Current Practice

Bacillary Dysentery

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Diseases, like nations, rise, expand, and fall, and it is as hard to explain the changing epidemic virulence of a micro-organism as to account for the waxing and waning energies of a people. One can cite social and economic impulses for the latter and varying hygienic and host factors for the former. One may in this way explain in part how dysentery ceased to be a scourge of gaols and became instead a nuisance in nursery schools, but it is more difficult to show why *Shigella flexneri* has given way to *Sh. sonnei* as the epidemic type in England, and why the same thing has not happened in America or even, to some extent, in Scotland. The forces and stresses underlying these changes are complex and the behaviour of micro-organisms, like that of man, can be mysterious and hard to understand.

Bacteriology

Classification

The *Shigellae* are members of the enterobacteriaceae and form a fairly homogeneous group of lactose-fermenting organisms. They are divided into four sub-groups, A, B, C, and D. Group A contains organisms which do not ferment mannitol, and has the group name *Sh. dysenteriae*. There are 10 serotypes differentiated by agglutination tests. *Sh. dysenteriae* type 1 is better known as *Sh. shigae*, and *Sh. dysenteriae* type 2 was formerly *Shigella schmitzii*. The other eight serotypes rarely cause disease in man. Group B organisms ferment mannitol and have the group name *Sh. flexneri*. There are 6 serotypes and 9 subtypes. The original *Sh. flexneri* is a member, and the organism once known as the Newcastle bacillus is *Sh. flexneri* type 6. Group C organisms resemble group B organisms biochemically but are antigenically distinct. There are 15 serotypes, and the group name is *Sh. boydii*. Group D contains only one serotype, *Sh. sonnei*; it ferments mannitol and is a late lactose-fermenter.

The organisms in the four groups can be further differentiated by phage typing. *Sh. flexneri* can be subdivided in this way into phage types which correspond fairly closely with the serotypes. *Sh. sonnei* can be subdivided into over 60 phage types, but it is easier in the laboratory to classify strains according to their ability to produce on blood agar substances known as colicines. The colicines are antibiotics and may inhibit the growth of other strains and of some related enterobacteria, and a series of indicator organisms, whose sensitivities to colicine are known, is used to detect the colicine pattern of the strain being tested. Strains which do not produce colicines are classed as untypable. This colicine typing can be used to trace the epidemic spread of Sonne dysentery, and in this way outbreaks which appear to be related may be shown to be due to different colicine types and so not connected at all. Similarly a strain excreted by a carrier can be compared with an epidemic strain and shown to be the same or different. It is of some therapeutic interest that untypable strains have tended to be sulphonamide-sensitive, while nearly all the typable strains have been resistant.

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Growth and Resistance

Shigellae are present in very large numbers in the faeces and intestinal mucus early in the disease. They survive in alkaline faeces for days but die in a few hours in acid faeces. Provided they reach the laboratory quickly rectal swabs give satisfactory results, but if these are taken early in the morning, exposed to ward temperatures and sunshine for most of the day, and plated in the evening *shigellae* may die out in the interval. If delay is likely faeces should be collected into a buffered 30% glycerol saline solution. Cultures are made on deoxycholate citrate agar or other suitable media, and, after overnight growth, colonies are investigated for their biochemical reactions and serotyped by slide agglutination. A preliminary report should be available within 24 hours.

The resistance of the organisms in varying conditions is of epidemiological importance. *Shigellae* are killed in one hour by heating at 55° C. (130° F.), but such exposure would not occur under natural conditions. More relevant are experiments in which metal tags, cotton balls, filter paper, cover slips, and wooden sticks were contaminated with *Sh. sonnei* and exposed to different temperatures.¹ The organisms survived on metal tags for 7 to 14 days at 4° C. (39° F.), 2 to 9 days at 15° C. (a room temperature of 59° F.), and for 1 to 4 days at 37° C. (98.6° F.). On the other articles the organisms survived longer—on cotton balls and filter paper for as long as a month at 15° C. If for cotton balls, metal tags, cover slips, and wooden sticks one substitutes blankets, bedsteads, locker tops, or benches it is easy to see how a bedroom, a hospital ward, or a laboratory bench could be contaminated with live dysentery germs for long periods.

Light and humidity also affect the survival of *shigellae*. In the shade *shigellae* may survive for a month, but if exposed to light at the same temperature they die within five days²; on dry linen in the dark they can survive for up to six weeks.^{3,4} Relative humidity is of great importance: in one experiment, with other factors constant, *shigellae* survived for 20 days at R.H. 93%, 10 days at R.H. 84%, and only 3 days at R.H. 0%.² The three factors—coolness, shade, and high R.H.—are all present in the environment of the water closet, and *Sh. sonnei* have survived for as long as 17 days on the wooden seat.² The size of the inoculum affected survival; if the drops of faecal suspensions applied to the seat contained over 27,000 organisms they survived for 17 days, but if fewer than 10,000 they were dead within 2 days. This is of epidemiological importance, for it has been shown that only the liquid stool of a patient with diarrhoea leads to heavy contamination of the seat, whereas the formed stool of a carrier does not.² The effect of the intensity of the infection was again shown when faeces were exposed to natural conditions. When the faeces contained over 20 million organisms/g. the *shigellae* survived for 19 days, but when as few as 10,000/g. survival was only 48 hours: when 10-g. samples were exposed organisms survived for 10 days, but in bulk samples they survived for over 3 weeks.² Temperature was again shown to be important: at 37° C. all the organisms in faeces samples containing 1½ million organisms/g. were dead in a week, but at temperatures between 12.8° C. and

18.8° C. (55° F. to 66° F.) shigellae could still be grown in large numbers.²

Shigellae have been grown from dust on schoolroom and bedroom floors, usually only when contamination from a nearby water closet could be traced.² They have been grown from moist garden earth kept at 15° C. for 9 to 12 days, so that contamination of children's sand-pits is a possibility. They can survive in water shaded from the sun at room temperature for over a week, and for similar periods in milk and food. Perhaps more relevant to the spread of the disease is the fact that *Sh. sonnei* has been frequently grown from the fingers several hours after contamination of hands.

Epidemiology

The organisms of bacillary dysentery are excreted from the bowel and ingested by the mouth. The disease is therefore essentially one of defective hygiene and sanitation. It has always been a great hazard in military campaigns, and even where the standard of field hygiene and camp sanitation is high dysentery still causes great wastage of man-power.^{5,6} In underdeveloped countries, especially in the tropics, methods of disposal of faeces may be primitive or absent, and drinking water and food are readily contaminated, causing widespread outbreaks of the disease.⁷ Flies multiply in the warmer part of the year, and flies emerging from maggots can find their way to the surface even if buried in faeces under several feet of sand.⁸ They carry the organisms on their feet and excrete it in their faeces and vomit, and can obviously be major spreaders of the disease in areas of primitive sanitation. In the hottest part of the year the heat of the tropical sun may sterilize exposed human faeces and kill the maggots of flies, so that after a rise in the earlier part of summer there may be a decline in the incidence of the disease in the later part.

In developed and temperate countries climate has no such direct effect. Sonne dysentery in Britain has become commoner in winter than in summer in the last 40 years, but this cannot be due directly to the climate, for there are no flies in winter and the summer sun is not hot enough to kill shigellae quickly. Improvement in hygiene and sanitation may have had some effect, but both were already of high standing when the change began. Moreover, the total incidence of notified cases has risen during this time. The oddest change of all has been in the type of infecting organism—*Sh. flexneri* has become uncommon, while *Sh. sonnei* is now the dominant organism. It may be that *Sh. flexneri* can cause illness only if the infecting dose is high, and it has died out in an environment where it finds it difficult to reach food or milk and multiply in it, whereas *Sh. sonnei* may be able to infect with the small dose which may pass from hand to hand and not require to multiply before ingestion. This would enable it to survive where sanitation was efficient but personal hygiene less than perfect, as is the case among children in modern homes and modern infant schools. All this is conjecture, but may fit the facts. When the epidemiology of Sonne dysentery is studied in nursery schools there is no difficulty in tracing the spread of infection from the water closet to fingers, and, directly or indirectly, to the mouth.²

While spread by water and food may be normal in backward countries, such outbreaks are uncommon where hygiene and sanitation are satisfactory. They can still occur when things go wrong and faults occur in water supply⁹ or sewage disposal, or when carriers gain access to food. Outbreaks have occurred when wells have been contaminated by cesspools,⁹ and food-borne outbreaks have followed the eating of pies, blanc-mange, water-cress, and cheese.¹⁰⁻¹² But such outbreaks are rare and attract attention because of their rarity. Dysentery in Britain, and this virtually means Sonne dysentery, is now a disease spread by personal contact in the home, the playground, or the school. It has become an endemic rather than an epidemic infection.

Pathology

Pathological changes in the bowel wall in bacillary dysentery vary with the type of infecting shigella. *Sh. sonnei* probably causes a catarrhal inflammation of the mucosa of the large bowel with some infiltration with polymorphs and plasma cells, but there is little engorgement of the blood-vessels or haemorrhage into the mucosa and submucosa except in a few scattered areas. These changes are enough to cause irritation of the bowel wall, increased secretion of mucus, and the passage of loose stools for a short period. Flecks of blood are often present in the stools, but red-currant jelly stools are not often seen in cases of Sonne dysentery. Many cases of Flexner dysentery are also mild, but both Flexner and Shiga bacilli can cause intense inflammatory changes in the mucosa and submucosa, with congestion and thrombosis of blood-vessels and large areas of haemorrhage. The mucosa may become necrotic and slough, leaving raw ulcerated areas, most marked in the rectum and sigmoid colon though sometimes affecting the whole of the large bowel and the last few feet of the small intestine. When these changes are severe, healing may be incomplete, the mucosa being replaced by fibrous tissue or granulation tissue, and in chronic cases transverse ulceration of the bowel may persist indefinitely. Such changes are rarely seen in cases of bacillary dysentery contracted in Britain, but it is well to remember that *Sh. sonnei* belongs to a family of organisms capable of destroying most of the mucosa of the large bowel.

Clinical Manifestations

Sonne Dysentery

The only common symptom is diarrhoea, usually not very severe. In a sharp attack the patient may have diarrhoea every 10 to 15 minutes for the first two to three hours, but this acute stage passes quickly and the bowels may then move only every three or four hours. The patient may have 10 to 12 loose stools in the first 24 hours, but in most cases the diarrhoea has largely subsided by the second day, though motions may continue to be loose for a few more days. The stools consist at first of faecal matter, later mainly of watery mucus. Babies' stools may be green and frothy. Flecks of blood are often seen, but frank bleeding is uncommon. If there is much blood in the stools, one should suspect a cause other than Sonne dysentery—intussusception in babies, or ulcerative colitis in adults. In many patients symptoms consist of nothing more than the passage of one or two loose stools, and the patient pays no attention to the incident until someone investigating an outbreak recalls it to his memory. Sometimes infection causes no diarrhoea at all, the patient being a symptomless excreter.

Vomiting is not common, though it may occur when the infecting dose is high, as in food- or water-borne outbreaks. Babies tend to vomit more than adults, and the vomiting and diarrhoea may lead to dehydration, though often babies are little upset by an attack of Sonne dysentery.

Usually Sonne dysentery is an afebrile disease, but sometimes there is a sharp rise of temperature to 102° F. or 103° F. (38.9° C. to 39.4° C.). In such patients the symptoms at onset may be deceiving with headache, generalized pain, and malaise. Sometimes there is neck stiffness and lumbar puncture may be carried out to exclude meningitis. Diarrhoea in such patients may not occur till after the first 12 to 24 hours of illness.

Abdominal discomfort is usually mild or absent, but sometimes pain is severe. Appendicitis may be closely simulated and appendicectomy be performed: usually the appendix is normal, but sometimes it is inflamed, possibly as a specific reaction to the presence of *Shigella sonnei*. In babies the possibility of intussusception must be kept in mind: if there is much blood in the stool or on the napkin, intussusception is a more likely diagnosis than Sonne dysentery. In the elderly

diarrhoea may be succeeded by severe abdominal pain, constipation, and general deterioration; these may be symptoms of acute mesenteric thrombosis.

Sonne dysentery is usually a mild disease, a nuisance rather than a serious illness. When the infecting dose is high it can be serious. I recall one woman with severe coffee-ground vomiting due to food-borne Sonne dysentery, and I have treated several elderly patients for tetany which developed within a few hours of the onset of a severe attack. In patients already debilitated by another disease, an attack of Sonne dysentery can be fatal—hence the reason for treating seriously an institutional outbreak, however mild the first cases may be.

Flexner and Shiga Dysentery

The illness caused by *Sh. flexneri* and *Sh. shigae* (*Sh. dysenteriae* type 1) may be no more severe than Sonne dysentery. Often the patient is much more acutely ill. Abdominal pain is present, the patient is febrile, and diarrhoea persists for most of a week. In more severe cases the patient's temperature rises to 101° F. to 103° F. (38.3° C. to 39.4° C.) and he rapidly appears toxic and dehydrated. He is flushed, anxious, and restless, with rapid pulse, pinched skin, coated tongue, and scanty urine. Diarrhoea is severe and the stool consists of blood and mucus. In most cases the illness persists for 10 to 14 days and then subsides; but in some there is a sudden flare-up of diarrhoea, with rapid death from dehydration and exhaustion, while in others symptoms drag on for weeks. Choleraic or gangrenous forms are usually caused by *Shigella shigae*. In the choleraic type the onset is acute with collapse and the passage of profuse watery stools, later replaced by altered blood. In the gangrenous form there are great abdominal pain and cramps and the passage of stools containing altered blood and sloughs. Both of these forms are usually fatal within a few days.⁶ They are not seen in Britain.

Treatment

General Measures.—Most patients with Sonne dysentery are only mildly ill and require little general treatment: if sent to hospital they are often over the worst before they get there. For patients more severely ill, especially patients with Flexner or Shiga infections, intravenous administration of fluid is often required, and this may be more important than the administration of antibiotics. For babies, fluid containing 4.3% glucose in 1/5 normal saline is satisfactory and intravenous administration is rarely required for more than 24 hours. Elderly adults with tetany usually respond to the infusion of a litre of isotonic saline, though sometimes the addition of 20% calcium gluconate may be required. For patients suffering from the severe forms of bacillary dysentery prolonged intravenous fluid administration may be required, and this should be controlled, if possible, by electrolyte estimations.

Drugs do very little to control diarrhoea, other than those which attack the bacterial cause. Mist. kaolin. et morph. is often prescribed, but I do not believe that it has any effect on the diarrhoea. It contains about 1/50 gr. (1.25 mg.) morphine hydrochloride in a dose. If morphine is thought desirable for a weary and anxious adult, it is much better to give a subcutaneous dose of 1/6 to 1/4 gr. (10 to 15 mg.). Other preparations containing agar, bismuth, or charcoal are in use, but their effect on diarrhoea is doubtful.

Specific Treatment.—Shigellae are sensitive to sulphonamides and to several antibiotics, but resistance develops quickly, and it is essential to know the sensitivity pattern of the organism one is treating, or at least the sensitivity pattern of the epidemic strain. This may vary from place to place. In Britain most strains of *Sh. sonnei* are at present resistant to sulphonamides, and it is useless to attempt to attack such strains with sulphon-

amides and wasteful to use mixtures of antibiotics and sulphonamides. If, however, the organism is sensitive to sulphonamides, the absorbable varieties are as effective as so-called non-absorbable sulphonamides. As much as 40% of sulphaguanidine may, in fact, be absorbed, and succinylsulphathiazole and phthalylsulphathiazole both release sulphathiazole in the bowel, and their activity may be due to this absorbable form: a drug which remains in the lumen of the bowel and does not penetrate the mucosa and submucosa can hardly be expected to attack shigellae in these sites. Sulphaguanidine and succinylsulphathiazole may be given in daily doses of 10 to 20 g., phthalylsulphathiazole 5 to 10 g., for five days. But it is just as logical to use an absorbable drug, and sulphadimidine in a dose of 1 g. every six hours for five days is one of the safest, for both the parent drug and its acetyl derivative are highly soluble in the urine.

Provided the organism is sensitive, streptomycin, neomycin, and nalidixic acid are all satisfactory drugs and are given by mouth. The dose of streptomycin for an adult is 2 g. every six hours, for young babies 0.5 g. every six hours. Neomycin adult dosage is 1 g. every six hours, 0.125 mg. for babies. Nalidixic acid dosage is 1 g. every six hours for adults, 0.15 mg. for babies. In each case the course lasts five days. Tetracycline may also be used if the organism is sensitive, but many are resistant. There can be no justification for using chloramphenicol. If, after any course, the faeces still give a positive culture the sensitivity of the organism must be determined again, for it may have become resistant to the drug, and it is useless to repeat the course. Another drug to which the organism is still sensitive must be tried.

Resistance to antibiotics has not so far proved a problem, and laboratory sensitivity reports correspond fairly well with clinical results, a situation very different from findings with salmonella infections, in which in vitro sensitivity results bear little relation to the in vivo efficacy of drugs. Infectious drug resistance may in the future cause trouble. In one outbreak of dysentery due to *Sh. flexneri* eight different resistance patterns to various antimicrobial agents were detected in shigellae isolated from the patients during the outbreak, and sensitivity patterns reported at the onset could not be relied upon as a basis for treatment throughout the outbreak.¹³ How serious such infectious drug resistance may prove remains to be seen.

As regards tests of bacteriological cure, the traditional three negative rectal swabs or specimens of faeces is a satisfactory standard in dysentery, provided there is an interval of a few days between the end of a treatment and the first test. Very few positive cases will be missed, and the few patients who do become positive after three negatives are, save in special circumstances, of little epidemiological importance, for it is the patient in the acute stage, not the carrier, who spreads the disease. Where the patient is a nurse or a food-handler or a baby who has to return to a residential institution, I usually require six or even 12 negative specimens.

Prevention

It is not possible in this space to discuss prevention, but the rationale of any preventive methods depends on the resistance of the organisms and the epidemiology of the disease. Essentially, prevention depends on blocking the spread of shigellae excreted in the faeces of one person from reaching the mouth of another. Where sanitation is primitive nothing short of major sanitary improvements is likely to be effective. Where sanitation is good infection may still spread from hand to hand, and prevention consists in breaking this contact. It is much easier to lay down rules than to carry them out. Sonne dysentery has been described both as a "highly preventable disease"¹⁴ and as "the commonest of the unpreventable diseases."¹⁵ It has also been stated that once it has gathered impetus "no convincing evidence has been produced that any deliberate measures

help to terminate an epidemic.”¹⁵ One may or may not wholly agree with this statement, but anyone who has tried to control an outbreak knows that there is some truth in it.

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TODAY'S DRUGS

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Treatment of Psychoneurosis

Anxiety states and symptoms are the most common psychiatric disorders encountered by practitioners, both in general practice and in general hospital outpatient departments. Anxiety may be an understandable reaction to a stressful situation; when this is resolved the anxiety will disappear. On the other hand, anxiety may be without apparent foundation, or out of all proportion to the supposed cause. Anxiety occurs as a symptom in almost any psychiatric syndrome or organic disease. It is essential to distinguish a primary anxiety state from one which is secondary to another psychiatric or organic disorder.

An anxiety state can present in a variety of ways. Prior knowledge of the basic personality of a patient with anxiety is helpful. An "inadequate" personality will react to relatively minor stress with excessive anxiety. The driving, capable personality will begin to develop overt anxiety symptoms only after prolonged and gradually overwhelming stress. Treatment must take the patient's personality into account, and an attempt should be made to help the patient reduce stresses which may be present. The value of tranquillizer and sedative drugs is to suppress symptoms and damp down tensions sufficiently to break a vicious circle and to help the patient to regain sufficient confidence for him to resolve the problem or conflicts behind his symptoms.

Barbiturates

In many cases the barbiturates are still unsurpassed in their ability to relieve anxiety, and they are far cheaper than tranquillizers. But they are apt to cause addiction in predisposed personalities, and a suicidal attempt with a barbiturate is more likely to succeed than with a tranquillizer.

In an acute panic attack a barbiturate in high dosage is probably the most effective treatment—for an adult 400 to 600 mg. of amylobarbitone sodium by mouth, with 100 mg. chlorpromazine if necessary, will produce deep prolonged sleep in 20 to 30 minutes. Subsequent treatment will depend on the circumstances.

The so-called medium-acting barbiturates, such as quinalbarbitone and amylobarbitone sodium, are the most useful both as hypnotics and as sedatives. They are particularly effective in the chronically tense individual with a reasonable personality. An effective sedative for an anxious or phobic patient is 50 to 100 mg. of amylobarbitone sodium up to three times a day. As tension is relieved it is sometimes replaced by a mild sense of euphoria. It is as well, therefore, to avoid giving barbiturates to a patient liable to become addicted. Some chronically tense patients may need to continue on such a dose continuously or intermittently for years. A number of phobic patients can be helped merely by the knowledge that they have 50 mg. of amylobarbitone sodium in their pockets to use in an emergency.

Longer acting barbiturates such as phenobarbitone are sometimes useful in the treatment of chronic anxiety states in patients who have always reacted to minor stresses with excessive anxiety. But acute anxiety does not respond well to phenobarbitone. The drug should not be used as a hypnotic. Phenobarbitone is a depressing drug, and its use is therefore contraindicated if there are signs of depression, particularly in older patients. Phenobarbitone is useful in children as a temporary means of reducing excessive excitement and hyperactivity and also as a hypnotic. Unlike adults, young children and infants will often sleep soundly on a small dose of phenobarbitone.

Compared with adults, children can tolerate relatively large doses of barbiturates, but they are not effective in children who are severely disturbed. A phenothiazine derivative such as promethazine (Phenergan), or one of the diazepam tranquilizers, is usually a better choice.

A common symptom of anxiety is difficulty in getting to sleep. Sometimes treatment of this symptom alone will effect an all-round improvement. Some patients displace all their anxiety on to difficulty in getting to sleep and work themselves into a state of panic as bedtime approaches. A hypnotic which ensures a good night's rest will break this pattern and lead to a lessening of anxiety; 200 mg. amylobarbitone sodium, or the equivalent dose of another medium-acting barbiturate, may be most satisfactory for this purpose. But sometimes a non-barbiturate hypnotic, such as diazepam (Valium) 10–15 mg., or glutethimide (Doriden) 250–750 mg., is more satisfactory. Where there is a tendency to waken frequently the hypnotic can be potentiated by adding chlorpromazine 50–100 mg. Promethazine is also a useful hypnotic in a dose of 25–75 mg.