A New Look at Infectious Diseases

Dysentery including Amoebiasis

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Bacillary dysentery is caused by the Shigellae, a group of Gram-negative, non-motile organisms which are pathogenic only to man and some primates. As classically described, the disease is characterized by acute onset of severe diarrhoea, abdominal pain, and fever and stools which contain mucus, pus, and blood. In very many cases, however, infection is mild and may cause only transient diarrhoea or be symptomless. Serious illness occurs most frequently among the very young, the aged, the debilitated, and the malnourished.

BACTERIOLOGY

The Shigellae are identified by their fermentation characteristics, the group as a whole being non-lactose fermentors. There are four subgroups—namely, (A) *Sh. dysenteriae*, (B) *Sh. flexneri*, (C) *Sh. boydii*, and (D) *Sh. sonnei*. Subgroups A, B, and C have a number of subtypes, which differ serologically; *Sh. sonnei* is the only member of subgroup D. The organisms are easily cultured from stools and rectal swabs, but blood and urine cultures give, for practical purposes, invariably negative results. Apart from one member of the *Sh. dysenteriae* group (*Sh. shiga*) the Shigellae do not produce exotoxins. Disease caused by *Sh. dysenteriae* tends to be the most, and that caused by *Sh. sonnei* the least, severe.

Bacillary dysentery tends to be prevalent wherever people live in overcrowded and unsanitary conditions. It is a well-recognized scourge of armies in wartime, and of refugee and prisoner-of-war camps. Faecal-oral transmission of Shigellae occurs directly by contaminated hands or through the intermediary of flies, food, and infected water supplies. The disease is more prevalent in warm than in cool climates, but paradoxically spread of bacillary dysentery in cool climates occurs most readily during winter, when people tend to live in closer personal contact than in the summer months.

The prevalence of the different subgroups of Shigellae varies from place to place, and may alter in the same location from time to time. In the U.K. at the present time *Shigella sonnei* accounts for over 90% of cases of bacillary dysentery; the remainder are usually due to *Shigella flexneri*, which is somewhat more prevalent in Scotland than in England.¹ In contrast, in many tropical countries *Shigella flexneri* tends to be the dominant species,²⁻⁴ while in North America *Sh. sonnei* and *Sh. flexneri* appear to be equally prevalent.⁵

In many underdeveloped tropical countries heavy faecal contamination of the environment, poor water supplies, unhygienic food handling, overcrowding, and the presence of

flies ensure that all age groups in the population are constantly exposed to infection with Shigellae. In more affluent societies exposure to infections is greatest among young children, especially in nursery schools and similar institutions where toilet seats, bedding, toys, etc. are liable to faecal contamination by an age group who are still learning to control their excretory functions and are not yet competent in the techniques of hand washing and hygienic food handling. Outbreaks of bacillary dysentery are also liable to occur in residential units for the aged or severely handicapped, especially in conditions of overcrowding and understaffing.

PATHOLOGY

Inflammation is usually limited to the colon and rectum but in severe infections may extend to the terminal ileum. In *Sh. sonnei* infections pathological changes are usually mild and may be limited to oedema and hyperaemia of the mucosa and submucosa, with some cellular infiltration of the gut wall, punctate haemorrhages, and an excess of mucus secretion. In more severe infections (as tend to occur with *Sh. flexneri* and *Sh. dysenteriae*) the entire mucosa may become grossly inflamed and oedematous with copious outpouring of blood-stained mucus and pus. The superficial epithelium may slough in an irregular fashion giving rise to shallow ulcers which bleed. Usually ulceration does not go deeper than the submucosa.⁶ Rarely, coagulative necrosis of the gut wall may occur, with the attendant risk of perforation and healing by scarring and stricture formation.⁶

CLINICAL MANIFESTATIONS

The incubation period is short, usually two or three days and rarely longer than one week. With *Sh. sonnei* infections many cases experience little more than some looseness of the bowels, or mild watery diarrhoea for a day or two, unassociated with any significant constitutional upset. Some of those who acquire the infection remain symptomless, even though they may be excreting the organisms.

In more severe infections there is an abrupt onset of fever, cramping abdominal pain—often associated with vomiting—followed by diarrhoea, which may be profuse. Initially the stools are watery and yellow-green in colour but later may contain mucus, blood, and pus. In very severe infections—especially with *Sh. flexneri* and *Sh. dysenteriae*—there may be considerable toxæmia, high fever, lower abdominal pain, severe tenesmus, and profuse diarrhoea, the stools consisting largely of watery mucus, blood, and pus. In cases in which there is a delay in onset of diarrhoea, the initial symptoms of vomiting, fever, and abdominal pain and tenderness may simulate acute appendicitis or another intra-abdominal lesion.

In young children the onset of bacillary dysentery may be associated with convulsions and signs of meningeal irritation,

such as neck stiffness and a positive Kernig's sign, suggesting the diagnosis of meningitis. The true nature of the illness may be masked by delay in the onset of diarrhoea. In these circumstances, a lumbar puncture may have to be done to exclude meningitis.

Very occasionally the disease strikes with catastrophic severity and may cause gangrene of the colon. *Sh. shigae*, one of the subtypes of the *Sh. dysenteriae* group is the organism usually incriminated in this severe form of the disease which leads to prostration and circulatory collapse and may be rapidly fatal.⁶

In most mild to moderate infections symptoms tend to subside, even without specific treatment, within a week to ten days, but in more severe cases the course is more protracted and convalescence may be slow.

PROGNOSIS

Sh. sonnei dysentery as seen in the U.K. has a good prognosis. The very young, the aged, or those who are chronically debilitated are, however, at special risk and may succumb from the effects of acute fluid and electrolyte derangements. In tropical countries the prevalence of more virulent strains of Shigellae, high environmental temperatures—that exaggerate the effects of dehydration—inadequate standards of medical care, and wide prevalence of malnutrition all contribute to a more serious prognosis in bacillary dysentery.

DIFFERENTIAL DIAGNOSIS

When watery diarrhoea is the main presenting symptom, the illness must be differentiated from food poisoning, Salmonella infections, and gastroenteritis due to pathogenic *Escherichia coli* in young children. The more classical dysenteric symptoms (especially the passage of blood and mucus in the stool) call for differentiation from amoebic dysentery and ulcerative colitis. The early symptoms of fever, abdominal pain, and vomiting may suggest appendicitis, urinary tract infection, and occasionally intussusception in the young—while convulsions and meningism at the onset of illness calls for differentiation from meningitis.

The Shigellae are easily cultured from rectal swabs or stools of patients. Isolation of the organism constitutes the only reliable way to confirm diagnosis. If rectal swabs are employed, care should be taken to avoid drying before culture. Rectal swabs should be placed in a transport medium if delay seems likely before culture can be undertaken.

TREATMENT

General

Early recognition and correction of shock and dehydration and the maintenance of normal fluid and electrolyte balance are the most important aspects of treatment. Abdominal pain and discomfort may be alleviated by the use of preparations such as kaolin and morphine, or antispasmodics such as Lomotil (diphenoxylate hydrochloride and atropine sulphate). In the most severe cases morphine by injection may be indicated. Control of high fever will reduce fluid losses and increase the patient's comfort. The use of purgatives, at one time a vogue in treatment, is to be denigrated.

Specific treatment

In the more severe 'form of the disease a broad-spectrum antibiotic such as tetracycline, ampicillin, or chloramphenicol should be administered for five to seven days and will in most cases achieve rapid control of infection. The sulphonamides,

formerly widely used in bacillary dysentery, can no longer be recommended as treatment of choice in Europe, where sulphonamide-resistant strains of Shigella are now widespread. In tropical countries, where sensitivity patterns may differ and where economic considerations limit choice of treatment, the soluble sulphonamides such as sulphadimidine still have a place in treatment. The usual adult dose is 2 g initially followed by 1 g six-hourly. The dose for children is 150 mg per kg per day (total daily dose not to exceed 6 g). If sulphonamides are used, care must be exercised to maintain adequate fluid intake to avoid the danger of crystaluria. Co-trimoxazole may be of value where resistance to sulphonamides and/or broad-spectrum antibiotics such as tetracycline pose a problem.⁷

The following drugs have also been found of value in the management of moderately severe infections.⁸

Streptomycin (adult dose) 2g four times daily for 5 days.

Neomycin " " 1g " " " " "

Nalidixic acid " " 1g " " " " "

The use of specific antimicrobial therapy in patients with mild, transient infections is debateable.

CONTROL OF INFECTION

Patients should be isolated and the strictest care exercised in disposing of their faeces and soiled bed linen etc. Test of cure of infection should be by at least three consecutive negative stool cultures. Outbreaks of dysentery in institutions such as nursery schools, residential homes, and general hospital wards may call for temporary closure of these units, and special attention must be directed at identifying carriers or other sources of infection. The most stringent tests of cure of infection must be applied to food handlers. It is difficult to lay down absolute criteria of cure of infection but six consecutive negative stools has been suggested as a reasonable requirement for food handlers who have had the disease.⁸

Amoebiasis

The term amoebiasis covers a wide range of disease in the gastrointestinal tract and includes also amoebic liver abscess and many other less common visceral manifestations. We shall be concerned here only with the "dysenteric" manifestations of amoebiasis.

Intestinal amoebiasis is one of the most perplexing entities in clinical practice. It is caused by the *Entamoeba histolytica*, a unicellular parasite that has a global distribution. In most people this causes little or no clinical illness but in certain circumstances it may cause catastrophic illness with serious morbidity and mortality. In general in affluent societies in cool temperate climates amoebic infection is usually symptomless. When symptoms do arise they tend to be mild and rarely constitute a threat to life. In less privileged communities in warm climates, however, amoebic infection—though symptomless in a high proportion of the population—is frequently the cause of gross disease in the gut attended by a high rate of varied and serious complications, of which amoebic liver abscess is the commonest. Different population groups in the same geographical environment may show remarkable differences in their response to infection. Among the white citizens of the city of Durban in South Africa, intestinal amoebiasis tends to be a "nuisance" rather than a "disease," whereas in the Bantu community in the same city amoebic dysentery is frequently an acute, devastating illness which ranks as a major cause of morbidity and mortality in the African population.⁹

The reasons for this extremely variable expression of infection by the same parasite are as yet not clearly defined, but host factors are implicated and, of these, malnutrition may be a major determinant of morbidity. Differences in the composition of the dominant types of gut flora may also have a bearing on pathogenicity.

There is a tendency to regard amoebiasis as an "adult" disease, but there is abundant evidence to show that infants and young children are frequently infected¹⁰⁻¹³ and may be severely affected even as early as the neonatal period.¹⁴ A recent report from a large children's hospital in Cape Town showed that *E. histolytica* was a more frequently identified cause of dysenteric illness in coloured children than *Shigellae* or *Salmonellae*.¹⁵

PARASITOLOGY

In the gut *E. histolytica* exist naturally in a motile vegetative form. When passed in stools they may be detected in this form or as cysts. Clinical illness is always due to vegetative amoebae, which invade the bowel by a process of colliquative necrosis. These invasive forms of the parasite are active phagocytes, which among other things ingest red blood cells. The only reliable parasitological criteria on which to base a diagnosis of amoebic dysentery is the detection of haematophagous trophozoites of *E. histolytica* in stools or intestinal secretions. Nevertheless *E. histolytica* may be difficult to demonstrate and may be confused with non-pathogenic amoebae and macrophages. Various serological tests have been developed which are of value in the diagnosis of invasive amoebiasis.

SEROLOGY

Extensive studies have established that the presence of antibodies to antigens of *E. histolytica* implies past or present invasion of tissues by the parasite.¹⁶ The gel-diffusion precipitation test has been shown to be simple, reproducible, and reliable,^{17, 18} but requires 48 hours at least for an unequivocal negative result. A very rapid amoebic latex agglutination test, recently reported, promises to be a helpful clinical tool, especially where amoebiasis is highly prevalent and where difficulties in diagnosis may arise, as in outpatient clinics.¹⁹ A negative result with either of these tests virtually excludes the diagnosis of active amoebic disease but positive results must be interpreted in the light of antibody studies in the general population, and with regard to the patient's clinical state. These tests have their main value in the diagnosis of extraintestinal amoebiasis. Examination of a fresh, warm stool remains the most reliable method of diagnosing amoebic dysentery.

PATHOLOGY

The range of the lesions found in amoebic dysentery varies from barely detectable superficial puntate ulceration in the most superficial layers of the mucosa of the colon to gross destructive changes involving all the layers of the gut and extending from terminal ileum to the perianal region. The caecum and recto-sigmoid region of the colon tend to be most frequently affected and typical findings include ulcers of variable size, depth, and extent which have undermined, irregular edges and in the walls of which *E. histolytica* can be found. Haematogenous spread may occur from the colon to the liver and other organs.

CLINICAL MANIFESTATIONS

Most patients present with mild diarrhoea, which may be chronic or relapsing and is unassociated with any significant constitutional disturbance. The stools may simply be loose, but characteristically there is some excess of mucus. Diagnosis is usually established by detection of haematophagous *E. histolytica* in the stools. When stool examination is negative or cannot be relied on, sigmoidoscopy and serological tests may be helpful in confirming diagnosis.

In more serious infections diarrhoea is more overt and persistent and the stools characteristically contain an excess of

clear mucus with variable amounts of blood. Abdominal discomfort, tenesmus, and tenderness over the colon may be present but fever and constitution disturbance may not be very evident. The severest form of the disease may have an acute onset and simulate bacillary dysentery. Diarrhoea may be profuse with an almost continuous discharge of watery mucus-containing blood-stained stools. Abdominal pain and tenderness may be appreciable. The presence of abdominal distention, hiccup or marked guarding should give warning of perforation of the colon. Shreds of mucosa may be passed in the stool and occasionally a ragged necrotic mucosal 'cast' of a segment of colon may be evacuated.

COMPLICATIONS

Hepatic invasion is a constant threat, and even mild inapparent intestinal infections may be complicated by amoebic liver abscesses and other systemic involvement at a later date. In endemic areas, lesions in the right lung base should always raise the suspicion for systemic amoebiasis. In the severer form of amoebic dysentery perforation of the colon and peritonitis may occur. This is a severe complication with a high mortality. Serious haemorrhage may also occasionally occur, and requires urgent and liberal blood transfusion.

Other complications include cutaneous ulceration in the perineal region, and inflammatory granuloma of the colon—the so-called amoeboma—and stricture of the colon.

TREATMENT

For patients with mild to moderate dysentery oral administration of metronidazole is the simplest, safest, and most effective treatment currently available. The recommended adult dose is 800 mg thrice daily for 5-7 days;²⁰ for children the dose is 50 mg per kg given orally in three divided doses daily for seven days. This regimen usually achieves rapid control of dysenteric symptoms and can also be relied upon to control systemic spread of the disease.

Alternatively, the following may be employed: (1) tetracycline (as oxytetracycline or chlortetracycline) 250 mg, 6-hourly for 10 days, plus (2) diloxanide furoate, 0.5 g. thrice daily for 10 days, plus (3) chloroquine, 600 mg initially, followed by 300 mg six hours later and then 150 mg twice daily for 14 days.²⁰

In very severe forms of the disease attention must be paid to correction of fluid and electrolyte disturbances and of anaemia. Specific therapy with a combination of metronidazole, tetracyclines, and diloxanide furoate is indicated.

Emetine hydrochloride, 1 mg per kg daily (maximum dose 65 mg daily) or dihydroemetine 2 mg per kg daily, by subcutaneous injection for 5 to 10 days, may be substituted for metronidazole in the above regimen, or may be given as *additional treatment* in very severe infections.¹³ These drugs are cardiotoxic and must not be used in the presence of cardiac failure. Their use in ambulant patients cannot be recommended.

In treating cyst passers diloxanide furoate, 0.5g-1 g thrice daily for 10 days, is effective in a high proportion of cases. Alternatively di-iodohydroxyquinoline 600 mg thrice daily, for three weeks, either alone or with tetracycline for 10 days, may be used.

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Any Questions?

We publish below a selection of questions and answers of general interest

Oral Contraceptives for Patients on M.A.O.I. Therapy

Which is the oral contraceptive of choice to prescribe for patients who are taking a monoamine oxidase inhibiting drug for depression?

There are no documented interactions between monoamine oxidase inhibitors and oral contraceptives.

Reaction to Immunization

A boy now aged 8 months had a reaction two hours after the second triple antigen injection, with pallor and vomiting, loose stools, and rapid respirations. The attack responded to anti-histamines. His father is sensitive to horse serum. Should the third dose of triple antigen be given and what action should be taken about future prophylaxis?

The features of the clinical reaction in this case are indicative of a severe endotoxin reaction which may have been due to (a) faulty storage of vaccine, particularly solid freezing on at least one occasion, or numerous cooling/warming cycles in and out of a refrigerator, (b) use of residual vaccine from multidose containers contaminated during a previous immunization session, (c) failure to evenly disperse the vaccine before use by shaking the multidose bottle, (d) inadvertent intravenous inoculation of the vaccine, or (e) temporary hypersensitivity to endotoxin following release of endotoxin by common intestinal commensals.

It is not possible to predict with confidence whether the child in this instance would have a similar or more severe reaction if given another dose of diphtheria/tetanus/pertussis vaccine. It would be prudent, under the circumstances, to omit giving further amounts of pertussis vaccine. The immunization course should be completed with one dose of combined diphtheria-tetanus vaccine only to be given six months after the second dose of D.T.P.

Tenosynovitis of Tendo Achillis

What is the treatment for persistent—and worsening—tenosynovitis of the tendo achillis?

Many cases of tenosynovitis of the achilles tendon are encountered in patients with an underlying rheumatic disease, the commonest being rheumatoid arthritis, but it may also occur in gout, ankylosing spondylitis, or psoriatic arthritis, which may not be overt at the time. Other cases can usually be attributed to repetitive trauma, such as wearing unaccustomed heavy footwear, for instance, ski boots.

Simple remedies and avoidance of repetitive trauma, usu-

ally suffice to cure the condition. Loose light shoes with a Sorbo pad behind the heel should be worn. Blocking the heel with a tapered raise of up to 2 cm may also help. An abnormal gait pattern arising from a valgoid or cavoid foot or even verrucas may be responsible. Local steroid injection can be most effective but it must be placed just within the tendon sheath and not forced into the tendon. In elderly patients with rheumatic disease the pain may be the result of partial fraying of the tendon and complete rupture may follow the injection.¹

If all these measures fail it may occasionally be necessary to immobilize the ankle in a plaster boot for four to eight weeks. Although tendon stretching exercises may be a prophylactic for ski novices they are unlikely to benefit—and might exacerbate—chronic tenosynovitis.

¹ Bedi, S. S., and Ellis, W., *Annals of the Rheumatic Diseases*, 1970, 29, 494.

Causes of Purpuric Enanthem

Are there any other causes for an enanthem which has a tendency to become purpuric other than that seen in infectious mononucleosis, enteroviral infection, or drug reaction.

Many other oral enanthems may become purpuric—for example, measles, erythema multiforme, and the blistering rashes. In other words the tendency to become purpuric is too non-specific to be used as a diagnostic feature.

Notes and Comments

Treatment of Orf.—Dr. F. E. GRAHAM-BONNALIE (Edinburgh) writes: With reference to the answer to this question ("Any Questions?" 3 February, p. 287) your expert states that orf takes six weeks to come, six weeks to go, and that there is no specific treatment. May I repeat an observation I made some years ago¹ The application twice daily of ung. hydrarg. ammon. dil. will within 72 hours leave a healthy granulating surface which will heal within another 7 days. May I add that it is not uncommonly also contracted from cows' udders.

OUR EXPERT replies: I suspect that Dr. Graham-Bonnalie is confusing milker's nodes with orf. They look very much alike clinically, indeed they may be totally indistinguishable, but they are quite a different disease, and caused by a different virus.

¹ Graham-Bonnalie, F. E., *British Medical Journal*, 1951, 1, 1265.