patient. There had been no history suggestive of coronary insufficiency before or since recovery from the illness, the blood cholesterol was within normal limits, and no Q waves were demonstrated although widespread injury was indicated cardiographically. Eight months after delivery (July, 1958) no change could be detected in the E.C.G. before and after exercise (stepping test at the rate of 30 steps a minute for two minutes).

Bashour and Winchell (1954) reported two cases of myocardial degeneration in pregnancy and the puerperium which fit into the clinical pattern of the picture previously described. They discovered a factor in each case which could account for the degeneration, sensitivity to sulphonamide therapy, and an epidemic respiratory infection respectively; and postulated that if each case history was analysed in sufficient detail a cause for the degeneration would be found.

A feature of this patient was the difficulty in obtaining therapeutic levels in most drugs used in her treatment. It was found impossible to lower the prothrombin time to therapeutic levels by phenindione and ethyl biscoumacetate; large doses of quinidine (4.7 g. a day) produced a blood level of only 2 mg. per litre, and 1.5 mg. of digoxin daily was required to maintain her digitalization. An intestinal cause was unsuccessfully sought to explain these factors; the stools had never been loose, bulky, or offensive, the patient was well nourished, and fat-balance studies showed normal absorption. The glucose-tolerance curve and the serum alkaline phosphatase were normal. The possibility that excessive tissue metabolism of these drugs might have occurred was considered but not investigated.

Summary

A case of myocardial degeneration occurring in late pregnancy and the puerperium is reported because of its rarity and its conformity to other reported cases. A satisfactory clinical recovery occurred.

The syndrome consists of congestive heart failure occurring in the last trimester of pregnancy and the puerperium with no previous history of cardiovascular disease. It is associated with sinus tachycardia, small pulse volume, triple rhythm, precordial systolic murmur, a loud second sound in the pulmonary area, profuse sweating, emboli, and cardiographic evidences of myocardial disease.

No satisfactory cause for the degeneration has been discovered.

I thank Professor R. E. Tunbridge and Dr. G. Watkinson for their advice on the manuscript and permission to publish the case history.

ADDENDUM.—Since this paper was submitted Benchimol *et al.* (1949) have published a series of 18 cases of post-partum heart failure occurring in the absence of pre-existent cardiac disease. In this series they state that they recognize five main groups classified according to aetiological factors: (1) cases undoubtedly due to toxæmia of pregnancy (8 cases); (2) cases probably related to toxæmia of pregnancy (3 cases); (3) cases related to non-specific myocarditis which may be seen associated with several types of infection; (4) cases with pre-existent hypertensive disease (chronic pyelonephritis, etc.); and (5) cases corresponding to specific myocarditis (Chagas's disease and miliary tuberculosis).

The cases reported in group 2 conform very closely in clinical, E.C.G., and radiological descriptions to those of the above case report.

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ACUTE BACILLARY DYSENTERY IN CYPRUS

A COMPARATIVE STUDY OF TREATMENT IN 332 CASES

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Bacillary dysentery has always been very common amongst British Forces in the Middle East. In the first world war its incidence and severity were extremely high, but in the second the disease was not so disastrous. However, it still produces more admissions to hospital than any other condition in these Forces. In the United Kingdom it is also of considerable importance, particularly in children. The annual notifications in England and Wales have risen from 2,860 in 1940 to 28,910 in 1957, with a peak of 49,009 in 1956.

Sulphonamides were introduced as the standard treatment of dysentery nearly twenty years ago, and were the subject of favourable reports by Fairley and Boyd (1943), Bulmer and Priest (1943), Hardy (1946), and Weil (1947). Controlled trials by Fairbrother (1944), Scadding (1944, 1945), Jamieson *et al.* (1944), and Brodie *et al.* (1946) suggested that these compounds were little better than supportive treatment, but they still remain the standard treatment for bacillary dysentery.

The Korean War provided the opportunity for a large scale trial of broad-spectrum antibiotics by Garfinkel *et al.* (1953), and they were also used in a smaller trial in England by Abbott and Parry (1955). Although the tetracyclines proved the most successful, the hazards attending their use are generally thought to outweigh their advantages. Oral streptomycin was recommended by Ross *et al.* (1949) and by Sangster (1956). A combination of sulphonamide and streptomycin was recommended on laboratory evidence by Klein and Kimmelman (1946) and tried with success on infants by Johnson and Landsman (1957).

A trial of dysentery treatment was undertaken at the R.A.F. Hospital, Akrotiri, Cyprus. The object was to

compare and evaluate the merit of symptomatic non-specific treatment with recognized specific treatment, using antibacterial agents. The second object of the trial was to compare small-dose soluble sulphonamide treatment augmented by oral streptomycin with the large-dose insoluble sulphonamide treatment that has been popular in this country.

Material and Methods

A fairly mild variety of bacillary dysentery is seasonal in Cyprus between May and November. All male patients with acute bacillary dysentery admitted to the hospital in 1957 and 1958 were included in the trial so long as they had not already received chemotherapy. All were young Service men between the ages of 19 and 30. The length of history before admission varied from 12 to 48 hours: this is in contrast to the cases reported from the Middle East during the last war by Fairley and Boyd (1943) and Scadding (1944, 1945), when two to four days was the usual period.

Three daily consecutive stool specimens were examined by microscopy and culture on desoxycholate citrate agar. The diagnosis of acute bacillary dysentery in a case with acute diarrhoea was made on either or both of the following findings: (1) isolation of a shigella identified by slide agglutination and sugar cultures; and (2) microscopical discovery of a "bacillary exudate," consisting of an inflammatory exudate containing a large number of pus cells and red cells with fewer macrophages and epithelial cells. Isolation of a shigella resulted in the diagnosis of "proved bacillary dysentery," while the finding of a bacillary exudate resulted only in a diagnosis of "clinical bacillary dysentery." The latter diagnosis was used by Fairley and Boyd (1943) and by other writers.

The organisms isolated from all the cases are detailed in Table I. Shigellae were isolated from 146 cases—in 130 (89%) from the first specimen and 10 of the

TABLE I.—*Dysentery Bacilli Isolated in 1957 and 1958*

Organism	Total No.	%
Flexner I	18	12.3
" III	2	1.4
" VI	52	35.6
Sonne	72	49.3
Boyd DI	2	1.4

remainder from the second. With only two exceptions, whenever a shigella was isolated the stool had shown a bacillary exudate.

Comparison of Treatment by Phthalylsulphathiazole with Non-Specific Treatment

The R.A.F. Institute of Pathology and Tropical Medicine recommends as routine treatment for bacillary dysentery a six-day course of 125 g. of phthalylsulphathiazole. This dosage is higher than that used in most dysentery treatment trials, but is in accordance with the recommendations of Fairley and Boyd (1943).

Alternate patients in 1957 were given either phthalylsulphathiazole in an initial dose of 9 g. followed by 4 g. five times daily for a total of six days, or "dummy" tablets labelled "K.110," inert except for homeopathic doses of mixed vitamins, twice daily for six days. The identity of these tablets was not revealed to patients or nursing staff. In addition, mist. kaolin et morph. B.P. was given to both groups in the usual dosage

as often as required. The seventh day after treatment was a rest day, and from the eighth to the thirteenth day the patient produced six daily clearance stools which were examined by the laboratory.

Results.—Clinical measurements were not made at this stage, but the impression gained was that the diarrhoea and colic of patients on the sulphonamide settled about one day before those of the control group. The relapse rates are shown in Table II: the difference between

TABLE II.—*Preliminary Trial Relapse Rates*

Type of Dysentery	Sulphonamide Group			Control Group		
	Cases	Relapsed	%	Cases	Relapsed	%
Flexner I ..	2	0	0	4	0	0
III ..	1	0	0	1	0	0
VI ..	2	0	0	2	0	0
Sonne ..	24	1	4.2	26	7	26.9
Boyd DI ..	0	—	—	2	0	0
Total proved	29	1	3.3	35	7	20.0
Clinical dysentery	58	5	8.6	51	8	15.6
Total ..	87	6	6.9	86	15	17.4

them in the proved cases is statistically significant ($D./S.E. = 2.01$), as is that in the total dysentery group ($D./S.E. = 2.10$). Those cases with proved dysentery which relapsed did so coincident with the discovery of the organism in a clearance stool, and those with clinical dysentery were found to have relapsed on the discovery of a shigella or the reappearance of a bacillary exudate alone. The vast majority of relapsed cases did not have more diarrhoea.

Comparison of Soluble Sulphonamide and Streptomycin with Phthalylsulphathiazole

Alternate patients in 1958 were given either phthalylsulphathiazole in the dosage detailed above, or "streptotriad," a proprietary preparation containing in each tablet 65 mg. of streptomycin, 100 mg. of sulphathiazole, 100 mg. of sulphadiazine, and 65 mg. of sulphamerazine. This was given as three tablets thrice daily for six days, the whole course being 3.51 g. of streptomycin and 14.31 g. of soluble sulphonamide. The identity of these tablets was concealed behind the name "K.111." In addition, mist. kaolin et morph. B.P. was given as required.

Follow-up.—The patients were seen daily by a medical officer and the duration of diarrhoea was noted. After the six treatment days one rest day passed before the six consecutive daily clearance stools were examined.

Results.—Since the time regime of treatment was the same, only two criteria of the effectiveness of the treatment have been chosen: the duration of diarrhoea from the beginning of treatment, and the clinical and bacteriological relapse rate during the six clearance days. Measurement of the duration of fever or abdominal colic was found to be of little value since only some 55% of the patients had a fever, and this settled in almost every case by the end of the second day.

The duration of diarrhoea is shown in the Chart, expressed as a percentage of those still having more than two loose stools daily on the various days of treatment. In the sulphonamide-treated group the average duration of diarrhoea of those with proved dysentery was 3.45 days, for those with clinical dysentery 3.43 days, and for the whole group 3.44 days. In the streptotriad-treated group the average duration in those with

proved dysentery was 2.84 days, in those with clinical dysentery 3.02 days, and in the whole group 2.95 days. These figures have been analysed statistically with the following results:

All phthalylsulphathiazole cases: mean, 3.44 days. Standard deviation, 1.18. All streptotriad cases: mean, 2.95 days. Standard deviation, 1.03. Difference of the means: 0.49. Standard error of the difference of the means: 0.176.

The difference of the means is statistically significant, being considerably more than twice its standard error. The relapse rates are shown in Table III; the difference between them in the proved cases is not significant (D./S.E.=0.28), nor is that for the total dysentery cases (D./S.E.=0.26).

TABLE III.—Main Trial Relapse Rates

Type of Dysentery	Sulphonamide Group			Streptotriad Group		
	Cases	Relapsed	%	Cases	Relapsed	%
Flexner I ..	5	2	40.0	7	2	28.5
.. VI ..	28	2	7.1	20	1	5.0
Sonne ..	12	0	0	10	1	10.0
Total Proved ..	45	4	8.9	37	4	10.8
Clinical dysentery	35	3	8.6	42	2	4.8
Total ..	80	7	8.7	79	6	7.6

The figures for 1957 and 1958 have been combined to show the clearance day on which the cases relapsed (see Table IV). This clearly demonstrates the importance of examining several clearance specimens.

TABLE IV.—Day of Relapse

Clearance day ..	1	2	3	4	5	6
Number relapsed	10	5	6	7	1	5

Discussion

One of the difficulties in comparing treatments for dysentery is that reported epidemics vary greatly, not only in the type of organism but also in severity. The pattern of dysentery in the Middle East has changed in recent years. Boyd (1946) reported the isolation of shigellae in 27,414 men of the Middle East Forces between 1940 and 1943; 19% *Sh. shigae*, 7% *Sh. schmitzii*, 62% *Sh. flexneri*, and only 7% *Sh. sonnei*.

In the present small series of 146, however, there were neither *Sh. shigae* nor *Sh. schmitzii*; 49% were *Sh. flexneri*, and *Sh. sonnei* had risen to 49%. Thus comparison between the present series and those of Fairbrother (1944) and Scadding (1944, 1945) becomes difficult. On the other hand, the series from the United Kingdom refer almost exclusively to *Sh. sonnei*, and the great majority of cases described are in infants and small children.

A further point of considerable importance in comparing one trial with another, even when the same drug is used, is the total dosage and the duration of administration. Thus for the insoluble sulphonamides this has varied from 31 g. in five days (Brodie *et al.*, 1946) and 56 g. in seven days (Abbott and Parry, 1955) to 90 g. in six to nine days (Fairbrother, 1944); while the dose used in the present series was 125 g. in six days. This large dose is recommended in the R.A.F. because of the unsatisfactory response to smaller dosages (W. P. Stamm, 1958, personal communication).

Finally, any test of cure must involve an adequate clearance check. Fairbrother stated: "It is obvious that the criterion of freedom from infection at present generally accepted—that is, three successive negative results—is quite unreliable." He therefore recommended that 12 daily specimens should be obtained, beginning six days after cessation of treatment. This, however, is impracticable, since it involves some four weeks' isolation. The method adopted here—six successive days, beginning two days after the cessation of treatment—is longer than in many of the reported trials.

The results recorded in this paper show that one week's symptomatic treatment alone allowed one in five of proved bacillary cases to flourish as intestinal carriers, whereas a full course of phthalylsulphathiazole produced bacteriological cure in 93.1% of cases as well as quicker symptomatic recovery. The difference between relapse rates with streptotriad and phthalylsulphathiazole was not significant, although with streptotriad the duration of diarrhoea was significantly shorter by half a day. In addition to this advantage, streptotriad is much more acceptable to the patients, since no large initial dose is required and the six-day course consisted of only 54 tablets, while phthalylsulphathiazole began with 18 tablets and a total of 250 tablets in six days. This is important when one considers that in many cases of acute bacillary dysentery nausea is a leading symptom. Finally, at these dosages, a course of streptotriad at current retail prices is 11s. 9d. cheaper. No side-effects were noted in the group on streptotriad, but one patient on phthalylsulphathiazole developed a transient macular rash.

Summary

A trial of treatment for acute bacillary dysentery is described.

A full course of phthalylsulphathiazole was shown to be significantly more effective, both clinically and bacteriologically, than supportive treatment alone.

A mixture of soluble sulphonamide and streptomycin in moderate dosage gave better clinical results than the full course of phthalylsulphathiazole, and is both cheaper and more acceptable to the patient.

The changing pattern of bacillary dysentery, the need for a standard dosage of sulphonamides, and the importance of adequate tests of cure are discussed.

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SULPHONAMIDES AND STREPTOMYCIN IN BACILLARY DYSENTERY

A CONTROLLED TRIAL

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Bacillary dysentery is very prevalent in many warm climates, and in recent years its incidence has greatly increased in temperate climates, especially during the winter and spring. Before the introduction of sulphonamides the course of the illness was not infrequently prolonged, disabling, and sometimes fatal. The use of the poorly absorbed sulphonamides in the early years of the second world war revolutionized treatment, and later the absorbable sulphonamides in smaller dosage were found to be equally effective, although special care must be taken with them, especially in the tropics, to keep the patient free from renal blockage by adequate hydration. The combination of three sulphonamides used in this trial has generally been found to be remarkably free from this defect. In recent years, however, sulphonamide-resistant strains, especially of *Shigella sonnei*, have been met with increasingly, and streptomycin given orally has been widely reported as a satisfactory though expensive substitute, but, again, some strains have become resistant to streptomycin. In some hospitals, therefore, the newer broad-spectrum antibiotics have been employed in moderate or low dosage. Marked success in the control of the dysenteric symptoms has been claimed with these, but there is a risk of side-effects, some very serious. In any case, the high cost

of these drugs makes their massive use out of the question in most tropical and semi-tropical countries.

In order to explore the factors of efficiency combined with cheapness in the mass treatment of bacillary dysentery, a small controlled trial was carried out in Zagreb with (a) sulphonamides alone, (b) tablets containing about 80% sulphonamides and 20% streptomycin, and (c) streptomycin alone. Patients with the acute dysenteric syndrome (abdominal pain, tenesmus, and acute diarrhoea with blood and mucus in the stools), who had had no specific treatment before admission to the hospital, were given the following treatment in successive groups, the dosage being suitably modified in children.

Group 1.—0.5-g. tablets of "sulphatriad" in dosage for adults of 1 g. six-hourly for seven days (total 28 g.). (0.5 g. sulphatriad=0.185 g. sulphathiazole + 0.185 g. sulphadiazine + 0.130 g. sulphamerazine.)

Group 2.—"Streptotriad" tablets (each containing 265 mg. sulphatriad and 65 mg. streptomycin sulphate) in dosage for adults of 2 tablets six-hourly for four days only (total 2.08 g. streptomycin and 8.5 g. sulphatriad).

Group 3.—Streptomycin tablets in dosage for adults of 2 250-mg. tablets six-hourly for four days only (total 8 g. streptomycin sulphate).

A fourth group of patients was started on symptomatic treatment only, but the first two patients remained ill so long that this was, temporarily at least, abandoned.

The numbers in each group are small because so many patients had had some specific treatment before admission and were therefore excluded from the trial. However, before treatment was begun each patient had a careful clinical evaluation, including daily inspection of the stools, a rectal swab, and three stools taken at the bedside, inoculated into desoxycholate medium and incubated immediately; in addition each stool passed during the treatment and for a few days thereafter was bacteriologically examined.

Results

Group 1 consisted of 12 patients—5 *Sh. flexneri* (types I, II, or VI), 5 *Sh. sonnei*, and 2 from whom no shigellae were isolated. In 7 out of 10 proved cases fever after admission ranged from 37.2 to 39.2° C. The treatment was started on the second or third day of disease in 8 of the 10 proved cases. The temperature became normal on the first day of treatment in 6 out of 7 febrile patients. In the proved cases the stools became normal between the first and sixth days of therapy except in two instances. Bacteriologically all the cases were free from shigellae after the fifth day of treatment, the *Sh. sonnei* cases taking longer than the *Sh. flexneri* cases to clear up.

Group 2 consisted of 15 patients—10 *Sh. flexneri* (types I, II, III, or IV), 2 *Sh. sonnei*, 1 *Sh. schmitzii*, and 2 bacteriologically negative. Fever after admission in 8 out of 13 proved dysentery cases ranged from 37.5 to 39.3° C. The treatment was started on the second or third day of disease in 9, on the fourth or fifth day in 2, and on the seventh and ninth days in 2. The temperature became normal on the first or second day of treatment in all 8 febrile cases. The stools became normal in appearance between the third and eighth days, mostly on the fifth or sixth day. Bacteriologically the stools became negative after the first day of treatment