Treatment of Sonne Dysentery

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Sonne dysentery still presents a problem in public health and general practice, and is one of the commonest of the treatable infectious diseases.

The average yearly notification of bacillary dysentery for the period 1954–63 in England and Wales was 34,661, and the number notified in 1963 was 31,759. Of the total of 32,626 isolations of dysentery organisms in 1963 98.2% were due to the Sonne strain. As a rule the clinical illness is mild and of short duration, but there may be grave illness in infants and in the elderly. In 1963 35 deaths were attributed to all forms of dysentery (Ministry of Health, 1964).

Management of patients with dysentery is normally the responsibility of the family doctor, but when the diagnosis is not clear, or the illness is severe or does not appear to be responding to treatment, the patient is often admitted to a hospital which has facilities for isolation and treatment. Cases occurring in nursery schools, orphanages, general hospitals or overcrowded homes, or among nursing staff and food-handlers, are also admitted.

It has been shown (Cruickshank and Swyer, 1940 ; Fairbrother, 1944) that of patients with Sonne dysentery treated symptomatically about 50% were excreting the organism in their stools two weeks after the onset of the disease, and 30% were still excreting it four weeks after the onset. The object of employing specific chemotherapy is to improve on this position as quickly and as cheaply as possible. The ideal drug for treating dysentery has been defined by Taylor (1957), who said: "What is required is a drug that is cheap and effective in quickly and permanently rendering an infected person negative, and which can be given in general practice to sufferers and their family contacts. The disease with which we are dealing is so mild that the drug used must be quite free from side-effects." During the last few years a number of different drugs have been used in the treatment of dysentery at Fazakerley Hospital, Liverpool, and one of our purposes has been to evaluate these drugs with respect to Taylor's criteria.

Material and Methods

The results of treatment of patients with Sonne dysentery admitted to Fazakerley Hospital between January 1958 and September 1964 are presented. In all, 1,392 patients were treated, and the age incidence is shown in Table I. The diagnosis was proved bacteriologically in all patients by the examination of rectal swabs. The patients were treated in hospital, and post-treatment swabs taken before discharge. In the same period six patients with dysentery due to *Shigella flexneri* were admitted, but these have been excluded from the report, although their illness was clinically indistinguishable from that due to *Shigella sonnei*.

TABLE I.—*Age Incidence of* 1,392 *Patients With Sonne Dysentery*

Age in years	0–	1–	5–	15+
No. of patients	265	720	212	195

In all cases supportive treatment was begun immediately after admission, as indicated. It included simple dietary measures, and occasionally intravenous fluids. Specific treatment was begun before the result of the rectal swab had been obtained if the illness was already bacteriologically proved—for example, when the patient was transferred from another hospital—or if the patient was ill. Otherwise specific treatment was withheld until a bacteriological diagnosis had been made.

The drugs used, and the dosages employed, are given in Table II. In all cases a "course" of treatment lasted for five days, and the drug was administered six-hourly. Tablets or capsules of the drugs were given to older children and adults, and suspensions and solutions were used in smaller children and babies. The dosages shown have not been strictly adhered to in all cases, individual variations being taken into account. For example, a large 14-year-old child would be given an adult dose.

TABLE II.—*Drugs and Dosage (in mg.) in the Treatment of Sonne Dysentery*

Age in Years	Streptomycin	Sulphaguanidine	Nalidixic Acid	Paromomycin	Tetracyclines	Chloramphenicol	Neomycin	Furazolidone
0–	250	250	150	125	62·5	62·5	62·5	50
1–	500	500	300	250	125	125	125	100
5–	750	1,000	600	500	125	125	Not used	Not used
15+	1,000	2,000	1,000	1,000	250	250	" "	" "

All doses given by mouth every six hours for five days.

Bacteriology and sensitivity testing was performed by the Liverpool Public Health Laboratory, and we are indebted to Dr. E. C. Armstrong for the following notes.

Rectal swabs were plated direct on to desoxycholate-citrate-agar (D.C.) and were then placed in selenite F broth ; after 16–18 hours' incubation these broth cultures were plated on to D.C. and the plates incubated for a further 24 hours. Strains were identified by biochemical and serological methods.

Sensitivity tests were carried out by the plate method, using nutrient agar which had been shown previously not to contain sulphonamide-antagonizing substances. The following diagnostic preparations were used: Mast sensitivity disks. Nalidixic acid (Negram), 30 μg. per disk. Evans Sentests tablets, of two concentrations, "high" and "low" according to the new formulation, for chloramphenicol, tetracycline, streptomycin, neomycin, and sulphonamide (sulphafurazole).

The amount of the agent in the reformulated Sentests is determined on the basis of controlled performance tests and not on extraction method. Labelling with antibiotic content would in some cases be misleading, as some of the antibiotics are absorbed by the inert base of metallic oxide used. The tablets are now made to conform to standards which coincide approximately with those recommended by the Food and Drug Administration of America. The concentrations formerly given were: chloramphenicol 40 and 100 μg. ; tetracycline 10 and 100 μg. ; streptomycin 20 and 80 μg. ; neomycin 10 and 100 μg. ; sulphonamide 0.1 and 1 mg.

Criterion of Cure

A rectal swab was cultured on three consecutive days, beginning 24 hours after completion of a course of treatment.

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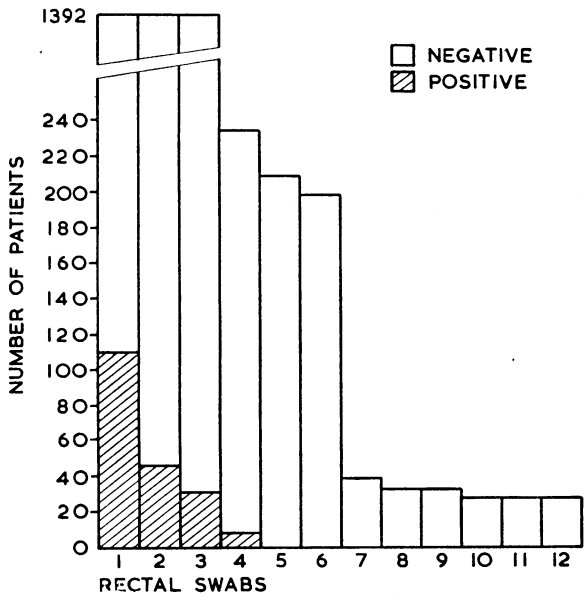
If all these were negative the patient was regarded as cured. If any one swab was positive treatment was counted a failure.

In 233 patients, who were food-handlers or nurses or patients awaiting transfer to general hospital, more than three swabs were obtained—usually six, and sometimes twelve—before the patient was discharged. In this group seven additional failures were found after three negative swabs—all on the fourth swab. In no case was a fifth or subsequent swab positive. These results are shown on the accompanying nomogram, which illustrates the distribution of the first positive swabs after treatment.



Distribution of positive rectal swabs after treatment.

Deaths

There were four deaths among the patients with Sonne dysentery in the period under review.

Case 1.—A man of 67, who was diabetic and had an old hemiplegia, was found on admission to have acute intestinal obstruction. His general condition made him unfit for operation ; he was treated conservatively, but died six days after admission. No specific treatment for dysentery was given. Permission for necropsy was refused.

Case 2.—A man of 82, this patient also had bronchopneumonia complicating chronic bronchitis and emphysema, and was incontinent of urine and faeces. He was treated with paromomycin and penicillin, but his condition deteriorated, and he died after eight days in hospital. Permission for necropsy was refused.

Case 3.—A male infant of 6 months, in very poor general condition on admission, was given intravenous fluids and whole blood. Neomycin was given by mouth. After two days chemotherapy was changed to intramuscular tetracycline as he could not retain oral neomycin, which was vomited together with small amounts of altered blood. After three days the antibiotic was again changed, this time for chloramphenicol, as the organism had proved resistant to tetracycline ; however, he died a day later. Necropsy showed a poorly nourished infant with aspiration pneumonia. Petechial haemorrhages were found in the stomach, and the lower ileum was congested and oedematous.

Case 4.—A male child of 1 year, who was in poor general condition on admission and who also had whooping-cough, was given oral tetracycline ; he was able to retain clear fluids. *Escherichia coli 0126* and *Sh. sonnei* were cultured from the stool, and polymyxin was added to the chemotherapy after two days. The *Sh. sonnei* was resistant to tetracycline, which was discontinued after three days. He appeared to be improving, but died suddenly on the fifth day after admission. Necropsy revealed no obvious cause for the sudden death. An intestinal swab yielded a profuse growth of *Sh. sonnei*.

Results of Treatment

The results are summarized in Table III. The effects of further treatment of those patients in whom the first course failed are not reported.

TABLE III.—*Results of Treatment of* 1,392 *Patients with Sonne Dysentery*

Drug	Success	Failure	Total
Streptomycin	867 (90%)	96	963
Streptomycin and sulphaguanidine	102 (89·5%)	12	114
Sulphonamide	5 (55·5%)	4	9
Nalidixic acid	99 (88·5%)	13	112
Paromomycin	47 (94%)	3	50
Tetracycline	39 (68·5%)	18	57
Oxytetracycline	3 (50%)	3	6
Chloramphenicol	12 (100%)	—	12
Neomycin	22 (43%)	29	51
Furazolidone	11 (61%)	7	18

Streptomycin orally was used throughout the seven-year period. Of 963 patients treated with this drug 867 (90%) were cured. This compares with Sangster's (1956) experience, when 86% of 1,111 patients were cured with the first course of treatment with streptomycin. A decrease in the number of patients who responded to a first course of treatment was noted at the beginning of 1963, and, whereas in the last three months of 1962 85% of patients treated with streptomycin were cured, this figure fell in the first three months of 1963 to 42%. After this the position improved again, and 86% were cured in the last quarter of 1963. The quarterly figures are shown in Table IV. These clinical results correlate well with *in-vitro* tests of sensitivity of the organism ; for while in 1960 of 120 strains tested all were found to be sensitive to streptomycin, in 1963 of 157 strains tested 26% were resistant. In the first eight months of 1964, of 115 strains tested only 8% have proved resistant *in vitro*, and there has been a corresponding improvement in the results of treatment with streptomycin. Except for one adult who could not tolerate oral streptomycin because of nausea, no side-effects were noted. It is clear that streptomycin gives consistently good results except when resistant strains emerge (Table V). Such strains are likely to emerge from time to time in any area, and W. M. Jamieson (personal communication, 1964), in Dundee, found a similar variation in the sensitivity pattern in 1958 coinciding with a decline in the efficacy of treatment with streptomycin. He also found that the results improved again in 1959 and 1960, as appears to have been the case in Liverpool in 1964.

TABLE IV.—*Results of Treatment with Streptomycin* 1962–3

Months		Success	Failure	Total
1962	1–3	29 (83%)	6	35
	4–6	54 (93%)	4	58
	7–9	28 (85%)	5	33
	10–12	23 (85%)	4	27
1963	1–3	5 (42%)	7	12
	4–6	27 (77%)	8	35
	7–9	32 (89%)	4	36
	10–12	30 (86%)	5	35

TABLE V.—*Results of Treatment with Streptomycin* 1958–64

Year	Success	Failure	Total
1958	108 (95%)	6	114
1959	121 (90%)	13	134
1960	205 (93%)	16	221
1961	178 (93%)	14	192
1962	135 (88%)	18	153
1963	94 (79·5%)	24	118
1964	26 (84%)	5	31

Streptomycin and Sulphaguanidine in combination were used in 1958 and 1959 only, and the cure rates were 89.5% in each year. This compared with 95% for streptomycin in 1958 and 90% in 1959. Furthermore, of nine patients given

sulphaguanidine or a soluble sulphonamide alone in 1958 only 5 (55.5%) were cured. As the combination of drugs appeared to confer no advantage over streptomycin alone, sulphaguanidine was not given after 1959. Sulphonamide resistance has for many years been recognized as an increasing problem in the treatment of bacillary dysentery (Garfinkel *et al.*, 1953 ; Adams, 1960 ; Turk, 1960). Of 120 strains of *Sh. sonnei* tested in 1960 88 were resistant and 10 only moderately sensitive to the drug, leaving 22 (17.5%) fully sensitive. In 1963 only 8% of 157 isolations were fully sensitive, and in the first eight months of 1964 only 3 (2.5%) of 115 isolations were fully sensitive to sulphonamides. Geddes and Sangster (1962) found 100% of 51 strains resistant to sulphonamides. These results strongly suggest that there is no longer any justification for using sulphonamides in the treatment of Sonne dysentery. They are contraindicated on the grounds of unnecessary additional cost, as well as the unpleasant side-effects which occur from time to time when soluble sulphonamides are used. It is interesting to note that they are still given prominence in some articles on the treatment of dysentery (Adams, 1960 ; To-day's Drugs, 1964), and also that 14 out of 20 proprietary antibiotic-containing mixtures listed in the September 1964 *Mims* recommended for the treatment of dysentery contain sulphonamides.

Nalidixic Acid (Negram) was provided by the manufacturers for clinical trial in 1964. It was given to 112 patients and cured 99 (88.5%). This compares with a cure rate of 84% for streptomycin in the same period (Table V). No side-effects were noted in any of our patients treated with this drug. All the 120 strains tested for sensitivity were found to be fully sensitive. We conclude that nalidixic acid is a useful alternative to streptomycin in the treatment of Sonne dysentery.

Paromomycin (Humatin) was used in 1963 when bacterial resistance to streptomycin was high. Given to 50 patients, it cured 47 (94%). This is similar to the experience of Geddes and Sangster (1962), who cured 91% of 34 patients, and that of Coles *et al.* (1960), who cured 25 (92%) of 27 patients, Paromomycin is poorly absorbed, and we observed no side-effects. It also appears to be a useful alternative drug to streptomycin.

Tetracycline was given to 57 patients, of whom 39 (68.5%) were cured. These indifferent results are undoubtedly due to increasing resistance of the organism to tetracycline. Abbott and Parry (1955) obtained a 96% cure rate with tetracycline, having encountered no drug resistance, while McKendrick and Medlock (1958) achieved a 94% cure rate. In 1960 17.5% of 120 strains isolated in Liverpool were either resistant or only moderately sensitive to tetracycline, and by 1963 39% of strains were resistant. In the first nine months of 1964 29% of strains have proved resistant or only moderately sensitive. This increase in resistance to tetracycline is matched by a rising failure rate in our patients, so far as can be seen from the small numbers treated. Because of this, and because of other objections to its employment as a routine, such as the possible development of staphylococcal enteritis, we have limited the use of tetracycline to those patients with a concurrent infection, at which the drug is primarily directed. For the same reasons, only six patients were treated with oxytetracycline, of whom three were cured. No side-effects were noted from either drug.

Chloramphenicol was given to 12 patients, and all were cured. The use of chloramphenicol in dysentery is restricted by fear of its dangerous side-effects in an illness which is usually trivial, although in none of our patients have side-effects been noted. Of 392 strains tested in 1960, 1963, and 1964 none was found to be resistant to the drug. We feel there is a place for chloramphenicol in the treatment of patients who are dangerously ill and cannot retain a reliable oral antibiotic.

Neomycin was used mainly in babies with a diagnosis of gastro-enteritis who were ill on admission. It was given to 51 such patients, who in fact had Sonne dysentery, and bacteriological cure was achieved in only 22 (43%). This is little better than the expected result with supportive treatment only, and is similar to the results found by Abbott and Parry (personal communication, 1964) in 1956, when 50 patients were treated with neomycin and a cure rate of 50% was obtained. It contrasts with the experience of Geddes and Sangster (1962), who cured 30 (88%) of 34 patients with this drug and concluded that neomycin was as effective as streptomycin or paromomycin in Sonne dysentery. The sensitivity to neomycin of 270 strains of *Sh. sonnei*, which included those strains isolated from the patients who eventually received the drug, was tested and all except two strains were fully sensitive. It is difficult to explain the poor results with neomycin, which we have found to be most effective in the treatment of infantile gastro-enteritis due to pathogenic *E. coli*. It is clear, however, that drug resistance was not the cause of failure.

Furazolidone was given in a small trial in 1959 to 18 patients ; of these 11 (61%) were cured. This compared with a cure rate of 90% for streptomycin in the same year (Table V). The trial was not extended because of these poor initial results.

Summary and Conclusions

The results of treatment with various antibiotics of 1,392 patients with bacteriologically proved *Shigella sonnei* dysentery are presented.

Oral streptomycin is the drug of choice in the specific treatment of dysentery. The sensitivity of the prevailing strains of the organism to streptomycin should be determined from time to time so that temporarily increased resistance will be found when it occurs, and another drug can be substituted.

Nalidixic acid (Negram) and paromomycin (Humatin) are both as effective as oral streptomycin in clearing the infection, but are more expensive. Either can be used as a substitute for streptomycin if it is found that the prevailing strains of *Sh. sonnei* are becoming increasingly resistant to this drug.

The tetracyclines are no longer very useful in the treatment of *Sh. sonnei* dysentery in this area because of the prevalence of resistant strains. Chloramphenicol should not be used routinely because of the danger of serious side-effects.

Neomycin and furazolidone do not give results good enough to warrant a recommendation for routine use in this disease.

The sulphonamide drugs, either alone or in combination with streptomycin, appear to have little if any effect in curing the disease, and it is doubtful if the continued use of this group of drugs in the treatment of Sonne dysentery can be justified.

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