

be carried, I would add that whilst no one device suggested by experiment can be capable of meeting every contingency, neither is any one likely to be destitute of value if it sufficiently reconciles a large number of obvious difficulties; this pattern seems to cover these more than any other I have tried.

AN INVESTIGATION INTO THE RESULTS FROM TREATMENT OF BACILLARY DYSENTERIES BY SERUM AND BY SALINES RESPECTIVELY.

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DYSENTERY of a bacillary type has been extremely prevalent amongst our troops in the Salonica area, and has resulted in the invaliding to England of a number of men. The following investigation was therefore undertaken in order to ascertain, if possible, the relative efficiency of the two more important methods of treatment at present in use. From the large amount of material to which I had access it was finally decided to select only those cases which occurred during 1916, and in which the diagnosis of dysentery had been confirmed by bacteriological examination. Such a limitation has necessarily resulted in the inclusion of an unduly large proportion of exceptionally severe and complicated types of the disease, since a laboratory examination for all was an impossibility and was naturally reserved for the more acute cases or for those presenting special features. It was found that in 535 cases a dysentery bacillus had been isolated. These have been divided into two groups which are dealt with separately, viz., cases due to an infection by the bacillus of Shiga, and those due to an infection by either the bacillus of Flexner or the bacillus of Hiss (Y). Those showing mixed infections, e.g., by the bacillus of Shiga + *Bacillus typhosus*, have been excluded throughout.

The methods of treatment under consideration are the two now most commonly adopted, namely, treatment by anti-dysenteric serum either alone or in combination with salines, and treatment by salines only. As will be shown later, the dosage both of serum and of salines as administered to these cases was extremely varied.

SHIGA DYSENTERY.

The bacillus of Shiga was isolated in 395 cases, eleven of which terminated fatally. Eighteen cases which recovered and six fatal cases were instances of double infections and are therefore excluded from the following figures. A further eighteen are also excluded as they received neither serum nor salines during the course of their illness. It is, however, interesting to note that several of these latter who received practically no treatment became chronic carriers of the bacillus of Shiga.

Of the remaining 348, anti-dysenteric serum was given to 176, whilst 172 received salines only. As affording some guide as to the efficacy of treatment the cases have been classified according to their mode of progress towards convalescence, and in order to render the results more strictly comparable the day

of illness on which treatment was commenced has always been taken into consideration.

Class I.—Convalescence rapid. A total of 157 cases received treatment *on or before the fifth day of illness.* Of these, sixty-four per cent who were given serum made a rapid recovery, as compared with forty-eight per cent who received saline treatment only. Of cases coming under treatment *between the sixth and tenth days of illness* twenty-six per cent of those who received serum, even at this late stage, could still be shown to have made a rapid convalescence as compared with only fourteen per cent who received salines. Even *after the tenth day of illness* it is still possible to obtain five per cent of rapid recoveries, when serum is administered, though not a single case treated with salines at this stage could be placed in this class.

Class II.—Convalescence slow, but generally quite satisfactory. The slow rate of progress of cases in this group was often accounted for by an intercurrent attack of malaria. The majority were able to be transferred finally to a convalescent camp, though a small number of severe cases which were treated with serum were sent to England for the completion of their cure. The figures of cases in this class are shown in Tables I and II, and not much is gained by a further study of them.

Class III.—Convalescence Unsatisfactory. By this is meant a failure to respond to treatment or the development of some complication. This group is one of considerable interest. Of 157 patients treated *on or before the fifth day of illness,* in only nine per cent of those who received serum could convalescence be said to have been unsatisfactory, as compared with twenty-five per cent of those who received salines only. Of cases coming under treatment *between the sixth and the tenth day of illness* as many as twenty-seven per cent of those who received serum fall into this class, a fact which serves to emphasize the necessity for *early* treatment with serum. High as these figures are they are even higher for those who received saline treatment only, where it was found that in fifty-eight per cent convalescence was unsatisfactory. The majority of cases in this class had of necessity to be invalided to England, some showing every indication that their disease was passing on into one of chronic dysentery. The appended tables set forth the actual figures on which the above percentages are based.

TABLE I.—SHIGA DYSENTERY, TREATED WITH ANTI-DYSENTERIC SERUM.

| Treatment begun on | Number of cases | Convalescence | | |
|--------------------|-----------------|---------------|------|----------------|
| | | Rapid | Slow | Unsatisfactory |
| 1st day of disease | — | — | — | — |
| 2nd " " | 9 | 8 | 1 | — |
| 3rd " " | 10 | 7 | 3 | — |
| 4th " " | 26 | 16 | 7 | 3 |
| 5th " " | 19 | 10 | 6 | 3 |
| 6th " " | 26 | 8 | 13 | 5 |
| 7th " " | 22 | 6 | 9 | 7 |
| 8th " " | 9 | 2 | 4 | 3 |
| 9th " " | 4 | 1 | 2 | 1 |
| 10th " " | 12 | 2 | 6 | 4 |
| After 10th day | 39 | 2 | 19 | 18 |

TABLE II.—SHIGA DYSENTERY, TREATED WITH SALINES ONLY.

| Treatment begun on | Number of cases | Convalescence | | |
|--------------------|-----------------|---------------|------|----------------|
| | | Rapid | Slow | Unsatisfactory |
| 1st day of disease | 2 | 2 | — | — |
| 2nd " " | 12 | 8 | 3 | 1 |
| 3rd " " | 30 | 14 | 10 | 6 |
| 4th " " | 29 | 13 | 6 | 10 |
| 5th " " | 20 | 8 | 6 | 6 |
| 6th " " | 16 | 5 | 3 | 8 |
| 7th " " | 20 | 3 | 7 | 10 |
| 8th " " | 9 | — | 4 | 5 |
| 9th " " | 6 | — | 4 | 2 |
| 10th " " | 5 | — | 2 | 3 |
| After 10th day | 23 | — | 6 | 17 |

It should be noted that not a single case with an unsatisfactory convalescence occurred amongst those treated with serum on or before the third day of illness, though such was not the case with those who received salines only. Moreover, after the seventh day of illness no single case treated with salines made a rapid recovery, whereas, even at this late stage, a small number who received serum thereafter made rapid progress.

Relapses.—It was noticed that there were several instances where patients, who appeared to have responded satisfactorily to treatment, suddenly developed a return of acute dysenteric symptoms whilst still in hospital. These have been termed relapses. All occurred within forty-five days of the original attack, and when finally invalided home several showed evidence of the condition becoming one of chronic dysentery. Of sixty-four patients who received serum *on or before the fifth day of illness* three per cent relapsed, whilst of ninety-three saline-treated cases, fifteen per cent relapsed. In those coming under treatment from *the sixth to the tenth day of illness* relapses occurred in 4 per cent who received serum, and in 19.6 per cent treated with salines only. Whilst of cases not treated until *after the tenth day* relapses occurred in five per cent of those who received serum and in 21.7 per cent of those who received salines only.

TABLE III.—SHOWING PERCENTAGE OF SERUM-TREATED AND SALINE-TREATED CASES WHICH BECAME CARRIERS.

| Treatment commenced | Carriers | |
|----------------------------------|---------------|----------------|
| | Serum | Salines |
| On or before 5th day of illness | 1.5 per cent. | 10.7 per cent. |
| On or before 10th day of illness | 2.7 " " | 7.0 " " |
| After 10th day of illness | 10.0 " " | 21.7 " " |

Carriers.—Any case in which it has been possible to isolate dysenteric organisms eight weeks or more after the onset of illness has been classed as a carrier. Only a small number of examinations were made at this late stage of the disease, so that these figures are necessarily incomplete. As already mentioned several instances of carriers occurred amongst men whose original attack of dysentery had been so mild that a restricted diet and a single dose of an aperient relieved them of all symptoms for the time, but as these had received neither salines nor serum, they are not included in the following figures. Of cases treated *on or before the fifth day* of illness only one who received serum is known to have become a carrier as compared with ten who were treated with salines

only, a percentage of 1.5 and 10.7 respectively. The value of serum in the *prevention* of these carriers is best shown in the accompanying table (Table III), and again it will be seen that to obtain the best results serum should be administered early in the disease. Trial was made of serum for the *treatment* of these carrier-cases but without any benefit.

Arthritis.—When examining the records of several thousand cases of dysentery, arthritis as a complication was found to occur in only a very small percentage. The majority developing this complication were, however, bacteriologically examined and hence an unduly high percentage is shown in the present series of bacteriologically proven cases. It is interesting to note that arthritis was often found associated with conjunctivitis or with iritis. In two instances patients with arthritis were found to be Shiga carriers. In 137 cases treated with serum *on or before the tenth day of illness* no single instance of arthritis occurred, whilst of thirty-nine cases which did not receive serum until after the tenth day arthritis occurred in one. Trial was made of serum for the *treatment* of this complication, but without any apparent benefit, and nearly all cases had finally to be invalidated home.

Cardiac Complications.—These comprise chiefly cases of cardiac dilatation, though there are included also a few instances of persistent tachycardia where no record has been made as to the condition of the heart. Of 157 patients treated *on or before the fifth day of illness* cardiac complications occurred in six per cent of those who received serum, and in fourteen per cent of those who received salines only. For cases treated *after the tenth day* cardiac complications occurred in 15.4 per cent of those who received serum and in nine per cent of those receiving salines. The smaller percentage amongst these saline-treated cases which came under treatment late in the disease can be readily accounted for by the milder, less toxic type of disease which these patients exhibited.

TABLE IV.—SHIGA DYSENTERY. COMPLICATIONS AND SEQUELÆ IN SERUM AND IN SALINE-TREATED CASES.

| Day of illness on which treatment commenced | Number of cases | | Relapsed | | Carriers | | Arthritis | | Cardiac complications | |
|---|-----------------|---------|----------|---------|----------|---------|-----------|---------|-----------------------|---------|
| | Serum | Salines | Serum | Salines | Serum | Salines | Serum | Salines | Serum | Salines |
| | | | | | | | | | | |
| On or before 5th day | 64 | 93 | 3 | 15 | 1.5 | 10.7 | — | 5.3 | 6 | 14 |
| On or before 10th day | 73 | 56 | 4 | 19.6 | 2.7 | 7 | — | 5.3 | 16.4 | 16 |
| After 10th day | 39 | 23 | 5 | 21.7 | 10 | 21 | 5 | 4.3 | 15.4 | 9 |

Deaths.—There were five fatal cases and death was found on post-mortem examinations to be due to *B. dysenteriae Shiga* infection, and only one received serum before the tenth day of illness. This was an acute case admitted very toxic on the second day and treated at first with salines only. On the seventh day he became slightly jaundiced. On the seventh, eighth and ninth days serum in twenty cubic centimetres doses was administered subcutaneously. On the tenth day the stools are noted as much improved in character, but on the thirteenth day the patient suddenly collapsed and died. Three fatal cases were instances of dysentery complicated by the occurrence of malarial attacks during

the acute stage. No serum was given until the fourteenth, thirty-fourth and fifty-sixth days of illness respectively, and death occurred on the fifteenth, forty-second, and sixty-eighth days respectively. The remaining case was treated with salines from the fifth to the eleventh day, when twenty cubic centimetres of serum were administered. Diarrhoea still continued. On the thirty-fifth day he began to pass much bright blood, which continued for six days. Emaciation became extreme. On the one hundred and fourteenth day symptoms pointing to perforation set in and death occurred four days later.

FLEXNER-HISS DYSENTERY.

Cases of dysentery due to an infection by the bacillus of Flexner or by the "Y" bacillus have been grouped together, there being only 140, and clinically they much resembled each other. With but three exceptions the cases were of a milder type than those due to an infection by the bacillus of Shiga, and there were no deaths. Ten patients had double infections, and are therefore excluded from the following figures, together with a further twenty-eight who received neither serum nor salines during the course of their illness.

Serum-treated Cases.—Only thirty-five cases of Flexner-Hiss dysentery received any serum treatment. Of eighteen treated *before the fifth day of illness* convalescence was rapid and satisfactory in fourteen. One became chronic and developed persistent tachycardia, two others developed cardiac dilatation and one relapsed and was known to be a carrier of the Flexner bacillus fourteen weeks after the onset of illness. Of seventeen cases treated *after the fifth day* convalescence was rapid and satisfactory in ten. Four showed signs of the condition becoming chronic and were invalided home, whilst three others developed cardiac dilatation. A point worth noting is the fact that cases with an infection by the "Y" bacillus did not respond to serum treatment as satisfactorily as did cases with an infection by the Flexner bacillus.

Saline-treated Cases.—Sixty-seven patients were treated with salines only. Of these forty-four received treatment *on or before the fifth day of illness*, and twenty-three made a rapid recovery. Convalescence was unsatisfactory in nine cases, four of whom had bad relapses. Cardiac complications occurred in five, and one case was known to have become a carrier. Of twenty-three patients treated *after the fifth day of illness* only six made a rapid recovery. Convalescence was unsatisfactory in eight, all of whom had finally to be invalided home. There were five cases which relapsed, five which developed cardiac complications, and three who were known to have become carriers.

In this group of Flexner-Hiss infections there was only one case of arthritis, and it is doubtful whether even this one could be classed as a true dysenteric arthritis, as the patient had for many years been subject to attacks of "rheumatism" associated with swelling of various joints. Whether arthritis ever occurs as a complication in dysentery of this group is a point requiring more accurate observation. There was, indeed, one other case of arthritis not included in the present series as no pathogenic micro-organisms could be isolated from the stools. His blood-serum, however, agglutinated the bacillus of Flexner sufficiently strongly to indicate that his dysentery had been due to infection by that organism. Neither of the above recorded cases of arthritis was associated with iritis or with conjunctivitis.

A summary of the results following treatment of Flexner-Hiss dysenteries is appended in Table V.

TABLE V.—COMPARING RESULTS FROM TREATMENT BY SERUM AND BY SALINES RESPECTIVELY IN FLEXNER-HISS INFECTIONS.

| Method of treatment | Convalescence unsatisfactory | Carriers | Relapsed | Cardiac complications |
|----------------------------|------------------------------|---------------|---------------|-----------------------|
| Serum before 10th day .. | 7 per cent .. | 3 per cent .. | 3 per cent .. | 17 per cent .. |
| Salines before 10th day .. | 22 „ .. | 6 „ .. | 14 „ .. | 15 „ .. |

Methods of treatment as exemplified in the present series of cases. In the treatment of these bacteriologically diagnosed dysenteries there is exhibited a marked degree of variation as to dosage and the frequency of administration of the doses both of serum and of salines.

Anti-dysenteric Serum.—The serum used was in the majority of cases a polyvalent one. A few cases of Shiga dysentery in garrison troops were treated by Dr. B. M. Cunningham with Shiga anti-dysenteric serum (Pasteur Institute) supplied through the kindness of Major W. Broughton-Alcock. Serum was at times given alone following a single dose of some aperient medicine, at other times in combination with salines administered more or less frequently. The smallest single dose was ten cubic centimetres—this patient (Flexner dysentery) received such a dose on the sixth and eighth days of his illness with but little benefit, followed by twenty cubic centimetres on the tenth day. Convalescence was slow, the man not being fit for convalescent camp until the end of the fourteenth week.

Another case received ten cubic centimetres on the tenth, eleventh and thirteenth days of illness; he developed severe serum sickness on the twenty-third day, followed by persistent tachycardia, but was transferred to the "Heart Clinic" of a convalescent camp at the end of fourteen weeks.

Several severe toxic cases received 100 cubic centimetres or more at one dose; one such case coming under treatment on the fourth day of illness was given 115 cubic centimetres of serum on the fifth day and 120 cubic centimetres on the sixth day. Convalescence was rapid, and the patient was transferred to camp at the end of eight weeks. The largest total amount of serum given to any one patient was 420 cubic centimetres. Treatment was not commenced until the seventh day; from then onwards to the twentieth this man received doses varying from 100 cubic centimetres to 20 cubic centimetres. He was transferred to camp at the end of eleven weeks. Another patient received between the sixth and thirteenth days a total of 340 cubic centimetres of serum together with intravenous salines and drachm doses of sodium sulphate by the mouth. He went to camp at the end of eight weeks. It is interesting to note that in both these cases serum sickness was mild.

From a study of the case-sheets of patients treated by serum it would appear that the best results are obtained where serum has been given in fairly large doses (forty to sixty cubic centimetres of polyvalent serum) and on consecutive days, salines being administered simultaneously by the mouth. The following examples serve to illustrate this point and its converse.

Salines.—The statement "case treated with salines only" in practice meant varying dosage and intervals, and largely depended on the severity of the case. Some medical officers would prescribe sodium (or magnesium) sulphate in drachm

or half drachm doses every hour for six, twelve or even twenty-four doses; others every two hours for twenty-four hours followed by less frequent doses. Other cases would receive these doses only every four hours and occasionally a mild case would be ordered salines only three times daily.

TABLE VI.—SERUM TREATMENT, WITH FAIRLY LARGE DOSES GIVEN ON CONSECUTIVE DAYS.

| Case No. | Treatment commenced | Days on which serum given | Daily dose of serum | Result |
|----------|---------------------|---------------------------|------------------------------|--|
| 7 | 6th day of illness | 6th, 7th and 8th | Centimetres 60, 40, 40 .. | Convalescence rapid and uneventful. To camp in 8 weeks |
| 11 | 4th ,, ,, | 4th, 5th, 6th and 7th | 60, 40, 40, 40 | To duty in 9 weeks |
| 25 | 7th ,, ,, | 7th and 8th .. | 60, 60 .. | To camp in 7 weeks |
| 104 | 2nd ,, ,, | 2nd and 3rd .. | 60, 60 .. | To camp in 6 weeks |
| 112 | 4th ,, ,, | 5th, 6th and 7th | 60, 60, 60 .. | To camp in 6 weeks |

TABLE VII.—SERUM TREATMENT, SHOWING EITHER TOO SMALL DOSAGE OR INTERVALS BETWEEN DOSES TOO LONG.

| CASE No. | Treatment commenced | Days on which serum given | Daily dose of serum | Result |
|----------|---------------------|-----------------------------|-----------------------------|---|
| 9 | 5th day of illness | 12th and 14th .. | Centimetres 40 and 20 .. | Slow progress. Invalided home |
| 21 | 2nd ,, ,, | 5th, 6th, 7th, 9th and 11th | 20 each dose | Slow progress. Cardiac dilatation. Invalided home |
| 57 | 7th ,, ,, | 8th and 11th .. | 60, 60 .. | Unsatisfactory result. Invalided home |
| 431 | 2nd ,, ,, | 3rd and 6th .. | 50, 40 .. | Slow progress. Invalided home |
| 86 | 4th ,, ,, | 4th, 6th and 11th | 20, 20, 40 .. | Unsatisfactory progress. Invalided home |
| 301 | 3rd ,, ,, | 5th, 6th and 11th | 20 each dose | Became chronic. Invalided home |

Summary.—It would be very difficult to obtain a parallel series of cases of equal severity and treated uniformly, on the one hand with serum combined with salines and on the other hand with salines only. Such an achievement could alone give strictly comparable results. Had it been possible to have included in this report every case of dysentery which passed through the hospital the results as obtained from *all* cases treated with serum would have still been by far and away the best, though at the same time the results from *all* cases treated with salines would have been better than in the present series of cases.

In spite of the severe type of case which was treated with serum the results have been shown to be vastly superior to those from cases which received salines only. All the figures, however, bring out the importance of early serum treatment. It should be noticed that no fatal case occurred amongst patients treated before the end of the first week. Even in Shiga dysentery eighty-eight per cent of cases treated from the second day and seventy per cent of those treated from the third day of illness made a rapid recovery, nor was there from amongst these cases a single one which had to be invalided home or which did not finally make a complete recovery. Even of those treated on or before the fifth day there were

only ninety per cent whose convalescence could in any way have been termed unsatisfactory.

Moreover, as a preventive of certain complications and sequelæ, serum holds a most important position. For example, it has been shown that not a single case of dysenteric arthritis occurred among patients who were treated on or before the fifth day of illness, and though data are necessarily incomplete, carrier cases would appear to be of far less frequent occurrence when serum has been used. Further, in spite of the toxic condition of so many of the patients when they first came under observation, only six per cent of those treated on or before the fifth day developed cardiac dilatation or persistent tachycardia. Not only was convalescence rapid when serum was given early, and repeated in adequate doses, but relapses were very rare, so that a more rapid evacuation of patients to convalescent camp was possible than in the case of those treated with salines only. The average duration of hospital treatment for the two classes of cases was found to be 8.6 and 9.6 weeks respectively.

It is therefore urged that there should be:—

(1) A more extensive use of anti-dysenteric serum which should be given at the earliest opportunity.

(2) That doses should be adequate, by that I mean at least 40 cubic centimetres of polyvalent serum, for a case of moderate severity.

(3) That two, three, or even four such doses should be given on consecutive days.

(4) That at the same time salines by the mouth should be administered frequently, drachm or half drachm doses every hour or every two hours until the stools become fæcal, and thereafter in gradually diminishing doses.

In conclusion I desire to tender my thanks to Lieutenant-Colonel G. B. Price, Officer Commanding Imtarfa Military Hospital, and to Major W. Broughton-Alcock, officer in charge of laboratory, Imtarfa Military Hospital, for facilities given to me for my work and for much encouragement and kindly advice.

Reviews.

THE CAUSATION OF SEX IN MAN. By E. Rumley Dawson, L.R.C.P.Lond., M.R.C.S. London: H. K. Lewis and Co., Ltd. Second Edition. 1917. Pp. 226. Price 7s. 6d. net.

In the second edition of his interesting monograph, Mr. Rumley Dawson has strengthened the evidence in support of his contention that the sex of an unborn child may not only be foretold but also even predetermined. The author's aim is to prove that unilateral ovulation occurs bimensually, and that the ovum proceeding from the right ovary is invariably endowed with male potentiality. Evidence in support of this theory is quoted from the results of operations and post-mortem examinations on cases of extra-uterine pregnancies and also by examples showing the interdependence of the succession of sexes and month of birth in large families. A careful scrutiny of the facts brought forward by the author leads one to the conclusion that his theory is worthy of serious consideration by all medical men,