflammation and tissue damage causes painful straining to pass stools, which can lead to rectal prolapse.

late in the course of the illness. Young children and elderly people are most likely to die from the effects of shigellosis. At the ICDDR,B Treatment Centre, children under 12 months of age account for 21 per cent of shigellosis admissions but up to 33 per cent of all fatal cases. Dysentery is especially severe and more likely to be fatal in young infants, the malnourished, children who are not breastfed, and following measles. Acute and particularly prolonged episodes of dysentery often change marginal malnutrition to overt protein energy malnutrition, and can lead to vitamin A deficiency.

What are the effects of *Shigella* infection?

Shigella infect the cells of the lining of the large intestine (colon). The bacteria invade and damage these cells, producing breaks (ulcers) in the mucous membrane lining the intestine. These ulcers are most common in the rectum, which is the lowest part of the large intestine. Ulceration of the intestinal lining results in increased production of mucus, and the loss of blood and serum

SHIGELLOSIS

proteins into the intestinal cavity. This causes the symptoms of dysentery, which include blood and mucus in the stool (bloody diarrhoea); fever is also common.

The effects of *Shigella* infection on the intestine usually differ from those of organisms such as enterotoxigenic *E. coli* and *Vibrio cholerae*, which cause watery diarrhoea, without fever. These organisms infect only the small intestine and cause little or no damage to the cells lining the intestine. Dehydration is the main complication resulting from these infections. Occasionally *Shigella* causes only watery diarrhoea and this will cause dehydration (unless appropriate rehydration fluids are given).

Shigella dysentery may also lead to a number of dangerous complications. These include:

- severe anorexia (loss of appetite)
- hypoproteinaemia (a low concentration of blood protein)
- hyponatraemia (a low concentration of blood sodium)
- dilation of the large intestine
- seizures
- anaemia
- kidney damage
- persistent diarrhoea
- weight loss and malnutrition

How can shigellosis be identified?

• Stool culture

The most accurate way to find out if a person with diarrhoea is infected with *Shigella* is to make a culture of the stool, to check if the bacterium is present. But this is often impractical in developing countries. Making a culture is expensive and facilities are often unavailable in the rural communities and urban slums where the incidence of shigellosis is greatest. Moreover, the results are usually only available after two or three days, and treatment should not be delayed — a decision regarding antibiotic use must be made immediately. Stool microscopy for pus cells to identify shigellosis is not necessary when visible blood is present in stools. It may help to identify cases of mild shigellosis, when stools are mucoid without blood, but this is too non-specific to be of any practical value.

Shigella bacteria are not always found in the stool cultures of children who are infected. Even in the best conditions, a stool culture may only identify about 70 per cent

of those infected. If antibiotics are given to children with shigellosis before they come to the clinic, the drugs may eliminate the bacteria from their stools. In most studies that have been conducted in developing countries, *Shigella* were recovered from a stool culture in half or more of all children who had dysentery (see Table 1).

• Clinical signs and symptoms

The use of clinical signs and symptoms is therefore very important in identifying patients with shigellosis. Dysentery (bloody diarrhoea) is a very reliable indicator of the infection in the majority of cases. In many developing countries *Shigella* infection is the most common, and potentially the most severe, cause of dysentery. After *Shigella*, *Campylobacter jejuni* and *Salmonella* are the next most common causes of dysentery, but these usually produce self-limited illness that is rarely as serious or life-threatening as shigellosis. The parasite *Entamoeba histolytica*, responsible for amoebic dysentery, is a rare cause of dysentery in children, accounting for less than 5 per cent of all episodes. Stool microscopy for protozoa may not be available and it is often unreliable. Amoebiasis can only be diagnosed with certainty when trophozoites of *E. histolytica* containing red blood cells are seen in fresh stools. The microscopic detection of cysts alone is not

Table 1: Percentage of stool culture showing positive for *Shigella* taken from children with dysentery

Study site (community and hospital based)	Year of study	Per cent of cases showing <i>Shigella</i>
Dhaka, Bangladesh	1979	55
Nonthaburi, Thailand	1986	44
Rangpur, Bangladesh	1988	50
Bangkok, Thailand	1991	37

sufficient for a diagnosis of amoebiasis. Treatment of dysentery should therefore focus on the management of shigellosis.

Mothers are usually accurate observers of their children's stools. If a mother reports that her child's stools contain blood and mucus, then it is reasonable to assume that the child is infected with *Shigella*. Many communities have local terms used to describe different types of diarrhoea, including dysentery, and health workers should become familiar with these terms.

Table 2: Appropriate antibiotics for shigellosis

Antibiotic ¹	Children	Adults	Comments
Cotrimoxazole (also called trimethoprim (TMP)-sulfamethoxazole (SMX))	TMP 5mg/kg and SMX 25mg/kg twice a day for 5 days	TMP 160mg and SMX 800mg twice a day for 5 days	Not recommended for use in jaundiced and premature infants under 1 month old
or:			
Ampicillin	25mg/kg 4 times a day for 5 days	1g 4 times a day for 5 days	Safe for infants, and pregnant or lactating women
Alternative if <i>Shigella</i> in the local area are resistant:			
Nalidixic acid	15mg/kg 4 times a day for 5 days	1g 3 times a day for 5 days	Not recommended for infants under two months

1. All doses are for oral administration. If a liquid form of the drug is not available for children, give the *approximate* dose as crushed tablets.

SHIGELLOSIS

Treatment of shigellosis in children

Children with visible blood in stools should be presumed to have shigellosis and be treated accordingly. The key components of shigellosis treatment are:

- giving an effective antibiotic
- continued feeding
- replacement of fluid losses
- follow up

Children treated early in their illness with an appropriate antibiotic will be considerably better 48 hours after therapy has begun. Those who do not receive effective drug treatment may develop persistent diarrhoea, malnutrition, and other life-threatening complications.

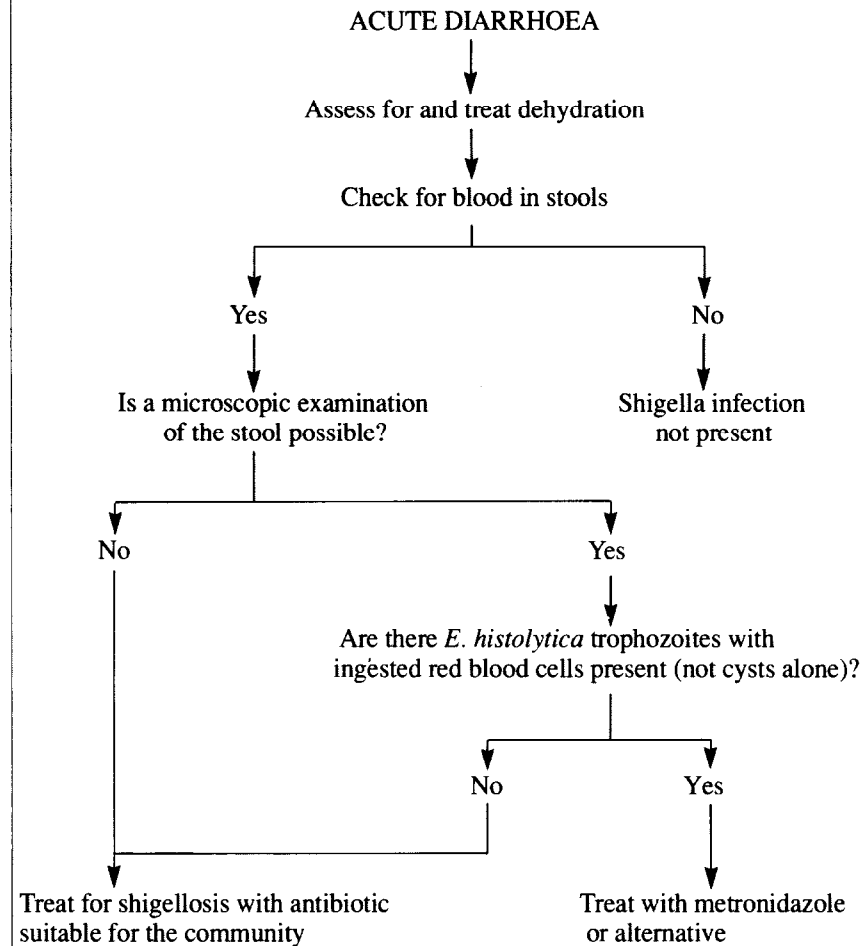
Those who are infected with *Shigella* who are already malnourished need special attention, as do infants under 12 months old, and those already dehydrated. The most severely ill should be cared for in hospital and the others should be followed up at least once every 48 hours until they are better. Infection of the bloodstream is common in these patients, and is caused by bacteria, other than *Shigella*, normally found in the gut. The signs of bloodstream infection are shock, low urine output and lethargy. Intravenous antibiotics such as gentamicin and ampicillin should be given in addition to an oral antibiotic for treatment of shigellosis. However, if ampicillin is given intravenously, it should not also be given orally.

• Antibiotic treatment

Antibiotic treatment should be started as soon as acute dysentery is identified. The chosen drug must be safe for use in children and inexpensive; a liquid formulation is preferable but not essential. Most strains of *Shigella* in the community must be sensitive to the drug, and it should have been shown to be effective in controlled clinical trials. Ampicillin and cotrimoxazole fulfil these criteria, and for the last 15 years have been the drugs of choice for treatment of shigellosis. Some doctors wrongly prescribe metronidazole, believing that the drug will cure both shigellosis and amoebic dysentery. Metronidazole should be used only if *E. histolytica* has been positively identified, or if treatment for shigellosis has failed.

Recently, however, resistant strains of *Shigella* have become common in some countries, such as Bangladesh. Where resistance to ampicillin and cotrimoxazole

Bangladesh: Treatment scheme used for children with bloody diarrhoea



exceeds 25 per cent, nalidixic acid is used as an alternative (see Table 2). This drug is more expensive than cotrimoxazole and ampicillin but is similarly effective. Unfortunately, in areas where nalidixic acid is widely used, *Shigella* bacteria often rapidly become resistant. It is important to use these drugs carefully to minimise the problem of resistance. Their use should be restricted to patients with dysentery: patients with watery diarrhoea do not require an antibiotic unless cholera is suspected. Health workers need to know the resistance pattern of *Shigella* in their community in order to make the right decision about which drug to use. Stool cultures should be obtained on a regular basis, and isolates of *Shigella* tested for sensitivity to drugs commonly used for treatment.

The new fluoroquinolones (e.g. ciprofloxacin and ofloxacin) are highly active and clinically effective when given by mouth, but because they cause cartilage damage in young animals, there is still concern about their safety in young children.

Studies are being carried out to determine how important this is in humans. Antibiotics known to be less effective and therefore not recommended include neomycin, gentamicin, the first generation cephalosporins, kanamycin, amoxicillin and sulphaguanidine. In many parts of the world, a significant proportion of *Shigella* strains show *in vitro* sensitivity to furazolidine and many doctors who use it as initial therapy in India report anecdotal favourable results. However, controlled clinical trials are lacking.

The diagram above shows a scheme which was developed for health workers to use when treating children with bloody diarrhoea in Bangladesh. Similar schemes could be established and evaluated for other countries.

• Continued feeding

Nutrient absorption continues during shigellosis, because the disease does not affect much of the small intestine, where most absorption takes place. However, the inflammation in the large intestine affects

SHIGELLOSIS



WHO/J Danois

Handwashing after defecation is the best way to prevent the spread of shigellosis.

nutritional status. Early effective antimicrobial therapy cures the infection and inflammation and the child's appetite will return, soon followed by weight gain. It is important to feed and/or breastfeed patients with shigellosis frequently to prevent them developing hypoglycaemia (low blood sugar) and losing weight during their illness. This can be difficult because they are often severely anorexic (suffering from loss of appetite). However, children need not eat as much at each feeding as they normally would. Small amounts of food should be given every three to four hours. This will also keep up the blood sugar level. Foods rich in potassium, such as bananas, are recommended. One extra meal should be given to the child every day for at least two weeks after the diarrhoea stops.

Continued feeding also helps to prevent the acute weight loss that occurs during diarrhoea. If a severely ill patient in hospital refuses to eat or to breastfeed, it may be necessary to feed with a nasogastric tube initially.

• Replacement of fluid losses

Mild to moderate dehydration is common in patients with shigellosis. Dehydration is caused by loss of fluid in stools, evaporation of water through the skin due to fever, and reduced fluid intake because of anorexia. Hyponatraemia (low levels of sodium in the blood) is a particular problem for those infected with *S. dysenteriae* type 1. Oral rehydration therapy should be given and in most cases fluids do not need to be given intravenously. Giving intravenous fluids increases the risk of infection and is expensive. Oral rehydration

solution contains enough salt (sodium) to increase the level of salts in the patient's blood, if it is low.

• Follow up

Follow up is important to determine whether patients have responded to treatment. Ask the mother to bring her child back to the health centre within 48 hours if the child is less than one year old, dehydrated when first seen, or still has blood in the stool. Diarrhoea may take longer than two days to stop altogether, but the visible blood in stools should disappear within that time. If the blood does persist, the child may be infected with a strain of *Shigella* that is resistant to the drug used. Such patients should be treated with a different agent for shigellosis unless another cause of dysentery is found. If there is still no improvement after two days of treatment with an alternative drug, the child should be taken to hospital. Amoebiasis should be considered.

How can shigellosis be prevented?

Shigella bacteria infect only humans and monkeys, and do not survive for long outside the body. Therefore, for infection to occur, *Shigella* bacteria must pass quickly from one person to another. This usually occurs through 'faecal-oral' transmission. This takes place when a person with shigellosis defecates, does not wash his or her hands adequately afterwards, and transfers *Shigella* germs to food (or water). The bacteria are then swallowed when the contaminated food is eaten by another person. Fewer than ten ingested bacteria are enough to cause a *Shigella* infection; in

contrast, thousands of *Vibrio cholerae* are required to cause disease. Once a member of the family has dysentery, infection can spread from person to person very quickly.

Community health education must include information on hygiene. The most effective way to reduce the incidence of shigellosis is to ensure proper washing of hands following defecation, and adequate disposal of faeces. It is not only adults who need to wash their hands. Children are probably the most common carriers of infection, and they must also be shown how to wash their hands. Adults caring for children need to wash their hands often too. Even if soap is not available, a good scrubbing with water, and use of an abrasive such as sand, is helpful in reducing the spread of infection. Household food and water also have to be protected from faeces and unwashed hands. There are no effective vaccines for the prevention of shigellosis, although research into vaccines, especially ones for oral use, is being carried out.

Steps to eradication

Of all the diarrhoeal illnesses, shigellosis is the one most closely linked with underdevelopment. Features of underdevelopment that produce a high incidence of shigellosis include poor housing and insanitary conditions, overcrowding, absence of adequate water supplies for cleaning and washing, and childhood malnutrition. In all countries where economic and social conditions have improved, the most virulent forms of shigellosis, caused by *Shigella dysenteriae* type 1 and *Shigella flexneri*, have virtually disappeared. Thus the prevention of shigellosis is closely linked to efforts to improve the economic and social conditions of people living in areas where shigellosis is now endemic.

On a national level, Diarrhoeal Disease Control Programmes need to research patterns of antibiotic use, investigate resistance of *Shigella* strains to drugs in different regions, develop treatment schemes appropriate for local conditions, and train doctors in the correct case management of dysentery.

Acknowledgements

This supplement is based on material prepared by Drs M Bennish and J Griffiths of the New England Medical Center (Tufts University), Dr A Salam of the International Centre for Diarrhoeal Disease Research, Bangladesh and Dr M Bhan, of the All-India Institute of Medical Sciences, New Delhi, India; and developed by the ADDR Project, Harvard Institute for International Development.