SONNE DYSENTERY

AN APPROACH

Thesis submitted for the Degree of

Doctor of Medicine

by

R. C. MACLEOD, M.B., Ch.B., D.P.H., D.T.M. & H.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

O B J E C T

To assess the Relative Value of the commonly used methods of treating Sonne Dysentery and to expound a rational method of coping with this disease.

SECTIONS

SECTION 1.

PREAMBLE AND LAYOUT OF THE INVESTIGATION.

The prevalence of infection with Shigella Sonnei was first recognised by Sonne in Denmark in 1913.

Dysentery was, for many years in this country, regarded as a disease of exotic origin (Reports of Chief Medical Officer up to 1925), but in 1933 the Chief Medical Officer wrote that "... it is now well recognised that bacillary dysentery due to Flexner and Sonne infections is endemic in this country".

Through the intervening years the bacteriological picture has changed, with Sonne infections becoming predominant (Glover 1947). He also stated that of 7,245 strains of dysentery bacilli isolated from patients suffering from the disease 87.5% were Shigella Sonnei.

Glover (1949) describes the great variations in notifications since 1925. Notifications (16,278) in 1945 being forty-seven times those for 1925, and the numbers falling to a low point in June 1947 (3,761) but rising to a third of the 1945 peak in 1948 (5,479). He goes on to state that the records of the Public Health Laboratory Service suggest that the great wave of incidence, its subsidence, and its subsequent rise were, in the main, due to variations in the frequency of infections by Shigella Sonnei.

Sonne Dysentery is similarly prevalent in Western Europe and America.

Roelcke (1941) states that of the 825 intestinal pathogens isolated in the Heidelberg Laboratory from 1932 to 1940, 56% were Shigella Sonnei. The increased incidence of dysentery in Europe after the 1939 to 1945 war was described by Stowman (1945) who showed that, in eight European countries, the dysentery level was 2.1 times the pre-war level, and that the Netherlands had had a fourteen fold increase mostly due to Shigella Sonnei.

American reports also show an increase in the incidence of bacillary dysentery, including Sonne infections. Felsen and Wolarsky (1953) stated that there had been a real increase in the amount of bacillary dysentery in the population, the reported incidence being but a fraction of the actual number of cases, though in 1934 on the occasion of an outbreak of Sonne Dysentery in a New York Hospital, it could be stated that the disease was practically unknown in the United States (Felsen 1934).

A disease existing in so many countries in such proportions must, even when the symptoms are generally mild, be regarded as of considerable importance, and the cases are not always mild. Nisbet (1938) reported an epidemic of 162 cases with 9 deaths in this country, and in Japan 40% of

a severe dysenteric infection known as EKIRI with a case mortality of 67.2% is due to infection with Shigella Sonnei. (Weil 1943). Lewis and Claireaux (1951) reported some very severe cases occurring mainly during the war years in this country.

The notifications of Dysentery in Liverpool over the years 1944 to 1953 are shown in Table I.

TABLE I

pulation	Year	Total Notifications of Dysentery	Proved Sonne	Others
66,230	1944	259	209	Flexner 50
81,120	1945	511	334	Flexner 173; Schmitz 1; Clinical 3.
34,620	1946	158	80	Flexner 76; Clinical 2.
53,340	1947	215	43	Flexner 37; Newcastle 135.
91,800	1948	285	61	Flexner 104; Newcastle 115; Schmitz 1; Clinical 4.
00,800	1949	444	388	Flexner 46; Newcastle 1; Clinical 9.
02,300	1950	200	163	Flexner 10; Clinical 27.
84,800	1951	553	498	Flexner 2; Bacillary Shiga 1; Clinical 44.
91,500	1952	300	291	Flexner 3; Clinical 6.
89,500	1953	755	730	Flexner 1; Newcastle 1; Clinical 22.

Taking the figure given by Hardy and Watt (1945) of 9.1 convalescent or passive carriers to each current case, the number of infected persons in the City in 1953 might be 6,500, but even this is far too small a figure as it is reasonable to suppose that with the mild symptoms prevailing and to be described in later pages, only a fraction of the cases can come to the notice of any doctor.

The efficacy or otherwise of the treatment of such a prevalent disease is obviously of importance in the maintenance of public health.

There is very close liaison in Liverpool between the Physician Superintendent of Fazakerley Infectious Diseases Hospital and the Medical Officer of Health's Department, where I deal with matters relating to Infectious Disease and when, in 1951, it appeared from bacteriological results in hospitalised and non-hospitalised cases that the sulphonamides were losing or had lost their effect, it was decided to begin an investigation into the comparative merits of various sulphonamides and antibiotics in the treatment of Sonne Dysentery. The investigation was also planned to cover such questions as the usefulness or otherwise of hospitalisation and what social conditions underlay the spread and continuance of the infection.

The investigation could not have been carried out without the interest and whole-hearted support of Dr. A.B. Christie, who afforded every facility in his hospital over a period of almost two years.

The layout of the investigation was as follows:-

Six drugs were on trial, namely: sulphathalidine, sulphasuccidine, sulphaguanidine, sulphadiazine, chloramphenicol, and oral streptomycin. A series treated with terramycin was also begun, but owing to the small number of cases admitted over a period, this series was stopped when six cases only had been treated.

Cases which had had treatment pre-admission were not included in the trial and cases admitted from other hospitals with a diagnosis of Sonne infection were not accepted as such until reported positive by the City Laboratory. There was one hospital excepted from this rule, as it had its bacteriology done by the City Laboratory.

Treatment was not, with the single exception noted, begun before a positive rectal swab had been obtained. Rectal swabs were taken daily, Sundays and public holidays excepted, and were examined by the City Laboratory which not only reported on the presence or absence of Shigella Sonnei, but gave a report on the number of colonies found on direct plating. When it was necessary to culture the organism in selenite broth to recover it, this fact was also given. Under five colonies was recorded as very small numbers, five to fifty as small numbers, fifty to two hundred as moderate numbers, and over two hundred as large numbers.

It was hoped by this means to obtain some guide, other than the mere presence or absence of the organism, to the course of the infection under treatment, and also some idea of the response of light and heavy infections to treatment.

It was realised, of course, that the method of taking the swab would have a great bearing on the results.

The cases as they were admitted to the wards were placed in groups of three according to a set rota, each group consisting of two cases on one or other of the drugs, and one on Mist.Kaolin, for example:

(1) sulphaguanidine (2) sulphasuccidine (3) Mist. Kaolin.

Three wards were at one time admitting cases, but this shrank to one and some re-arrangement of groups was, from time to time, necessary.

Patients were not discharged until twelve successive negative rectal swabs had been obtained.

The ex-patients were followed up after discharge. Two rectal swabs per week for four weeks was aimed at, and this was extended according to results. Illnesses in other members of the family were recorded, and where the ex-patient became an excretor again, the family was swabbed or stooled when possible. In the later stages of the investigation, the family was stooled as soon as the case was confirmed bacteriologically.

When the patient was a child, the history of previous illnesses and whether or not the child was breast fed was noted, and also whether or not the child was upset by its stay in hospital.

Social particulars were gathered under the following headings:-

(1) Type and size of home;
(2) Numbers in home;
(3) Sleeping arrangements;
(4) Provision of bed clothes;
(5) Cleanliness;
(6) Standard of mothercraft;
(7) Mother at work or not;
(8) Father's occupation, wages and social grade.

SECTION 2.

THE SULPHONAMIDES.

The rise and fall in the belief in, and the efficacy of the sulphonamides in the treatment of Sonne Dysentery can be traced quite clearly in the literature.

Libby and Joiner (1940) found sulphathiazole more effective than sulphapyridine and sulphanilamide against the colon - typhoid - dysenteric group of organisms and suggested its use in the dysenteries.

Marshall (1941) reported on the usefulness of sulphaguanidine in producing bacteriological cure in bacillary dysentery. He was successful in fifteen out of seventeen cases. Poth (1942) reported that succinyl

sulphathiazole had a marked bacteriostatic effect against strains of Shiga, Flexner and Sonne Dysentery bacilli. Hardy and Watt (1942) found that sulphaguanidine cleared up a mixed series of 51 cases of Flexner and 6 cases of Sonne infection in ten days, while 76% of the controls remained positive. Their dosage was six grammes T.I.D. for an adult or .3 grammes per kilo per day for four days. One case, however, was still positive at the end of 22 days and after 330 grammes of the drug.

A Public Health Laboratory Service Report (1942) describes an outbreak of Sonne dysentery in a nursery school where there were 13 cases, two of which died, and ten symptomless excretors including three nurses. They were treated with sulphaguanidine, the clearance criterion being three negatives at first, later eight consecutive negatives in four weeks or six negatives in four to six weeks in hospital. Dosage of sulphaguanidine was 1 gramme twice daily for three to four days. Nine cases cleared in between 0 - 9 days; two in 10-19 days. Nine carriers cleared in 0 - 9 days and one in 36 days. Two cases excreted intermittently for 2 - 3 months respectively, and were frequently positive after three negatives. Failure with sulphaguanidine thus occurred even early in its use in Sonne Dysentery.

Yannet, Leibovitz and Deutsch (1942) used sulphathiazole in an epidemic of Sonne Dysentery involving 44 cases and 13 carriers. 27 were treated with sulphathiazole, 3-6 grammes for four days. Diarrhoea continued for $1.5 \pm .2$ days, and in the controls for $2.9 \pm .4$ days. However, in the treated cases 33.9 days lapsed before the first negative specimen was obtained and 19.7 days in the controls. These findings do not appear to have been repeated.

Hoagland, Harris and Raile (1943) unlike some earlier authors quoted reported complete success with sulphaguanidine and also sulphasuccidine in a mixed group of Flexner and Sonne carriers, thirty of whom were treated with sulphaguanidine and thirteen with sulphasuccidine. The dosage was 30 grammes per day for six days and the follow up was thorough, an average of eleven negative swabs being obtained over a 17 - 60 day period.

Hardy and Cummings (1943) reported on 21 cases (mixed) of Sonne and Flexner infection treated with sulphadiazine found that all temperatures became normal in 24 hours. On the second day 67% had no more than two stools and these looked normal. The rest became normal in 3, 4 or 5 days. There was general clinical improvement in 6 - 12 hours even in critically ill infants, and all recovered. The authors found that sulphadiazine gave better results than sulphaguanidine.

Isinoff and Goldstein (1943) on the other hand, treated cases occurring in an orphanage with sulphathiazole and sulphadiazine at the rate of 1 grain per pound and with sulphaguanidine and sulphasuccidine at the rate of two grains per pound for an average period of four days, and found that all the drugs seemed reasonable effective, but that sulphadiazine was somewhat less so than the others. Out of the 83 cases involved, eight were left positive after treatment. Of these, six cleared on a course of a different sulphonamide.

Adams and Attwood (1944) reported a complete failure with sulphaguanidine and sulphasuccidine in Sonne dysentery. Of 251 cases of dysentery occurring in an Army camp they stated that 10% were Sonne dysentery and that some of the more severe illnesses were due to Sonne. Neither sulphaguanidine or sulphathiazole benefitted the 23 cases of Sonne and the symptoms were not affected. The stools remained positive for as long as six weeks.

Hardy and Watt (1944) reported that they found that cases and carriers of Sonne dysentery responded less well than those of other types of dysentery to sulphonamides and that poorly absorbed sulphonamides were no more successful than the others. They agreed with Brewer in finding that sulphasuccidine was, in their opinion, better than sulphaguanidine in Sonne dysentery.

Osborne and Jones (1944) however, found only eight out of 71 cases treated with sulphaguanidine resistant.

Fairbrother (1944) in a series of 92 cases of Sonne dysentery treated 76 by rest in bed, saline porridge, light diet and no sulphonamides. 52% gave 22 consecutive negative rectal swabs at the end of the second week. Where infection persisted the excretion was often intermittent. Two persistent carriers excreted the organisms for nine months in spite of repeated courses of sulphaguanidine and sulphasuccidine. In the earlier series Fairbrother found the Shigella Sonnei reappearing after three negative specimens.

Painton and Hautman (1945) reported on 181 cases in a U.S. army camp, stating that on treating 33 patients symptomatically only, 21 on 4 grammes sulphaguanidine daily for 7 days; 7 on 8 grammes sulphaguanidine for 7 days; 71 on .25 grammes sulphasuccidine per kilo daily for 7 days; and 49 on polyvalent dysentery bacterio phage for 2 days, and on beginning clearance examinations three days after stoppage of treatment and on the ninth day in controls, they found that sulphasuccidine gave 1.5% failures, large doses of sulphaguanidine one failure in the 7 cases, and that there was no significant difference between the results achieved with bacteriophage, small doses of sulphaguanidine, and with symptomatic treatment only each giving 18% to 24% failures.

Swyer and Yang (1945) compared the action of sulphanilylbenzidine, sulphanilylamidobenzamide and sulphasuccidine mainly on convalescent carriers in Sonne dysentery, giving a five-day course according to weight, six grammes being given for a 14-pound infant, up to 44 grammes for an adult. Daily rectal swabbing was done in the case of the first drug, and rectal swabbing each second day in the case of half dosage, and of full dosage in the second drug and in the case of sulphasuccidine. There was bacteriological cure in 1.8 days in 38 out of 41 patients on the first drug, cure in 2.5 days in 29 out of 30 patients on half dosage in the second drug, cure in 3.6 days in 71 out of 82 patients on full dosage if the second drug, and cure in 2.4 days in 17 out of 26 patients on sulphasuccidine. Treated cases were

followed up for 14.8; 10.9 and 13.2 days respectively. In four failures Sonne re-appeared after 4, 6, 8 and 14 consecutive negative faecal specimens over 2 - 5 weeks. This was suggested to be due to ward re-infection. Absorption from the gut in the case of the first two drugs was midway between that for sulphaguanidine and sulphasuccidine. There was some intermittent nausea with the first two drugs, but no apparent effect on the leucocytes.

Hardy (1945) reporting on the relative efficiency of ten of the more absorbable sulphonamides in a series of 1,423 cases and carriers (no infants) of which 382 were Flexner, 246 Schmitz, and 795 Sonne infections found that on giving the drug six-hourly with a double dose at the start, that Sonne was least affected. Of 621 cases infected by a highly resistant strain, 19% were still excreting after 7 days. The best drugs were sulphadiazine, sulphapyrazine and sulphasuccidine. Sulphathalidine was much less effective. Amongst the least effective was sulphaguanidine. He recommended sulphadiazine first and sulphasuccidine second for treatment. He thus in recommending sulphasuccidine supported Swyer and Young (1945) Painton and Hautman (1945) Hardy and Watt (1944) Brewer (1944), Hoagland (1943) and Isinoff (1943), but conflicted with Fairbrother (1944). Fairbrother, however, illustrated the rapid natural disappearance of the S. Sonnei in most cases and the long continued excretion in a small percentage.

Hardy's first choice was, however, sulphadiazine which was also recommended by Hardy and Cummings in 1943, but regarded as less effective than sulphaguanidine and sulphasuccidine by Isinoff (1943).

Watt (1945) also found Shigella Sonnei affected by sulphadiazine, sulphapyrazine, and sulphamethazine, than other types. He also reported that the last two were too toxic for routine use.

Hardy (1946) in assessing sensitivity of Shigella Sonnei to sulphadiazine reported that 54% of the strains required more than 5 micrograms per 100 ml. of the drug to inhibit. By comparison, Flexner strains only required 1 microgram. Some strains of Shigella Sonnei were not inhibited by 100 micrograms per 100 ml. and were thus completely resistant. He recommended sulphadiazine for treatment, stating that it gives rise to few toxic reactions and is one of the most effective drugs in the treatment of cases and carriers.

Vollum and Wylie (1946) in an outbreak of Sonne in two preparatory schools treated ten cases at first with 6 grammes of sulphasuccidine daily for five days. Nine cleared. All however became "re-infected". All the boys in the other school (37) were cleared by sulphasuccidine, and the 11 cases left in the first school were cleared by another course of sulphasuccidine. No tests of clearance are given.

Tateno (1950) in Japan investigating the resistance of Sonne organisms to sulpha drugs reported that:-

1. Most cases occurring and organisms isolated in 1950 were resistant.

2. Strains requiring more than six days to disappear from the stools were all resistant in vitro.

3. Resistance increases relatively fast in vitro, but in vivo, even after 7 days, only one ninth of the strains showed an increase.

4. The presence of sulphonamide resistant strains early in 1947 and even in earlier years is suggested.

Cooper and Keller (1950) reporting on 5 cases of Sonne dysentery occurring in a unit of a children's hospital over ten days, stated that all the children had been in the hospital for some 8 - 135 days prior to onset, and that sulphadiazine caused the fever to subside in 1 - 5 days. The drug was continued for 7 days, but in all cases the stools continued positive up till 12 days when treatment was changed to chloramphenicol. All the strains isolated were highly resistant to sulphadiazine, but sensitive to chloramphenicol.

Boyd (1951) stated that in bacillary dysentery the sulphonamides still retained their value.

Tateno (1951) reported that 80% of the Shigella strains isolated were sulphonamide resistant, but sensitive to streptomycin, chloramphenicol, terramycin, and aureomycin. Concentration - 10 microgrammes per millimetre.

Strang (1951) gave prophylactic sulphasuccidine in a day nursery where 12 out of 105 children were reported to be excreting the organism. The course was 6 grammes per day for 7 days. No new cases were reported after the completion of the course. All children were still positive, but two had discontinued the tablets several days before the elapse of the seven days.

Against this failure, Roberts (1951) states that he cleared 46 children in a rural school epidemic with sulphasuccidine.

The monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service (1953) contained a report on an outbreak of Sonne Dysentery in a Village Settlement. Ten persons were not cleared by sulphaguanidine and sulphasuccidine. Nine were given oral streptomycin but cleared no more rapidly than the one not so treated. It was suggested that the giving of streptomycin to the inmates for their tubercular infection might have had something to do with the resistance to the drug.

Ross (1954) in reporting on Sonne Dysentery in Day Nurseries found children becoming infected in spite of prophylactic courses of sulphasuccidine and sulphathalidine. Three staff members treated in

hospital with apparently a course of sulphathalidine (6 days) followed by one of oral streptomycin (3 days) were also found still to be excreting S. Sonnei.

The continued excretion following sulphonamides is not surprising as, if the seven strains of S. Sonnei tested for sensitivity were representative, the organisms were all resistant to the sulphonamide drugs used in a concentration of 10 micrograms/100 ml. It is, however, contrary to general experience that three persons all treated with oral streptomycin should remain excretors.

Presumably the conflict on the question of the efficacy of the various sulphonamides was due to their use against strains of differing sensitivity, to differing courses of treatment and to differing clearance standards resulting in different estimates of success or failure.

Some writers seem to be arguing against their own facts in continuing to advocate the use of sulphonamides where they themselves report that the strain of Shigella Sonnei they are dealing with is resistant to these drugs.

CHLORAMPHENICOL AND ORAL STREPTOMYCIN

These two drugs have only been used fairly recently in the treatment of Sonne dysentery. They had, of course, been used earlier in the other Shigella infections.

Hardy and Halbert (1948) in treating a series of cases due to Shigella Flexner Type 'Z' found that streptomycin and sulphadiazine were both very effective, but that streptomycin would clear up cases resistant to sulphadiazine. They found no significant toxic reaction to the streptomycin. The authors note that with streptomycin all cultures were negative on the sixth day following treatment, but by the fourteenth day, six out of the 37 patients had had a recurrence of positive cultures, and two additional recurrences took place in the following week. Dosage did not affect this result. However, Philbrook, Barnes, McCann and Harrison(1948) in dealing with 14 cases and 46 asymptomatic carriers infected by sulphonamide resistant Flexner Type 'Z' strain, did find that large doses of oral streptomycin were very much more effective than small doses. Two courses of 1.5 grammes oral streptomycin daily for three days had no effect, whereas 30 grammes of oral streptomycin over ten days was effective. They observed the patients for a period of up to 154 days, taking 5 swabs per week and they found that the number of consecutive negative specimens between positive specimens varied from 1 to 37 with a mean of 12.6. They advocated 20 negatives for clearance.

Ross, Burke, Rice and Bischoff,(1949) in comparing the results of treating Shigella Enteritis with oral streptomycin (34 cases) Aerosporin (16 cases) and sulphadiazine (20 cases) found them all about equally effective, but recommended the use of streptomycin as it could be used more safely than sulphadiazine in the tropics and could be used with resistant strains.

Ross, Burke, Rice and Stevens (1950) in treating Shigella Enteritis with chloramphenicol, oral streptomycin, and aerosporin, found them all effective to about the same degree. In 35 cases treated with chloramphenicol at the rate of 250 mgms. 4-hourly for an average of 8.6 days, the faeces became negative in 36 hours, in 33 out of the 35 cases. In the other two, it became negative in between 2 to 6 days. The cases were clinically improved about the same time. The average total dosage was 11.5 grammes.

Cooper and Keller (1950) reported that chloramphenicol cleared up five cases of Sonne dysentery due to sulphonamide resistent S. Sonnei. All stools were negative in an average of four days. The range of chloramphenicol blood levels was 1.6 to 25 micromilligrammes per millilitre of serum.

Tatino (1951) working in Japan found that:-

1. About 80% of the Shigella strains isolated were sulphonamide resistant, but sensitive to streptomycin, chloramphenicol, terramycin, and aureomycin, at concentrations below ten micromilligrammes per millilitre.

2. Streptomycin was the most active; chloramphenicol and terramycin next, and aureomycin least so.

3. Streptomycin alone was bacteriicidal, whereas the others alone or in combination were bacteriostatic.

4. The highest grade of resistance was acquired against streptomycin, whereas to chloramphenicol, terramycin and aureomycin strains became moderately or only slightly resistant in vitro. Anti-biotic dependent micro-organisms were obtained in the case of streptomycin only.

5. The presence of streptomycin resistant micro-organisms among a large number of sensitive organisms was demonstrated.

afaunus?

Hardy, Mason and Martin (1951) dealing with dysentery in troops in Korea, the infecting being mainly Flexner IV and Flexner III (Z) found that the antibiotics chloramphenicol, terramycin and aureomycin were each superior to the sulphonamides. The clinical superiority was as marked as the bacteriological, the patients being relatively free of complaints within 24 hours. The recommended dosage for all three antibiotics was an initial 2 grammes with 1 gramme at 12 and 24 hours thereafter. The clearance rate for patients on non-specific or sulphonamide thereby was approximately 10% per day. With the antibiotics, on the other hand, at the end of 25 hours the proportion which had changed from culturally positive to negative were, for aureomycin 56%, chloramphenicol 67%, and terramycin 68%. Of 225 Shigella strains isolated, 60% were resistant to sulphadiazine. One case was resistant to terramycin, four to chloramphenicol, and 23 to aureomycin.

Ross, Burke and Rice (1952) investigated the use of chloramphenicol palmitate in infants and children. They found that the drug itself was inert, but was hydrolised to the active form in the intestine. Blood levels were lower but better sustained than with chloramphenicol itself. They recommended a daily dosage of 100 to 150 milligrammes per kilogramme in four or more doses. They stated that clinical results were satisfactory, and that there were no toxic effects.

McFadyen and Stewart (1952) used chloramphenicol with sulphadiazine as control in a series of cases of Shigella dysentery (Flexner). They treated 96 cases with chloramphenicol and 92 with sulphadiazine. The age and sex of the patients was similar. The patients treated with chloramphenicol were given an initial dose of 30 milligrammes per kilogramme and thereafter 30 milligrammes per kilogramme daily in divided doses four-hourly. This was continued for three days after the first negative stool. The sulphadiazine group were given 2 grammes of sulphadiazine and thereafter 1 gramme four-hourly. In both cases this was continued for three days after the first negative stool, or in the case of sulphadiazine until 30 grammes had been given. Stool cultures were made daily until three consecutive negative findings were obtained. Sigmoidoscopy was done in all cases after cessation of the acute diarrhoea.

With chloramphenicol the average time required for the disappearance of the organism from the stool was 16 hours. Stools of all patients in this group were negative four days after the start of treatment. In the sulphadiazine group, 9 patients had positive stools at the end of the course of 38 grammes. In eight of these, sensitivity tests showed the organism to be resistant to sulphadiazine. Chloramphenicol cleared up these eight cases, the ninth case was cleared by a second course of sulphadiazine. There were no relapses in either group but, of course, it should be noted that only three negative specimens were obtained.

The average total dosage of chloramphenicol was 9.5 grammes, the range being 7.75 to 16. Five patients developed mild pruritis, which rapidly disappeared on cessation of treatment. In the sulphadiazine group one patient had severe haematuria on the fourth day and later developed acute intravascular haemolysis with haemoglobinuria.

Forbes (1953) in a sensitivity study on Shigella Sonnei found that at a concentration of 10 microgrammes per millilitre streptomycin exerted bactericidal action on Shigella Sonnei killing all organisms in less than five hours, whereas chloramphenicol, aureomycin and terramycin were essentially bacteriostatic. He showed that streptomycin produced resistance in Shigella Sonnei strains more readily than did other antibiotics. Chloramphenicol less favoured this development.

MacLeod (1953) (unpublished) in an outbreak in a residential school where eleven cases and ten carriers were discovered, found nineteen of them still excreting S. Sonnei after a five-day course of sulphatriad. All twenty-one were then given a five-day course of chloramphenicol and nineteen then produced eight consecutive negative rectal swabs over six weeks. The other two were transferred elsewhere after three negative swabs. The dosage of chloramphenicol was that used in this investigation.

Forbes treated 16 cases and one carrier with oral streptomycin, five grammes twice daily for two to three days. He states that clinical cure was achieved within 24 hours of beginning treatment, and bacteriological cure as judged by an average of 4.3 negative stools, was prompt and complete in all but one case. This case became negative later. No case relapsed clinically or bacteriologically during the follow-up period which, in some cases, was as long as six months. He also stated that the drug cleared up a case which had not cleared up on chloramphenicol. He states, however, following Welch(1950), that streptomycin is not absorbed from the bowel. This I shall attempt to disprove.

Gray (1953) in discussing the effect of chloramphenicol in the gut, with particular reference to salmonellae infections, stated that"it would appear that 'some excretors' could only be rendered free by the use of some other antibacterial compound, the absorption of which is not as complete as that of chloromycetin". This may also apply to carriers of other organisms. "It was found that the maximum stool concentration of chloromycetin is reached on an intake of 75 milligrammes per kilogramme per day".

The toxicity of chloromycetin has been reviewed in this country by Hodgkinson (1954) and he states that:-

1. In adults the total dose should not exceed 26 grammes.

2. In children the total dose should not exceed the equivalent of 100 mgms. per kgm. of body weight daily for seven days.

3. The length of treatment should not exceed ten days.

The American Council of Pharmacy and Chemistry reported in 1954 that: "Because of the occurrence of serious and fatal blood dyscrasias it is advisable to restrict the use of chloromycetin to the treatment of typhoid fever and other serious infectious diseases caused by organisms controlled by chloromycetin but resistant to the other antibiotics or other form of treatment".

It has been pointed out by Spears (1954) that chloromycetin palmitate yields lower serum and urine levels and higher stool levels than does the crystalline form.

It would appear that it is, therefore, safer to use in children, and it was used for the younger age groups in this investigation.

Stocks (1954) has shown the usefulness of streptomycin in controlling an outbreak of Sonne dysentery and in clearing up cases which remained bacteriologically positive after a course of sulphonamide. His article does not show the number of negative specimens required before clearance was presumed; also the clearance of cases treated at home in his outbreak took considerably longer than that of cases treated in hospital, both in this investigation and in others. He also quotes in a letter to The Medical Officer following some correspondence on his article, that

virtually all the strains of Shigella Sonnei in his area were found to be resistant to sulphonamides in vitro. He adds that in other areas where the predominant strain was found to be sensitive, results of treatment with sulphonamides were far from satisfactory.

White, Bell, Bone, Depsey and Lee (1945) in their search for an ideal drug, stated that:-

> "...the idea was to find the drug which would be active in the gut and in the gut wall. Such a drug would need to be highly soluble at intestinal PH values and be absorbed and excreted in such a way as to maintain a high intestinal and a moderately low blood concentration. Ready solubility in urine is also necessary for safety..."

SECTION 3.

RESULTS ACHIEVED AND COMPARISON OF RESULTS ACHIEVED IN THIS INVESTIGATION.

The sensitivity of strains of Shigella Sonnei in Liverpool during the years 1953 and 1954, to the drugs used is shown in Table I. The tests were largely done at the City Laboratory (Professor Robinson and Dr. McEntegart) but a number were done in the Newsham General Hospital Laboratory (Dr. Blewitt and Mr. Spencer).

It was not possible to get sensitivity tests done on the organism isolated from every case owing to laboratory difficulties, but some were done on strains from cases in each group. These are shown in Table IA.

It will be noted in Table I that Terramycin occupies a middle position between the other two antibiotics and the sulphonamides. Although the Terramycin treated group was not proceeded with, the results in the six cases so treated are given in the tables and tend to bear out the drug's sensitivity position.

Table II shows the age groups of patients treated. Though not exactly balanced the numbers under ten years for Kaolin, Chloramphenicol and Streptomycin are 42 (89%), 45 (88%), and 41(82%) respectively. The number under ten in the sulphonamide group was 59 (93%). The individual sulphonamide groups were stopped before completion for reasons to be given. The combined group is rather larger at 63 patients than the others, but not markedly so.

TABLE I

SENSITIVITIES

LIVERPOOL

1953 and 1954

	Resistant	Slightly Sensitive	Moderately Sensitive	Sensitive
Sulphonamides	79	3	1	-
Terramycin	16	1	30	78
Chloramphenicol	-	-	-	135
Streptomycin	2	-	9	124

TABLE IA.

SENSITIVITY TESTS.

S. Sonnei ex patients in this investigation.

	Resistant	Slightly Sensitive	Moderately Sensitive	Sensitive
Sulphonamides	12	3	-	-
Chloromycetin	-	-	-	63
Streptomycin	-	-	5	58
Terramycin	1	2	14	46

TABLE II

AGE GROUPS

	Under 1	1-2+	3-4+	5-9+	10-14+	15-29	30-44	45-	Total
Mist. Kaolin	4	18	10	10	1		1	3	47
Sulphathalidine	2	8	5	4			1	1	21
Sulphasuccidine	3	5	1	5		2			16
Sulphaguanidine	1	3	5	4					13
Sulphadiazine	1	5	3	4					13
Total Sulphonamides	7	21	14	17		2	1	1	63
Chloramphenicol	5	20	14	6	3			3	51
Oral Streptomycin	10	13	7	11	2			7	50
Terramycin	1	4			1				6
Total:	27	76	45	44	7	2	2	14	217
	88.48%				11.52%				

Table III shows that over one-third of the cases were admitted from other institutions, and of these a little less than a third were admitted without symptoms on a positive rectal swab only. One quarter of the cases had blood in the stools, and this is a cardinal symptom in creating anxiety in the patients, but only 2% of the cases were classified as being in poor condition on admission and even in these the poor condition was not so much due to the dysentery as to the child's "normal condition". Almost 7% of the cases were admitted on a diagnosis of diarrhoea only.

TABLE III.

	From whence admitted. Condition on admission.							Ostensible reason for admission.					
	Home	Hospital	Babies Home	Infected in other Institutions	Good Condition	Fairly Good	Poor	Pos. swab only.	Pos. swab and symptoms	Diarrhoea alone	Diarrhoea and other symptoms (vomiting, abdominal pain)	Diarrhoea with blood, with or without other symptoms.	Total Cases.
Mist. Kaolin	43	4		6	34	11	2	6	11	5	13	12	47
Sulphathalidine	10	11		8	14	7		2	8	3	4	4	21
Sulphasuccidine	7	9		5	11	4	1	2	8		4	2	16
Sulphaguanidine	7	4	2	4	8	4	1	3	3		1	6	13
Sulphadiazine	5	8		4	9	4		1	7	1	4		13
Chloramphenicol	29	22		11	43	8		1	22	1	15	12	51
Oral Streptomycin	31	19		14	43	7		4	17	4	9	16	50
Terramycin	4	1	1	2	6			1	1	1	1	2	6
Total:	136	78	3	54	168	45	4	20	77	15	51	54	217
%	63	37		25	77.5	20.5	2	9.22	35.48	6.91	23.5	24.88	

The courses of treatment on which the groups of patients were placed were as follows:-

PHTHALYL SULPHATHIAZOLE
(THALAZONE) (SULPHATHALIDINE)

(one drachmemulsion - .5 gramme)

Age	Dose	Daily Dose	Total Dosage
0-1	1 drachm - 4 I.D.	2.0 grammes	14 grammes
1-3	2 drachms - 4 I.D.	4.0 grammes	28 grammes
4-10	3 drachms - 4 I.D.	6.0 grammes	42 grammes
11-15	4 tablets - 4 I.D.	8.0 grammes	56 grammes
Adults	12 Tablets T.I.D. for 2 days. 6 Tablets T.I.D. for 5 days	18.0 grammes 9.0 grammes	81 grammes

SUCCINYLSULPHATHIAZOLE
(SULPHASUCCIDINE)

(1 drachm of emulsion - .5 gramme)

Age	Dose	Daily Dose	Total Dosage
0-1	1 drachm - 410	2 gm.	14 gm.
1-3	2 drachms - 410	4 gm.	28 gm.
.4-10	3 drachms - 410	6 gm.	42 gm.
11-15	4 tablets - 410	8 gm.	56 gm.
Adult	12 tablets T.I.D. for 2 days. 6 tablets T.I.D. for 5 days	18 gm. 9 gm.	81 gm.

SULPHAGUANIDINE

(1 drachm of the emulsion - 0.75 grammes)

7-day course

Age	Dose	Daily Dose	Total Dosage
0-1	1 drachm - 4 I.D.	3.0 grammes	21 grammes
1-3	2 drachms - 4 I.D.	6.0 grammes	42 grammes
4-10	2½ drachms - 4 I.D.	8.0 grammes	56 grammes
11-15	5 tablets - 4 I.D.	10.0 grammes	70 grammes
Adult	12 tablets - 4 I.D. for 2 days 6 tablets - 4 I.D. for 5 days	24.0 grammes 12.0 grammes	108 grammes

SULPHADIAZINE

(1 drachm emulsion - .25 grammes)

7-day course

Age	Dose	Daily Dose (after first day)	Total Dosage
0-3	2 drachms repeated in 4 hours. Then 1 drachm 4-hourly 5 times a day.	1.25 grammes	9.25 grammes
4-10	4 drachms repeated in 4 hours. Then 2 drachms 5 times a day.	2.5 grammes	18.5 grammes
11-15	3 tablets repeated in 4 hours. Then 2 tablets 5 times a day.	5.0 grammes	36.0 grammes
Adults	4 tablets repeated in 4 hours. Then 2 tablets 5 times a day.	5.0 grammes	37.0 grammes

CHLORAMPHENICOL

(5-day course)

Age	Dosage 75 mgm. per Kg.	Daily Dosage
3 months (75 mgms. per Kg.)	1 drachm palmitate 6-hrly.	500 mgms.
1 year	1½ drachms palmitate 6-hrly.	750 mgms.
2 years	2 drachms palmitate 6-hrly.	1 gramme
5 years	2½ drachms palmitate 6-hrly.	1¼ grammes
12 years	500 mgms.(2 capsules) 6-hrly.	2 grammes
Adult	75 mgms.(3 capsules) 6-hrly.	3 grammes

ORAL STREPTOMYCIN

(5-day course)

Age	Dose
0-3+	.25 grammes 6 hourly (1 gramme daily)
4-14+	.5 grammes 6 hourly (2 grammes daily)
15 Upwards	1 gramme 6 hourly (4 grammes daily)

TERRAMYCIN

(5-day course)

Age	Dosage	Daily Dosage
3 months (40 mgs. per Kg.)	50 mgms. or 9 drops 6-hrly.	200 mgms.
1 year	100 mgms. or 18 drops 6-hrly.	400 mgms.
2 years	150 mgms. or 27 drops 6-hrly.	600 mgms.
5 years	200 mgms. or 36 drops (1 c.c.) 6-hrly.	800 mgms.
12 years	500 mgms.(2 capsules) 6-hrly.	2 grammes.
Adult	750 mgms.(3 capsules) 6-hrly.	3 grammes.

The dosage of Kaolin given as a mixture varies from 3½ ounces given over a week for a child of up to three; 7 ounces to a child of up to nine; 10½ ounces up to fourteen, and 14 ounces for patients of the age of 15 years and upwards.

Table IV shows the more prominent symptoms and the mean number of days diarrhoea pre admission, pre treatment, and after the start of treatment.

Discarding the small Terramycin group, and bearing in mind that the number of days diarrhoea, pre admission, depends on the parents' stories, there does not appear to be any difference between the number of days diarrhoea occurring in the cases in each group. Nor does the number of days diarrhoea after treatment has begun appear to vary to any extent. The figure for chloramphenicol is the lowest, but then the pre-treatment figure is high, the distribution thus resembling that for Kaolin and probably being simply due to treatment beginning later in a fairly standard period of diarrhoea.

TABLE IV

	Number of cases with:-			Mean number of days on which diarrhoea occurred:-			
	Blood in Stools	Vomiting	Pyrexia	Total	Pre-admission	Pre-treatment (including pre-admission)	Post start of treatment.
Kaolin 47 cases	15	20	14 4 over 100F.	6.85	3	4.36	2.49
Sulpha-thalidine 21 cases	9	5	9 2 over 100F.	6	1.8	3.4	2.6
Sulpha-succidine 16 cases	5	7	3 2 over 100F.	6.75	2.31	3.56	3.19
Sulpha-guanidine 13 cases	6	6	5 1 over 100F.	6.76	2.31	3.53	3.23
Sulpha-diazine 13 cases	5	6	4 2 over 100F.	7.53	3.23	4	3.53
Chloro-mycetin 51 cases	18	17	17 6 over 100F.	6.35	2.47	4.35	2
Oral Strep-tomycin 50 cases	24	14	16 7 over 100F.	7.4	2.02	4.18	3.22
Terramycin 6 cases	2	4	2 1 over 100F.	6.6	4.4	5.6	1 3 cases nil
	84 or 38.68%	79 or 36.38%	70 or 32.23% 25 over 100F or 11.51%	6.61 mean	2.53 mean	4.02 mean	2.59 mean

Table V shows the mean number of days in hospital required to allow the accumulation of twelve successive negative rectal swabs post treatment in each case. The mean days in hospital shows a not particularly impressive difference between the two antibiotics (ignoring Terramycin) the sulphonamides, and the control series, but sub-division into groups shows a very marked difference, the percentage of cases cleared in 20 to 29 days being 19%, 23%, 68% and 60% in the control, sulphonamide, chloramphenicol and streptomycin groups respectively.

Two cases in the chloramphenicol group and one case in the streptomycin group remained positive for long periods. Sensitivity tests were done in two of these three cases, one on each drug, and the organism was fully sensitive to both drugs in vitro.

TABLE V.

Number of days in Hospital (to produce 12 negatives)

	Number of cases.	Mean days in hospital.	20-29 days	30-39 days	40-49 days	50-70 days	Over 70 days
Kaolin	47	43.58 45.81 *	9 or 19.14%	14	10	9	5 * 98;82;79;148;78
Sulphathalidine	21	41.47	5	6	6	4	
Sulphasuccidine	16	34.25	5	6	4	1	
Sulphaguanidine	13	38.54	3	4	4	2	
Sulphadiazine	13	51.23	2	4	1	4	2
Total Sulphonamides	63	41.09	15 or 23.8%	20	15	11	1
Chloromycetin	51	31.71	35 or 68.6%	10	2	2	2 76 days;83 days
Oral Streptomycin	50	32.08	30 or 60%	11	6	2	1 71 days
Terramycin	6	39.33	2	3			1 (one of 90 days)

* The case taking 148 days raised the mean days in hospital for the Kaolin group from 43.58 days to 45.81 days.

Table VI shows the numbers of rectal swabs taken and the results.

The number taken in the two antibiotic groups was, as would be expected from Table V, the lowest, and the number of positive swabs less than half that in the control group. The sulphonamides would appear to occupy an intermediate position.

The difference between the control and sulphonamide group and the antibiotic group is further brought out in the following breakdown of the mean positive swab figures.

Numbers of Positive Swabs

	1-4+	5-9	10-14	15-19	20-29	30-45	Total
Kaolin	12	15	9	7	2	2	47
Sulphonamides	20	20	18	3	2	-	63
Chloramphenicol	33	13	3	2	-	-	51
Streptomycin	34	12	3	1	-	-	50

It will be seen that the number of cases having under five positive swabs is very much greater in those treated with antibiotics. The percentages are: Kaolin 25.5%; Sulphonamides 31.7%; Chloramphenicol 64.7%; Streptomycin 68%.

TABLE VI.

Numbers of Rectal Swabs Examined and Results

	Mean Total	Positive	Negative	Negative post Treatment
Mist. Kaolin	30.32	10.55	19.78	12.12
Sulphathalidine	27.09	8.76	18.33	12.05
Sulphasuccidine	23.81	6.31	17.5	11.5
Sulphaguanidine	27.61	7.38	20.23	12.15
Sulphadiazine	26.61	9.84	16.77	11.15
Total Sulphonamides	26.27	7.98	17.76	11.55
Chloromycetin	21.74	4.63	17.31	12.04
Oral Streptomycin	21.82	4.1	17.72	12.06
Terramycin	26.5 1 case over 62	4.83 1 of 17	21.66	12

Numbers of Organisms recovered from rectal swabs positive for Shigella Sonnei.

It was found that in general the numbers of colonies recovered on plating the rectal swab or, on putting the culture through selenite broth where necessary, remained remarkably even. It was thought that should a patient after a number of negative specimens produce a positive specimen it might be possible to gain some idea from the number of organisms as to whether or not the positive result was due to re-infection.

The numbers of colonies were recorded in 158 cases, and in only 12 cases did a culture showing a large number of organisms follow abruptly one showing a small number.

The method of recording the number of organisms was as follows:-

++	- large numbers
+	- moderate numbers
+-	- small numbers
+==	- very small numbers
+-==	- recovered from selenite broth.

The numbers of colonies recovered from swabs taken on each side of a number of negative rectal swabs is shown below. The very marked failure of the later positive swab to show any increase in the number of colonies is at once apparent.

+-==	7 N.	+-==	+	8 N.	+-==	+-==	8 N.	+-==
+-==	8 N.	+-==	+==	12 N.	+-==	+-	8 N.	+-==
Same Case	++=	7 N.	+-	+==	8 N.	+-	+==	10 N.	+==
	+-==	11 N.	+-==	+	9 N.	+	+==	10 N.	+==
				+	11 N.	+==	+-==	12 N.	+==
	+==	11 N.	+==				+-==	10 N.	+-==
	+	9 N.	+==	+==	8 N.	+-==			
	+-==	12 N.	+==	+	8 N.	+-	+-==	9 N.	+-==
	+-==	6 N.	+-	+-==	13 N.	+-==	+	9 N.	+-==

It may be, of course, that a person re-infected shortly after his original infection has sufficient resistance to prevent multiplication of the organisms to any extent.

Table VII shows the mean number of days from the start of treatment up to and including the day on which the last positive swab occurred. It also shows the numbers and percentages of cases which failed to show an abrupt change from positive to negative rectal swabs, but rather tapered down to negative with a series of intermingled positives and negatives.

The number of cases having one, two, three and upwards intermittent positive swabs or groups of swabs is also shown. The last column shows for the total cases on each drug, the larger numbers of negative swabs between intermittent positive ones.

The clearance period of 18.44 days for the control group agrees approximately with that of Watt (1952) who found the mean duration of infection with S. Sonnei to be 22 days. Fairbrother (1944) found that 52% of a group of 92 cases of Sonne Dysentery treated symptomatically were clear at the end of the second week, and Gorman (1950) in a group of 121 cases found the clearance period to the first negative to be 17 to 18 days and to the third negative 32 to 35 days.

There would not appear, therefore, to be any very obvious change in the clearance rate in the case given no drug therapy.

The question of intermittent excretion with which Table VII is largely concerned is of the greatest importance in determining what criterion of cure is to be adopted.

The criteria of cure adopted by various authors have, in general, been low. Hardy (1944) adopted two negatives as his standard. Brewer in the same year adopted three to eight negatives over six to twenty days. Fairbrother (1944) used a four-day gap following treatment and then three consecutive negatives. The Monthly Bulletin of the Ministry of Health and Public Health Laboratory Service (1942) recording an outbreak of Sonne Dysentery in a Nursery School states that three negatives were first adopted as standard but was later changed to six negatives over six weeks.

Strang (1951) in a Day Nursery outbreak used three consecutive negatives.

Garfinkel (1953) in a group of cases mostly infected by a Flexner strain and mostly really ill used a standard of eight negatives with a terminal sigmoidoscopy. The Infectious Disease Committee of Papworth Village Settlement (1953) had a standard of six consecutive negatives for food handlers and three for others.

The fact that carriers of S. Sonnei often excreted the organism intermittently was noted by Fairbrother (1944) who wrote that S. Sonnei was often recovered after three consecutive negative stools, and he quoted positive results after four, six, eight, and fourteen consecutive negative faecal specimens. His results have been amply confirmed by this investigation, and the last column in Table VII shows for the whole 217 cases, a total of 95 observations of three and over consecutive negative rectal

TABLE VII

Clearance Time and Intermittency.

	Mean No. of days from start of treatment to end of positives.	Number of cases without intermittent positives.	Number of cases with intermittent positives.	One intermittent positive or group of positives.	Two	Three	Four	Five	Six and over	Numbers of negatives between intermittent positives.
Mist. Kaolin	18.44	7	40 (85.1%)	14 (35% of preceding column)	9	8	3	5	1	40 observations of 3 and over including a 12, three 10s, two 9s, and three 8s.
Sulphathalidine	16.05	7	44 (66.6%)	5 (35.7%)	3	5		1		6 observations of 3 and over, including a 13, a 12, a 10 and an 8.
Sulphasuccidine	11.12	6	10 (62.5%)	4 (40%)	3		1	1	1 (6)	7 observations of 3 and over including a 9, two 6s and a 5.
Sulphaguanidine	14.92	5	8 (61.5%)		4	3	1			7 observations of 3 and over including one of 14, 8 and two of 7.
Sulphadiazine	14.4	4	9 (69.2%)	5 (55.5%)	2			1	1 (6)	4 observations of 3 and over, including one 11, one of 10 and two of 8.
Total Sulphonamides	14.22	22	41 (64.9%)	14 (34.1%)	12	8	2	3	2	
Chloramphenicol	6	32	19 (37.25%)	10 (52.6%)	5	1	1	2		14 observations of 3 and over, including three 11s, one 8 and two 7s.
Oral Streptomycin	3.5	30	20 (40%)	11 (55%)	4	3	1		1 (8)	12 observations of 3 and over, including two 12s, a 9, and two 8s.
Terramycin	13 1 of 59	3	3	2			1			5 observations of 3 and over, including an 18 and a 10.

swabs followed by a positive swab. Many observations of from 8 to 12 consecutive negatives followed by a positive are recorded. An attempt (page 23) has already been made to determine whether positive results following many days of negative results are, in fact, due to re-infection.

It would require a very heavy and continuing degree of re-infection to produce the results shown in Table VII.

The clearance standards generally adopted would, therefore, appear to be too low but, of course, a balance must be struck between the ideal and the possible.

The difference, in the time taken for cases to become bacteriologically negative, between the control and sulphonamide groups and the two antibiotic groups is very striking (Table VII). It was the clear emergence of this difference which led to the abandonment of the plan to complete each individual sulphonamide-treated group to fifty cases. The complete resistance of the infecting strains of S. Sonnei in vitro to the sulphonamides was apparently paralleled by their resistance in vivo.

While chloramphenicol and streptomycin are both markedly superior to the control and sulphonamide groups in the mean number of days taken to clear the case, bacteriologically there is a definite bias in favour of streptomycin, this drug taking 3-5 days against chloramphenicol's 6. This difference is further brought out by Table VIIA.

TABLE VIIA

		Under 4 days	4	5-10	11-Upwards.
Time in days from the start of treatment to the last positive.	Streptomycin (50 cases)	39	3	5	3 cases. 15, 27 and 43 days.
	Chloramphenicol (51 cases)	31	6	7	7 cases. 14,19,31,24,27,36, 54 days.

It would appear, therefore, that though sensitivity tests showed not one strain of S. Sonnei even slightly resistant to chloramphenicol in vitro no less than seven cases in this series took clearance times equivalent to those of the control group.

The result with streptomycin was the reverse of this, for while sixteen strains (Table IA) were moderately or slightly resistant and one wholly resistant to streptomycin, only three cases took more than a few days to clear.

Both antibiotics not only cleared the cases more quickly than the sulphonamides or kaolin, but where intermittent positive swabs did occur they were much fewer in number. The percentage of cases producing intermittent positives where only one such positive was produced was over 50% both with

chloramphenicol and streptomycin, whereas with the sulphonamides and kaolin it was 34% to 35% only.

Results can be summarised as follows:-

1. The sulphonamide-treated cases required, to produce twelve negative rectal swabs, a period in hospital one-third longer than that required by those cases treated with chloramphenicol or streptomycin.

2. If it had not been for one case in the control group which took 148 days to clear, there would have been an insignificant difference between the sulphonamide and control groups in the number of days in hospital.

3. The numbers of positive rectal swabs obtained per case was with the two antibiotics less than half that of the control group. The sulphonamide-treated cases produced a number midway between the two.

4. The number of days from the start of treatment to the day on which the last positive rectal swab was taken showed a gradation from the control group through the sulphonamides and chloramphenicol to streptomycin. There was a drop of four days between the control group and the sulphonamide group and a drop of eight days between the latter and the chloramphenicol group. The drop between this group and the streptomycin group was less at two-and-a-half days.

5. Streptomycin was superior to chloramphenicol in producing earlier clearance but three cases did not respond readily. Seven cases did not respons to chloramphenicol although the organism was sensitive to the drug in vitro. These numbers are, of course, small.

6. No toxic symptoms were produced by any of the drugs.

Additional Investigations.

Some further investigation was done on the antibiotic-treated cases.

A few estimations of the stool level of chloramphenicol gave the following results:-

Case (1) 12.5 units per gr. gramme of faeces.
Case (2) 1.6 " " " " " "
Case (3) 1.8 " " " " " "

The estimation in case three was done on the third day of treatment and a second estimation in this case on the day following the cessation of treatment did not reveal the presence of any chloramphenicol.

These cases were all treated with the palmitate and the results of the assays were towards the lower level of the range given by Spiers (1954).

Some assays of the stool level of streptomycin gave these results:-

Case (1) - 213 units per gramme of faeces.
Case (1) - (one day later) 213 units per gramme of faeces.
Case (2) - 2,300 units per gramme of faeces
Case (3) - 200 units per gramme of faeces
Case (4) - 800 units per gramme of faeces
Case (5) - 250 units per gramme of faeces.

The method employed in these assays was as follows:-

Chloromycetin.

5 grammes of faeces were added to 5 ml. of distilled water, mixed well and autoclaved for 15 minutes at 15 pounds pressure (121°C). After cooling the mixture was centrifuged and 0.5 ml. of the supernatant fluid used for assaying.

Streptomycin.

5 grammes of faeces were added to 5 ml. of distilled water, mixed well and then centrifuged for 10 minutes at 3,000 R.P.M. The clear supernatant fluid was transferred to a Seitz filtering flask (E.K. pad) and negative pressure of about 300-400 inches of mercury applied. 0.5 ml. of the filtered extract was used for assaying.

On some occasions it was necessary to add a further 5 ml. of distilled water to prepare a solution suitable for filtering.

The test organism was Klebsiella pneumoniae in an overnight broth culture and by a tube dilution technique the effect of the faecal extract on the organism was compared to that of a standard (fresh) suspension of chloramphenicol or streptomycin as the case might be.

The results were as is shown rather variable though in Case (1) two results were similar.

One further investigation was done on the streptomycin-treated group. Several authors, Welch (1950) Forbes (1953) have stated that streptomycin is not absorbed from the bowel. This I thought to be a doubtful statement. It may be that streptomycin should not be widely used in mild illnesses such as Sonne Dysentery because of the possibility of raising the resistance to the drug of the tubercle bacilli infecting the general population. This would appear to be a rather improbable danger on the grounds of numbers treated alone, but it may not be so, and accordingly an attempt was made to estimate the blood levels of streptomycin in cases treated with this drug.

The following technique was used:-

Organism:- Klebsiella H. Sensitive to from 0.03 - 0.1 unit Strep/ml.
Medium:- Horse serum 2 volumes
10% Glucose 1 volume
Distilled water 2 volumes Sterilised
Phenol Red (ag.sat.soln.) 1.5 ml.

Standard Streptomycin 1 unit/ml.

This was produced by weighing the actual amount of StrepSulphate present and multiplying this by the potency indicated per mg.

Patient's serum inactivated at 56°C for ½-hour to destroy complement.

To every 20 ml. of Medium 0.4 ml. of an 18-hour culture of K41 was added and distributed in tubes as follows:-

	Final 0.25 ml.	0.125.	0.06.	0.03.	0.01.	
Patient's serum	0.5 ml.	0.5 ml.	0.5 ml.	0.5 ml.	0.5 ml.	(0.5 ml.
Medium	0.5 ml.	0.5 ml.	0.5 ml.	0.5 ml.	0.5 ml.	(discard
Control Strep.	0.5 ml.	0.5 ml.	0.5 ml.	0.5 ml.	0.5 ml.	(0.5 ml.
Medium	0.5 ml.	0.5 ml.	0.5 ml.	0.5 ml.	0.5 ml.	(discard

Dilution: 1 in 2 (-0.25) 1 in 4 (0.125) 1 in 8 -(0.06) 1 in 16 (0.03) 1 in 32(0.01)

When growth of K.41 occurs the organism utilises the glucose present forming an acid, this acid changes the PH of the medium and consequently changes the phenol red to yellow. Range phenol red (Red-ph 7.4, yellow at ph 6.4 and below.)

Therefore, by comparing the dilution of the serum with the control, the amount of streptomycin in the latter being known, the amount of antibiotic in the serum could be ascertained.

Eg: Serum dilution 1 in 8 inhibits K.41 - (0.06 ml. actual serum present).
Control " 1 in 8 " K.41 - 0.06 unit present.

. . 0.06 ml. contains 0.06 unit of streptomycin - 1 ml. contains 1 unit of streptomycin.

Or $\frac{\text{Test}}{\text{Control}} \times \text{Standard Conc/ml.} = \frac{8}{8} \times 1 = 1$ unit/ml.

Sera for examination were obtained pre-treatment, and three days after the start of treatment. One odd fact at once emerged and that was that some of the sera inhibited the growth of the test organism before treatment. An effort was made to distinguish between inhibition before and during treatment and by a process of dilution and incubation it was found that the pre-treatment inhibition was bacteriostatic only while the treatment inhibition was bacteriicidal.

Results of the assays were as follows:-

Streptomycin Units per millilitre of Serum

39 cases

Pre-treatment		Third day of Treatment						
	.06	.125	.25	.5	1	2	4	Nil
Inhibition 10		2	5	1	2			
No Inhibition 29	4	7	1	7	2	2	1	5

It would appear, therefore, that streptomycin given orally is absorbed from the bowel, though to a limited extent.

I am indebted to Mr. Stainton of the Fazakerley Hospital Laboratory for the devising and operation of this laboratory investigation.

Costs.

A factor to be reckoned with in treatment is cost, and the cost of the various course of drugs used is of some importance.

The cost of treating a child of five years with a course of each of the drugs is shown below.

The sulphonamide courses were for seven days, and the antibiotic courses for five days.

(1)	Sulphathalidine	8/9¼
(2)	Sulphasuccidine	12/3½
(3)	Sulphaguanidine	2/6¾
(4)	Sulphadiazine	4/6
(5)	Chloramphenicol	39/5
(6)	Oral Streptomycin	19/2
(7)	Terramycin	23/8

The cost of the drugs used is, however, of small importance compared

to the inclusive cost of hospital treatment. This, in Fazakerley Hospital in 1953, came to no less than £17.18.11., per week. Therefore, on the mean days in hospital given in Table V a case treated with a sulphonamide, say sulphathalidine, might cost £106.5.4., that treated with chloramphenicol £81.8.2., and with streptomycin £82.4.1. That is if twelve negatives are sought.

The advantages of streptomycin are brought out when it is seen that the time in hospital could be greatly reduced for patients on this drug as the figures given in Tables VII and VIIA justify a reduction of the clearance negatives to three. Only three cases would have been missed in this series by such a reduction. There are, however, other factors to be taken into account and these I shall discuss later.

SECTION 4.

Follow-up of cases after discharge.

Table VIII gives the results of the follow-up and it will be observed that 32 or 15.16% of the cases produced positive rectal swabs post discharge. This may have been due to re-infection at home or to intermittent excretion. Either way it would appear that a large amount of time and money had been wasted by admitting these children to hospital.

The patterns of excretion of S. Sonnei in these 32 cases was as follows:-

P - positive. N - negative.

(1) 5N 1P 7N over 83 days.
(2) 3P 1N 3P 2N over 49 days.
(3) 1P 4N 1P 3N over 53 days.
(4) 2P 5N 1P 3N over 114 days.
(5) 4N 1P 4N over 47 days.
(6) 1P 8N over 39 days
(7) 2N 5P 5N over 67 days
(8) 2N 1P 5N 1P 1N over 53 days.
(9) 1P 1N over 48 days
(10) 1P 6N 1P over 35 days
(11) 1P 7N over 53 days.
(12) 1P 7N over 68 days.
(13) 1P 3N 1P 5N over 55 days
(14) 1N 1P 6N over 33 days.
(15) 1P 5N over 145 days
(16) 4N 1P 5N 1P 3N over 240 days.
(17) 2N 1P 8N over 33 days.
(18) 3N 1P 3N 1P 2N over 83 days.
(19) 7N 1P 3N - 3N over 261 days.
(20) 2P 8N over 83 days.
(21) 2N 1P 3N 1P 10N over 68 days.
(22) 3N 1P 6N over 77 days.
(23) 6N 3P 12N over 40 days.
(24) 1N 3P 4N - 3N over 102 days.
(25) 7N 1P over 34 days.
(26) 1P 7N over 34 days.
(27) 7N 1P 1N over 39 days.
(28) 2N 1P 4N 1P 2N over 45 days.
(29) 4N 1P 9N over 101 days.
(30) 5N 4P over 50 days.
(31) 3N 1P 1N 1P 5N over 99 days.
(32) 3N 1P 3N over 41 days.

It is rather interesting that eight cases should show their positive results in the first one or two specimens only. Here again the finding may be due to the change to home feeding and conditions causing a final intermittent excretion or to the patient's resistance overcoming a re-infection.

The families of 16 of the 32 cases found once again to be excretors had been investigated at the time of the original infection, and a total of 23 excretors or cases were discovered in them. Nineteen of the families of the 32 ex-patients were investigated after the discharge of the patient, (including 12 of the 16 originally examined) and only 5 excretors were found.

These figures, as far as they go, would seem to indicate that the 32 patients were discharged into a diminished pool of infection, but a pool of infection nevertheless.

TABLE VIII.

Treatment	Total Cases	Follow-up completed to eight negatives	Less than eight negatives or interrupted follow-up.	Positives recurring	Follow-up not possible.
Mist. Kaolin	47	30 mean days follow up 42.83	6	10 21.27%	1
Sulphathalidine	21	10 mean days follow up 46.1	2	7 33.33%	2
Sulphasuccidine	16	11 mean days follow up 48.2	2	2 12.5%	1
Sulphaguanidine	13	9 mean days follow up 39.33	3	1 7.69%	-
Sulphadiazine	13	9 mean days follow up 44.55	2	2 15.38%	-
Total Sulphonamides	63	39	9	12 19.05%	3
Chloromycetin	51	43 mean days follow up 77.74	2	6 11.76%	-
Oral Streptomycin	50	38 mean days follow up 38.61	8	4 8.00%	-
TOTAL:	211	150	25	32	4
Percentages		71.09%	11.85%	15.16%	1.89%

SECTION 5

Home conditions; background of illness and breast feeding; upset of child occasioned by hospitalisation.

The home conditions of the patients admitted from their own homes are shown in the following tables. Table IX shows the type of home occupied. The term "old row" implies an old two-storied dwelling with the front door opening direct on to the street and a toilet in a small yard at the back. There is no bath and the house is dilapidated. The same type of house well maintained and well fitted has been termed "old row - good condition". The terrace house is one set back from the street generally with steps to the front door. It has indoor sanitation and has bigger rooms. This type of property in good condition has been shown separately.

The "old block" type of accommodation consists of rooms in old, very large, well-built blocks of terrace houses generally three and sometimes four storeys high. These were once palatial residences occupied by the wealthiest in Liverpool, and are now slums falling into ruin. The centre of Liverpool around the University is composed of this type of property. In all these houses the conveniences are shared by many families and the baths, if still there, are no longer usable.

The few private homes listed are modern houses in good condition with baths and all the usual conveniences. The "cubicles" are local authority accommodation for homeless persons where each family has one room.

TABLE IX

Council House	Council Flat	"Prefab"	Private House	Old Row	Old Row good condition	Old Terrace	Old Terrace good condition	Old Block	Cubicles
27	23	6	4	27	9	28	3	41	5
35%				65%					

It will be observed from this table that 65% of the patients came from families occupying inferior type accommodation. This, however, does not imply that Sonne Dysentery is more prevalent in such families, but merely reflects the housing position in Liverpool. The fact that 35% of the cases lived in good homes is rather more noteworthy as indicating the universal prevalence of the disease.

Table X shows the mean density of occupation and Table XI the sleeping arrangements as they affected the patient.

TABLE X

Families	Numbers in home	Adults	Children	Rooms	Bedrooms
173	990	483	509	668	381

The mean number of individuals per house is 5.72. All children of ten years and over have been classified as adults in order to conform to Housing Act standards. A further subtraction to complete the conformity to the Acts is required, namely, that of forty-five babies under one year which are disregarded under the Acts. The remaining children are counted as one-half each. The total number of "persons" is, therefore, 715, and they occupy 668 rooms or 1.07 "persons" per room and 1.87 persons per bedroom.

The Registrar General's One Per Cent. Sample Tables from the 1951 Census give the number of individuals per room in Lancashire as 1.01. The actual mean number of individuals in this investigation was 1.48 per room, that is approaching the Central Clydeside figure of 1.55 individuals per room. The number of individuals per bedroom was 2.6.

TABLE XI

Number in patient's bedrooms	Number in patient's beds	Patient with own bed	Bedclothes		
			Good	Adequate	Inadequate
538	308	84	53	96	24

There being 173 patients the mean number of individuals sleeping in the patient's bedroom is 3.11 and sleeping in the patient's bed 1.77. However, 84 of the patients had their own bed or cot, so that the other 89 patients had a mean number of 2.62 individuals per bed.

An attempt was made to assess the adequacy of the bed clothes partly as a guide to the mother's efficiency and partly because it was thought that inadequate blankets might make the family tend to huddle together, and thus facilitate the spread of infection. The percentage of cases where bedding was thought to be inadequate was 13.8%.

The mean number of breadwinners per family was 1.17, there being only one breadwinner in 158 cases and more than one in 15. The average household in the country is supported by 1.75 breadwinners (The Economist, 1954). Furthermore, the mean number of individuals per house in our cases was 5.72 whereas the mean number of individuals per industrial household is 3.77. (The Economist, 1954).

Our families in this investigation, therefore, had more members and fewer wage earners than the average. This would be expected in families where the children are young, and of course, this is the type of family where S. Sonnei infection is most obvious.

Social Grades.

The Registrar General in his Decennial Supplement for 1951 shows the percentages of the working population in each social grade as follows:-

Social Grade I - 3.4%
" " II - 15.2%
" " III - 51.9%
" " IV - 15.7%
" " V - 12.3%

The percentage of unemployed males is usually between 2% and 3%. The percentage of unemployed fathers in our families was 12.8% and the percentages in the social grades are shown beneath:-

Social Grade I - 0%
" " II - .61%
" " III - 47.85%
" " IV - 9.81%
" " V - 28.834%

Cases of Somne Dysentery in families of Social Grades I and II are rather unlikely to come to our notice, being dealt with privately by their own doctors and not often notified, so that the social scale of the cases which are notified would tend to be weighted to the lower end. However, in view of the relative numbers involved, this weighting could not be great.

There is little difference between the Registrar General's percentage in Social Grade III and the percentage in that grade in the group under investigation.

The real differences lie in Grades IV and V and in the unemployed, the Registrar General's figure being 28% and 2% to 3%, as against 38% and 12.8%.

Somne Dysentery would seem from these figures to be more prevalent in the lower social grades.

Standard of Mothercraft.

The standard of mothercraft was estimated on the basis of the mother's feeding, clothing, and handling of the children, together with the cleanliness and equipment of the home, rather on the lines of Thwaites (1952).

The standard was classed as good in 39.4%, average in 46.46% and poor in 14.2%. The homes themselves were assessed as clean in 58.95% of cases, fairly clean in 27.06% and dirty in 13.87%. Only 18, or 10.5% of the mothers went out to work, and some of these said that they did not do so regularly.

Previous Illnesses.

The previous illnesses of 176 children were recorded and are shown below:-

TABLE XII

Chicken Pox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
45	73	34	12	18	9	27	26	10	4	3

As well as these common illnesses two children had had tuberculous meningitis, one pleurisy, one a pelvic abscess, two infective hepatitis, two scarlet fever, two asthma, one rubella, one rheumatic fever, one malnutrition and three convulsions. Two children suffered from retrolental fibroplasia, one had a hare lip and complete cleft palate, one had been operated on for congenital narrowing of the oesophagus, and one was mentally defective.

The distribution of these illnesses amongst the children and the ages of the children are shown in Appendix I.

I cannot say for lack of a standard for Liverpool children whether this incidence of disease is within normal limits or not, but certainly as far as the first four illnesses are concerned it is within such limits.

The number of children previously affected by gastro-enteritis or dysentery was 37 and of these 31 were under five years, seven being under one, seventeen between one and three and seven between three and five. The numbers of children in these age groups in children under investigation was 27, 76 and 45 respectively (Table II). The percentages having previously had gastro-enteritis or dysentery were, therefore, 25.9%, 22.3% and 15.5%.

25.9% of the children under one year were, therefore, having their second experience of intestinal infection.

The full list of previous illnesses is set out by age groups in Appendix I and is also shown in relation to breast feeding.

Breast Feeding.

26.25% of 160 children had been wholly bottle fed, and 73.25% had received at least some breast feeding. The percentage of mothers who had abandoned breast feeding in each month is shown in Table XIII.

TABLE XIII

Under 1 month	1+	2+	3+	4+	5+	6+	7+	8+
16.94	18.64	13.52	16.94	10.16	4.24	5.93	3.38	10.16

Hughes (1948) found that 29% of mothers had abandoned breast feeding by the time the infant was three months old. The percentage shown in Table XIII is 49%. Dimmer (1949) stated that 49.7% of his cases had given up breast feeding at three months.

Ross (1951) stated that in 1929/30 only 23% of mothers had given up breast feeding at three months, whereas in 1949 no less than 63.8% had done so. Westropp (1953) however, found that only 16.2% of her cases had ceased to breast feed at three months.

The breast feeding experience of the children in this investigation would, therefore, appear to have been reasonably good by British standards.

EFFECT ON THE CHILD OF HOSPITALISATION

It is stated by Bowlby (1952) that the phases of development of the child's capacity for human relationships can be broadly placed in three groups:-

1. The phase during which the infant is in the course of establishing a relationship with a clearly identified person - his mother; this is normally achieved by five or six months of age.

2. The phase during which he needs her as an ever-present companion; this usually continues until about his third birthday.

3. The phase during which he is becoming able to maintain a relationship with her in absentia. During the fourth and fifth years such a relationship can only be maintained in favourable circumstances, and for a few days or weeks at a time; after seven or eight the relationship can be maintained, though not without strain, for periods of a year or more.

Some degree of upset would, therefore, be expected in young children admitted to hospital for periods of a month or more. 68% of the children in this investigation were under five years of age and 88% under ten years. 34% of the under-five group displayed greater or lesser departure from their pre-admission characters on return home.

The material does not lend itself to summarisation, and the reports on each child are presented individually, in brief, by age groups:-

Under 1 Year

Days in Hospital	Age	Particulars of Upset.
30	9/12	For six weeks was fretful and would not have mother out of sight.
43	6/12	Fretful and refused to use pot. Was not retrained four months later.
49	11/12	Fretful for a few days only.
54	8/12	Child fretful for a week, but there was a new baby in the home.

Under 2 Years

27	1.8/12	Cried and screamed a great deal for a few days, then settled down.
32	1.8/12	For 6 to 7 weeks was very difficult to handle, woke up screaming at night, would not eat or leave mother.
24.	1¾.	For 2 months cried a great deal and would not leave mother, also screamed at night. Still nervous of strangers 6 months later.

Under 2 Years (continued)

Days in Hospital	Age	Particulars of Upset
33	1.5/12	Would not go into cot. Had screaming attacks and was very fretful for 2 weeks.
24	1½. (Twins.)	Was nervous and had screaming attacks. These began to wear off after 2 weeks.
24	1½. (Twins.)	Fretful for 2 weeks. Reacted to visitors by incontinence.
28	1.8/12	Upset and fretful for some weeks.
22	1 year	Fretful for 2 days.
50	1 year	Fretful for a few weeks.
28	18/12	Aggressive and bad-tempered for 3 to 4 weeks.
26	18/12	Bad-tempered for one week.
52	1 year	A little fractious for 2 weeks.
50	1.4/12	For 2 to 3 months hated to be left alone and refused to go into cot.
37	1.4/12	Very nervous and fretful, also lost control of bladder for over 2 months.
44	1.7/12	Appeared rather wilful, and often cried with rage over 2 to 3 weeks.

Under 3 Years.

40	2 years.	For 3 to 4 weeks would not eat, sleep, nor leave mother.
45	2.5/12	For 3 to 4 weeks cried a great deal and clung to mother.
33	2½.	Upset for one month. Cried a lot, would not leave mother, would not go to sleep at night.
26	2 years	Was difficult to retrain to pot and rather fretful for 3 weeks.
71	2.3/12	Rather disobedient and naughty for about 2 months.

Under 3 Years (continued)

Days in Hospital	Age	Particulars of Upset
47	2 years	Screamed and cried a lot for 14 days.
42	2½.	Upset badly for 6 weeks, still frightened of strangers. Has temper tantrums and is restless at night, frequently waking up.
61	2 years.	Naughty and disobedient for 3 to 4 weeks.
26	2.3/12	No affection for mother at first - improved in 5 weeks. Disobedient with screaming fits for 3 weeks.
34	2½.	Bad-tempered for 3 weeks.
62	2.11/12	For 4 to 5 weeks very naughty and disobedient.
47	2½.	Very fretful and difficult with food for over 2 months.
	Under 4 Years.	
53	3 years	Very bad-tempered, and woke up at night for 2 months. Still rather short-tempered 6 months later.
46	3½.	Would not eat for 2½ weeks, restless at night, cried a great deal.
43	3 years	Frightened of strangers and still terrified of ambulances 6 months later.
32	3.2/12	Cried a lot, was restless at night, bad-tempered and would not leave mother for about 1 month.
28	3½.	For 3 weeks had to be carried to bed, and occasionally woke up screaming.
25	3 years	Temper tantrums, with kicking and screaming for ten days; continued fretful for 3 weeks.
	Under 5 Years.	
78	4½.	For 2 to 3 weeks cried a great deal and was very restless at night. Was very obstinate and bad-tempered.
30	4 years	Cried a great deal and clung to mother for 3 months. Still distrusts strangers 6 months later.

Under 5 Years (continued)

Days in Hospital	Age	Particulars of Upset.
53	4 years	For 4 to 5 weeks she ate little, clung to her mother and cried a great deal.
46	4½ years	For 6 to 7 weeks was very obstinate, refused to eat, and was restless at night.
28	4 years	Off food for a few days.
83	4 years	Very fretful, easily tired. Not back to normal in one month.
60	4½ years	For 3 to 4 weeks rather whining and difficult with food and sleep.
	Under 6 Years	
59	5 years	For 4 months cried easily, woke up at night, and was very obstinate.
24	5½ years	Poor appetite for one week.
30	5 years	Very fractious and difficult for 3 to 4 weeks. Impossible to rectal swab. (R.C.M)
31	5½ years	Very upset for 6 weeks. He shouted, swore and would not eat or sleep. Tried to stab me (R.C.M) with a pair of scissors. Still difficult, though much calmer, 3 months later.
26	5¼ years.	No appetite, cried easily, and was very sensitive for over six weeks.
	Under 7 Years.	
28	6½ years.	Listless, nervous, and with no appetite. Did not sleep. Began to recover after ten days.
60	6½ years.	Sullen, obstinate, and bad-tempered for 4 to 5 weeks.
	Under 8 Years.	
26	7 years.	Loss of appetite for some weeks.
	Under 12 Years.	
29	11 years.	Bad-tempered and irritable for about a week.
39	10 years.	Listless for a few days.

TABLE XIV

Children affected by hospitalisation

SUMMARY

Ages to 9+ (not including one case of 10 years and one of 11 years)

	-1	1+	2+	3+	4+	5+	6+	7+	8+	9+
Numbers affected at each age	4	15	12	6	7	5	2	1		
		1-2+		3-4+		5-9+				
Numbers in the whole group at these ages	27	76		45		44				
Percentage affected	148%	35.5%		28.8%		18.27%				

Section 6

Is it necessary or advisable to admit cases of Sonne dysentery to hospital?

1. Cases and carriers occurring in general hospitals and other institutions must be transferred to an isolation hospital. These comprised 37% (81 cases) of the group under investigation.

2. Only 2% of the cases admitted were in poor general condition.

3. The symptoms were mild. 38% had blood in the stools but this was small in amount 11.5% of the cases only had a temperature of 100°F or over. Only 32% had a temperature above normal at all.

4. The diarrhoea lasted approximately seven days (6.61) and of this period one third was over before admission and two thirds over before treatment began.

5. The follow up after discharge revealed that 15.16% of the cases again became excretors after discharge.

6. Table XV shows the amount of infection in seventy nine families.

Table XV.

	0-2 yrs.		3-5 yrs		6-9 yrs		10-14 yrs		15 yrs....
	Male	Fem.	Male	Fem.	Male	Fem.	Male	Fem.	
Total Nos.	57	32	39	37	30	24	17	10	177
Infected	41	24	23	29	16	13	8	2	21 6M : 15 F
Percentage	72%	75%	59%	78%	53%	54%	47%	20%	12%

These figures agree with those of Shaw (1953) in that children of nine years and under are most heavily affected but a preponderance of infections in males is not shown until the ten to fourteen years age group is reached. The percentage of adults affected is less than half that found by him. Another divergance from Shaw's figures is that he found babies of under one year less heavily infected than older children,

but of the nineteen babies under one year in these seventy nine families, 14 or 73% were infected. The admission of one or two cases from each family would hardly affect this pool of infection.

7. The previous illness and breast feeding history of the children would seem to indicate that they had not suffered from any particularly adverse factors under these headings except in that the babies had had a heavy previous experience of gastro enteritis and dysentery. The numbers involved in this group were, of course, small.

From a consideration of all these matters it would seem that there is little if any medical or epidemiological reason for admitting cases of Sonne dysentery to hospital. However social factors must be taken into account. The cases tended to come in greater proportion from the lower social grades and also by reason of the families being "young" families there was not so much money per head available as in the "average" family. 65% of the families occupied old or cramped accommodation. In spite of this 84 or 48.5% of the patients had their own bed or cot at home.

The standard of mothercraft was assessed as poor in only 14.2% of cases. There is one very important reason for not sending young children to hospital unless it is absolutely necessary and that is the extent to which the children are disturbed by being removed from their parent's care.

To sum up. There is no medical reason for admitting cases of Sonne dysentery to hospital and where the child has its' own bed and the standard of mothercraft is considered adequate the child should be nursed at home.

Section 7.

Conclusions.

1. Oral streptomycin is, in Liverpool, at the present time, the cheapest and most efficacious drug for the treatment of sonne dysentery.

2. Cases, unless there are adverse home circumstances, should not be admitted to hospital but should be treated at home.

3. The Isolation Hospital should, when treating those cases and carriers of Sonne dysentery from other hospitals and those from unsuitable homes, continually investigate

the efficacy of established and new drugs.

4. Arrangements should be made for the results of these investigations to be passed on to the general practitioners.

Section 8.

Summary.

1. A brief review of the rising tide of Shigella Sonnei infection and of the literature concerning it has been given.

2. An attempt covering 211 cases has been made to assess the relative value, in the treatment of Sonne dysentery, of the commonly used sulphonamides, sulphathalidine, sulphasuccidine, sulphaguanidine and sulphadiazine, of chloramphenicol and or oral streptomycin. These drugs were assessed against each other and against a control group treated with kaolin. Streptomycin was superior to the others as it produced bacteriological clearance in a mean period of 3.5 days, as against 6 days for chloramphenicol, 14 for the sulphonamides and 18 for the control group.

3. 15.16% of the cases once again became excretors of shigella sonnei within a short time of discharge from hospital.

4. The home background of the case was investigated and it was found that the lower social grades were rather heavily represented. Nevertheless 48.5% of the patients had their own bed or cot at home and in only 14.2% of cases was the standard of mothercraft classed as poor.

5. The necessity or otherwise of admitting cases of sonne dysentery to hospital was discussed. It was shown that few of the children were really ill only 2% being classed as in poor general condition. The diarrhoea lasted for approximately seven days and one third of that period was over pre admission and two thirds pre treatment.
The heavy family infection from which the child was taken and to which it returned was shown.
It was recommended on medical and financial grounds that cases should not be admitted to hospital unless the home conditions were adverse.

6. The medical grounds for refusing admissions included the definite danger of disturbing the child by separating it from its mother. Such an upset did occur in 34% of children under five years.

7. It was further recommended that the Isolation Hospital should continually investigate established and new methods of treatment and that arrangements should be made for passing information so gained to general practitioners in the area.

APPENDIX I

UNDER ONE YEAR

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Castro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
1	6/12	1/12							+				
2	9/12	6/52								+			+
3	11/12	6/52		+									
4	10/12	3/12											
5	7/12	1/52							+				
6	11/12	6/52	+	+	+					+			
7	10/12	3/12											
8	4/12	B						+					
9	10/12	2/12								+			
10	10/12	2/12							+				
11	11/12	8/12											
12	3/12	2/52											
13	7/12	2/12											
14	8/12	B							+				
15	14/12	3/365	Premature 4lbs.14oz.					+	+				
16	10/12	3/12								+			
17	6/12	4/52								+			
18	8/12	4/12											
19	9/12	3/12							+				
20	9/12	2/12							+	+			

Continued

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
21	6/52	4/52											
22	11/12	3/52							+				
23	7/52	B											
24	10/12	3/12											
25	10/12	4/12											
26	6/12	B	Hare lip and complete cleft palate										

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
					AGE I+								
27	1.11/12	N.K	+										
28	1.8/12	2/12								+			
29	1.8/12	6/12							+ + +				
30	1.4/12	N.K	+								+	+	
31	1	B			+						+ Some		
32	1¾	6/12		+									
33	1.4/12	3/12											
34	1	B		+			+		+			+	
			Retrolental Fibroplasia										
35	1.4/12	2/52											
36	1½	6/12		+	+								
37	1.4/12	2/52	+										
38	1.2/12	B								+			
39	1.7/12	3/12											
40	1.4/12	5/12	+						+				+
41	1.5/12	2/12											
42	1.3/12	2/12					+					+	
43	1½	9/12											
44	1.8/12	3/52		+									
45	1.9/12	B	+	+					+	+		+	
46	1½	N.K											
47	1.5/12	B								+			

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
48	1.1/12	4/12											
49	1.8/12	6/52											
50	1	4/52											
51	1.3/12	6/52							+				
52	1.3/12	3/12							+				
53	1.3/12	3/52											
54	1	2/52								+			
55	1.5/12	4/12											
56	1	3/365											
57	1½	2/12											
58	1½	B											
59	1½	B											
60	1.5/12	B	Operation for congenital narrowing of the oesophagus					+					
61	1.5/12	2/12								+			
62	1½	B		Convulsions						+			
63	1½	B								+			
64	1.11/12	4/12		+	+								
65	1	2/12											
66	1.10/12	NK								+			
67	1.8/12	NK	+				+		+				
68	1.2/12	3/52						+					
69	1.10/12	NK	Malnutrition 1953				+						

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
					AGE 2+								
70	2	3/12	+		+				+				
71	2.5/12	1/12							+				
72	2½	6/52		+			+						
73	2.11/12	3/52	+	+									
74	2	3/12											
75	2½	7/52											
76	2	4/12	+	+									
77	2	B											
78	2.11/12	3/12		+									
79	2½	NK						+	Infective		Hepatitis		
80	2	7/12		+	Infective Hepatitis				+		+		
81	2½	9/12											
82	2	NK									+		
83	2½	9/12						+					
84	2.9/12	NK	+	+	+								
85	2½	3/12		+									
86	2.10/12	2/12		+									
87	2¾	2/12	+	+	+	+			+				
88	2	3/52	+	+									
89	2.2/12	B	+	+									
90	2.3/12	6/52		+					+				
91	2.1/12	3/365				+							
92	2.9/12	NK								+			
93	2	1/52					+				+		
94	2.5/12	4/12		+	+								
95	2.3/12	7/52											

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
					AGE		3+						
96	3	3/12		+									
97	3.10/12	6/12		+	Tuberculous Meningitis								
98	3	2/52		+									
99	3	2/12			Mentally Defective								
100	3.2/12	3/12						+					
101	3	3/12		+									
102	3.2/12	9/12		+									
103	3½	4/12	+	+	+	+			+	+			
104	3½	NK											
105	3½	NK			+				+	+			
106	3.4/12	4/12					+		+	+			
107	3½	4/52		+	+		+		+	Convulsions			
108	3½	1/12					+			Convulsions			
109	3	NK	+	+	+								
110	3½	4/52											
111	3	B											
112	3	2/12											
113	3	5/52	+										
114	3.9/12	B											
115	3½	B		+					+				
116	3	B											
117	3	B											
118	3.11/12	B	Retrolental Fibroplasia										

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
						AGE 4+							
119	4½	B											
120	4.11/12	3/12	+	+									
121	4	6/52	+	+	+								
122	4½	6/12		+									
123	4	5/12		+	+	+							
124	4	4/12	+	+	+							+	
125	4.2/12	B	+	+	+								
126	4	NK		+		+							+
127	4½	2/12	+	+	+								
128	4	B	+	+		+							
129	4	3/12											
130	4	B	+		+		+						
131	4½	11/365		+	+	Tuberculous Meningitis				+			
132	4	5/52	Rheumatic Fever								+		
133	4	NK	+	+							+		

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
					AGE		5+						
134	5	B	+	+		+	Pleurisy			+			
135	5 1/12	3/12	+	+	+				+				
136	5	9/12		+	+	+							
137	5	5/12		+		+							
138	5 1/4	B											
139	5.2/12	B			+								
140	5	6/52	+	+									
141	5 1/2	B		Pelvic abscess									
142	5 1/12	3/12					+						
143	5.6/12	1/12											+
144	5	2/52											
145	5 1/12	1/52		+						+			
146	5 1/2	6/12	+	+	+								
147	5	B		Scarlet Fever									
148	5 1/2	9/12	+	+	+						+		
149	5 1/2	9/12	+	+		+							
150	5.11/12	9/12	+	+	+				+				

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
					AGE	6+							
151	6½	B		+									
152	6	B		Asthma						+		+	
153	6½	5/12	+	+	+		+	Rubella			+		
154	6½	3/12	+	+	+								
155	6	4/12		+	+								
156	6	NK			Colds only								

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
					AGE	7+							
157	7	2/12	+	+	+								
158	7	3/52		+	+	+							
159	7	NK	Convulsions				+						
160	7	6/52	+	+		+							
161	7	B		+									
162	7	B	+	+	+	Hernia			+				

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
					AGE	8+							
163	8	6/12			Epilepsy								
164	8	B		+									
165	8	B	+				+						

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
					AGE	**9+**							
166	9	1/12	+	+			+						
167	9	9/12	+	+									
168	9	B		+	+		+						
169	9	B		+				+					
170	9	B	+	+	+								

Case Number	Age	Breast Feeding	Chickenpox	Measles	Whooping Cough	Mumps	Pneumonia	Broncho-Pneumonia	Gastro-enteritis	Bronchitis	Dysentery	Otitis Media	Tonsillitis
			AGE	10	and	upwards							
171	10	9/12		+						+	+		
172	11	B	+	+									
173	11	B	+	+		Scarlet fever							
174	12.9/12	9/12		? Rheumatic fever									
175	12	NK	+	+									
176	13	4/12		+	+		Appendicitis						

REFERENCES

(1) "On the State of the Public Health", Report of the Chief Medical Officer, Ministry of Health (1933) 52.

(2) Glover, J.A., Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service. March 1947.

(3) Ibid. July, 1949.

(4) Roelcke, K., Neuberger, M. (1941) Muench Med., Woch 88, 643. (Summary from J. Amer, M.Ass. (1941) 117, 2105). Reviewed Bulletin of Hygiene 1941.

(5) Stowman, K. (1945) Epidemiological Information Bulletin of U.N.R.R.A. Health Division (Washington D.C.) 1, 101. Reviewed Bulletin of Hygiene, 1945.

(6) Felsen, J., Wolassky, W. 1953. "Journal of the American Medical Association", 153, 1069.

(7) Felsen, J. (1934) Quoted by Weil, A.J. 1943. Journal of Immunology. 46. 13.

(8) Nisbet, B.R. (1938) "Medical Officer" 59, 87.

(9) Weil, A.J. (1943) Journal of Immunology 46, 13.

(10) Lewis, I.C., Claireaux, A.E. (1951) Lancet 769.

(11) Hardy, A.V., Watt, J. (1945) Public Health Reports (Washington) 60, 261.

(12) Libby, R., Joyner, A.L. (1940). Journal of Infectious Diseases, 67, 67.

(13) Marshall, E.K., Bratton, A.C., Edwards, L.B., and Walker, E. (1941) Bulletin Johns Hopkins Hospital, 68, 94. (Bulletin of Hygiene 1941).

(14) Poth, E.J., Chenoweth, B.M., and Knotts, F.L. (1942). Journal of Laboratory and Clinical Medicine 28, 162.

(15) Hardy, A.V., Watt, J. (1942) Public Health Reports (Washington) 57, 529.

(16) Monthly Bulletin Emergency Public Health Laboratory Service (1942) Nov.2-5.

(17) Yannet, H., Leibovitz A., Deutsch, J.V. (1942). Journal American Medical Association, 120, 184.

(18) Hoagland, R.J., Harris, F.H., Raile, R.B. (1943). "War Medicine" Chicago 4, 400 (Bulletin of Hygiene, 1944).

(19) Hardy, A.V., Cummins, S.D. (1943) Public Health Reports, Washington 58, 693.

(20) Eisenoff, H.H., Goldstein, H. (1943) Journal of the American Medical Association 123, 624.

(21) Adams, J.W., Atwood, R.T. (1944) "War Medicine" Chicago 5, 14. (Bulletin of Hygiene 1944).

(22) Hardy, A.V., Watt, J. (1944). American Journal of Public Health 34, 503.

(23) Brewer, A.E. (1944). Lancet 471.

(24) Osborn, W.H., Jones, R.N. (1944) Lancet 470.

(25) Fairbrother, R.W. (1944). British Medical Journal 489.

(26) Painton, J.F. Hantman, S. (1945). Journal of the American Medical Association 128, 1152.

(27) Swyer, R., Yang, R.K.W. (1945) British Medical Journal 149.

(28) Hardy, A.V. (1945). Public Health Reports (Washington) 60, 1037.

(29) Watt, J. (1945) Public Health Reports (Washington) 60, 1355.

(30) Hardy, A.V. (1946). Public Health Reports (Washington) 61, 857.

(31) Vollum, R.L., Wylie, J.A.H. (1946). Lancet 91.

(32) Tateno, I.(1950) Japanese Journal of Experimental Medicine 20, 795. (Bulletin of Hygiene 1951).

(33) Cooper, M.L. Keller, H.M. (1950). American Journal of Diseases of Children, 80, 911.

(34) Boyd, J.S.K. (1951). British Medical Journal, i, 1440.

(35) Tateno, I. (1951) Japanese Journal of Experimental Medicine 21, 79.

(36) Stang, F. (1951). The Medical Officer, 86, 183.

(37) Roberts, E.W. (1951). The Medical Officer, 86, 35.

(38) Bulletin of the Ministry of Health and P.H.L.S. (1953) November.

(39) Ross, A.I. (1954). The Medical Officer, 91, 95.

(40) Hardy, A.V., Halbert, S.P. (1948) Public Health Report (Washington) 63, 790.

(41) Philbrook, F.R., Barnes, La V.A., McCann, W.J. (Jr.)., Harrison, R.R. (1948) United States Naval Medical Bulletin, 48, 405. (Bulletin of Hygiene 1948).

(42) Ross S., Burke, F.G., Rice, E.C., Birchoff, H., Washington, J.A. (1949). Journal of the American Medical Association, 141, 183.

(43) Ross, S., Burke, F.G., Rice, E.C., Washington, J.A., Stevens, S. (1950). Journal of the American Medical Association, 143, 1459.

(44) Cooper, M.L., Keller, H.M. (1950). American Journal of Diseases of Children, 80, 911.

(45) Tateno, I. (1951). Japanese Journal of Experimental Medicine, 21, 79. (Bulletin of Hygiene, 1952).

(46) Hardy, A.V., Mason, R.P., Martin, G.A. (1951). Annals New York Academy of Science, Vol. 55. Dec. 30th, 1952.

(47) Ross, S., Burke, F.G., Rice, E.C. (1952). "Antibiotics and Chemotherapy", New York, 2, 199.

(48) McFadyean, A.J.S., Stewart, P.H. (1952) Lancet 2, 166.

(49) Forbes, G.B. (1953) British Medical Journal 1139.

(50) Welch, H. (1950) Annals New York Academy of Science 53, 253.

(51) Gray, J.D. (1953). The Journal of Hygiene 51, 326.

(52) Hodgkinson, R. (1954). Lancet, February 6th.

(53) American Council of Pharmacy and Chemistry (1954). Journal of the American Medical Association, 154, 144.

(54) Speirs, A.L. (1954) British Journal af Pharmacology and Chemotherapy, 9, 59.

(55) Stocks, A.V. (1954) The Medical Officer, 92, 85.

(56) White, H.J., Bell, P.H., Bone, J.F., Dempsey, J.C., and Lee, M.E. Journal of Pharmacology and Experimental Therapy. 85, 247. (Bulletin of Hygiene, 1946).

(57) Watt, J., Hardy, A.V., De Capito, T.M. Public Health Reports (Washington) 1942. 57, 524.

(58) Fairbrother, R.W. (1944) . British Medical Journal 489.

(59) Gorman, J. (1950) The Medical Officer, 83, 241.

(60) Hardy, A.V., Watt, J. American Journal of Public Health (1944) 34, 503.

(61) Brewer, A.E. 1944. Lancet 471.

(62) Fairbrother, R.W. (1944). British Medical Journal 489.

(63) Bulletin of the Ministry of Health and P.H.L.S. (1942) November.

(64) Stang, F. (1951). The Medical Officer, 86, 183.

(65) Garfinkel, B.T., Martin, G.M., Watt, J., Payne, F.C., Mason, R.P., Hardy, A.V. Journal of the American Medical Association (1953) 151, 1157.

(66) Bulletin of the Ministry of Health and P.H.L.S. (1953) November.

(67) Fairbrother, R.W. (1944). British Medical Journal 489.

(68) Welch, H. (1950). Annals New York Academy of Science 53, 253.

(69) Forbes, G.B. (1953) British Medical Journal 1139.

(70) The Registrar General. One per Cent. Sample Tables 1951 Census.

(71) "The Economist" (1954) February 13th.

(72) The Registrar General. Decennial Supplement to the 1951 Census.

(73) Thwaites, E.J., Sutherland I. (1952) Archives of Diseases of Childhood, Vol. 27, No. 131.

(74) Hughes, E.L. (1948) British Medical Journal i, 597.

(75) Dimmer, F.H.M. (1949) British Medical Journal 2, 14.

(76) Ross, A.I. (1951). The Lancet, 1, 630.

(77) Westropp, C. (1953) The British Medical Journal 1, 138.

(78) Bowlby, A.H. (1952) World Health Organisation Publication, 1952.

(79) Shaw, C.H. (1953) Bulletin of the Ministry of Health and P.H.L.S. February.