others is prevented. All other forms of osteomyelitis are indications for x-ray therapy combined with the necessary surgical treatment. Amputations with their consequent disability may be avoided. Great claims have been made in the United States for the use of this treatment in gas gangrene. Parenthetically, as an example of failure of medical treatment post-herpetic neuralgia may be mentioned. The treatment of the posterior root ganglia by x rays is followed by quick cure. Trigeminal neuralgia also responds to irradiation of the Gasserian ganglion.

Acute Inflammations.—Carbuncles of the upper lip, some forms of erysipelas, cellulitis, lymphangitis, gas gangrene, and osteomyelitis of the skull should be treated at once with x rays. No harm whatsoever can be done by using small doses on a limited field, whereas delay may sometimes prove fatal. In very few cases of infection, however, the treatment fails to improve the condition.

Subacute and Chronic Inflammations.—The number of these conditions is very large; we will instance only a few. Good examples are actinomycosis, local tuberculous infections as of lymph nodes or mucous membrane, chronic osteitis, septic fingers, and other local septic conditions.

Prevention of Disfigurement.—Scars are much better, thinner, and less obvious in wounds that are treated by x rays, and keloid will be prevented if irradiation takes place soon after trauma. This treatment is now often employed by plastic surgeons.

Social Indications and Wartime Purposes.—Delay in healing of all kinds of inflammation may be of importance from its economical or its wartime aspect. Healing can be much accelerated by irradiation and the period of incapacity therefore considerably shortened.

Dosage

The wave-length does not seem to be of great importance if the lesion receives the same biological dose. This is not the same thing as the physical dose, because a larger number of roentgens (*r*) have to be given if the wave-length is shorter, in order to produce the same biological result. Nevertheless, Fukase has shown experimentally that the shorter wave-lengths give better results. Grenz rays* are not sufficiently penetrative to give the requisite lesion dose.

The accurate modern methods of measurement enable us to calculate the dose received by the lesion whether it is superficial or deep. Though a very large dose is definitely harmful and the optimum dose is very small, there is considerable latitude. Thus, double the optimum dose will still give a good result, though not the best. The dose to be received by the lesion lies between 30 *r* and 80 *r*. The former dose may be applied twice a week and doses from 50 *r* upwards once a week. This dose presumes the use of x rays of about 140 kV constant current with a filter of Al 5 mm. With higher voltage and filtrations the number of *r* must be larger to give the same biological dose; with lower voltages and filtration the number is smaller. Radium γ rays filtered by Pt 0.5 mm. necessitate a lesion dose double that used with medium x rays.

In acute cases it is best to use the smaller dose, repeating in 3 days, and again in 4 days if necessary. With chronic cases treatment may occasionally have to continue a long time—two or three months or even more. A case of extensive abdominal actinomycosis even took one of us a year to cure finally. The dosage rate is 10 to 80 *r*/min. The necessary dosage is so small that even the routine fluoroscopy is occasionally enough to stop the inflammatory reaction. Children with enlarged bronchial glands and constantly raised temperature sometimes lose this temperature rise if screened for about 5 minutes. A repeated dose of 150 *r* or more is likely to be followed by bad results.

Conclusions and Summary

Owing to the war the present is an important time to bring this method of treatment forward. The use of radiations in these cases is a very valuable one, and will without doubt much increase in the future, when experience has confirmed

* X rays of very long wave-length on the border (Grenze) of the ultra-violet.

the good results, which cannot be achieved by any other means.

The treatment of acute, subacute, and chronic inflammations by small doses of x rays is described, as well as the experimental and research work on which this treatment is based. The accelerated healing of wounds and fractures by irradiation is also described. The effect of x rays is due to the influence on local cellular reaction and local immunity. The reasons for the neglect of this treatment are gone into. The necessity for small doses is stressed, both for the better results and for the absence of late bad effects.

THE USE OF SULPHAGUANIDINE IN BACILLARY DYSENTERY

BY

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The cases surveyed in this paper were selected for treatment from 600 patients suffering from bacillary dysentery admitted to a general hospital in the Middle East over a period of 8 months. Of these, 77 were treated with sulphaguanidine. Its use was authorized only in severe or refractory cases. Hence the acute cases described represent those which from general experience of dysentery could not be expected to do well on standard treatment, and the chronic cases those which had already failed when so treated. There was occasionally a temporary shortage of supply, but every effort was made to give what was considered to be an adequate course of the drug. Sulphaguanidine consists of sulphanilamide in which one of the hydrogen atoms of the amino group is replaced by a guanidine ring, and is thus homologous with sulphathiazole and sulphapyridine. Experimental investigation has shown that sulphaguanidine, although water-soluble, is poorly absorbed by the intestinal mucous membrane. This would allow large concentrations to be maintained in the gut, with only a low tissue fluid and blood concentration resulting, and a correspondingly slight danger of toxic poisoning from large or prolonged dosage.

Of the 77 cases 26 were classed as acute and 51 as chronic. This differentiation was based mainly on the day of disease, and all cases giving a history of less than 2 weeks from the onset were considered acute. Duration of symptoms in the cases termed chronic varied from over 2 weeks to many months.

The Acute Series

Treatment and Routine

In these cases the malaise and toxæmia were severe and the motions very frequent, consisting of blood and mucus only. The majority had not received any treatment, although a few had had castor oil and sodium sulphate during their evacuation to this hospital.

Dosage of Sulphaguanidine.—With no previous experience as a guide the following arbitrary indications were used as a means of gauging the dosage required: 3.5 g. 4-hourly until (a) the patient's general condition showed marked improvement as evidenced by a drop in temperature, clean moist tongue, absence of toxæmia, and general feeling of well-being; and (b) the stools had been reduced to five or less in 24 hours and were faecal. 3.5 g. 4 times a day until the infrequent stools became a semi-solid with only slight traces of blood and mucus present. 3.5 g. 3 times a day until 2 or 3 days after the stools had become normal. Stools were considered normal when not more than two solid or nearly solid stools without blood were passed in a day. No particular attention was paid to a small excess of mucus, which was almost invariably present. In the early cases treated this latter part of the plan was not strictly adhered to and sulphaguanidine was stopped on the day the stools were free from blood.

On admission the patient was generally somewhat collapsed. He was put to bed, rested and warmed, and his clinical condition observed for the first few hours. During this time the frequency and character of stools were noted and specimens sent to the laboratory for plating and microscopy. Treatment with sulphaguanidine was started with an initial dose of 7 g. in the form of a powder stirred up in 2 oz. of water. In very severe cases this was followed by 3.5 g. in 2 hours, and again after 2 more hours. Otherwise the 3.5-g. doses were repeated at 4-hourly intervals. The diet was limited to fluids for the first 24 hours of treatment, after which mashed potatoes, fish, chicken, junket, and bread-and-butter were gradually added until on the third or fourth day the patient was receiving a full diet. No difficulty was encountered in getting patients to eat, as the desire for food returned almost invariably in the first 48 hours. Every effort was made to encourage a large fluid intake by mouth in the early stages to replace fluid loss. In no case was intravenous fluid found to be necessary.

The following adjuvant treatment was carried out: (1) In the case of Shiga infections, 30,000 units of antiserum; (2) mist. bismuth. c. creta, 1 oz. every hour, in the initial stages of treatment to aid in reducing the frequency of the bowel motions; (3) tinct. opii in 10-minim doses, or occasionally 1/4 gr. of morphine, to relieve abdominal pain.

Sigmoidoscopy was carried out during the week after treatment, and subsequently if a normal mucosa was not seen the first time. Sigmoidoscopy as a routine measure before treatment did not seem justifiable. The rectum was, however, examined in a few cases, and showed a typical picture of sloughs separating to leave intensely congested and bleeding surfaces with varying oedema and induration. In acute cases the general condition and a stool examination would seem to be an adequate means of assessing the intensity of the infective process. The urine was tested daily and a blood count done at completion of treatment.

TABLE I.—Acute Cases

No. of Case	Clinical Nature	Day of Disease	Bacteriology	No. Days Treatment	Total Dosage (g.)	Day of Marked General Improv.	Day Stools Faecal	Day No Abdom. Tender	Day No Abdom. Pain	Day Stools Normal	Remarks and Sigmoidoscopic Findings
13	Very severe	6	Shiga	17	266	10	10	10	9	14	Healed
10	"	10	"	11	199	7	5	7	7	9	"
12	"	12	"	13	192.5	6	7	6	4	11	"
20	"	6	"	11	171.5	4	7	4	4	8	"
17	"	3	"	12	161	9	6	5	3	10	"
21	"	4	"	10	154	4	5	5	6	8	"
18	"	10	"	10	150	5	8	7	3	8	"
6	"	5	"	11	143.5	3	5	5	5	9	"
8	Severe	2	"	9	133	2	3	3	3	7	"
15	"	8	"	10	133	4	5	4	2	8	"
9	"	12	"	9	117	3	4	4	2	8	"
26	"	7	"	9	108.5	4	4	4	2	7	"
7	"	12	Flexner	9	136	4	4	4	3	8	"
22	"	8	"	8	98.5	3	3	4	4	6	"
24	"	10	"	7	98	2	2	4	4	5	"
11	"	1	"	7	91	2	2	3	3	5	"
14	"	2	"	7	91	2	3	3	3	5	"
19	"	12	Not identified	7	112	4	4	4	3	6	"
25	"	7	"	7	98	3	2	3	4	4	"
23	Very severe	10	Shiga	20	350	—	always faecal	—	—	—	Mucosa remained injected and oedematous (catarrhal). See case notes
16	"	4	"	7	136	5	5	6	3	7	Mucosa showed marked induration and oedema with ulceration
4	Severe	9	"	7	101	4	3	6	3	7	Hyperaemic granular mucosa in patches and loose faecal stools with blood after a few days. Degrees of induration and oedema of bowel wall, with occasional bleeding ulceration
3	"	3	"	7	101	3	3	4	4	7	
2	"	4	Flexner	5	60	5	3	4	4	—	
1	"	5	Not identified	5	77	2	4	3	3	5	
5	"	10	"	8	123	4	4	5	5	7	

Out of a total of 26 acute cases treated 16 were Shiga, 6 Flexner, and 4 undetermined culturally but having a typical bacillary exudate in the faeces. Table I gives the cases in descending order of dosage and grouped according to cultural findings, except that those not completely cured and not showing a healed mucosa on sigmoidoscopy are grouped at the bottom. The cases are classed as severe or very severe according to their clinical condition on admission to hospital.

Cases Completely Cured.—Of the 26 cases 19 were cured, of which 11 were severe and 8 very severe. Table II shows the days on which recovery from symptoms occurred.

TABLE II.—Showing Days of Recovery from Symptoms

	Severe Cases (11)	Very Severe Cases (8) (All Shiga)
Average total dose	110 g. over 9 days	180 g. over 12 days
Marked general improvement	2 to 4 days	3 to 10 days
Stools became faecal	2 to 5 days	5 to 10 days
No abdominal tenderness	3 to 5 days	4 to 10 days
No abdominal colic	2 to 4 days	3 to 9 days
Normal stools	5 to 8 days	8 to 14 days

It is interesting to note the quick response to treatment of Cases 11 and 14 (Table I), both of which were severe Flexner infections treated on the first and the second day of onset respectively. Treatment lasted a week, with a total dosage of 91 g., and in spite of the severity of the infection stools were formed, and without blood, on the fifth day, the patient being discharged from hospital in full health 14 days from the onset of disease.

Cases Not Completely Cured.—These cases numbered 7—5 severe and 2 very severe. In the severe cases the average total dose was only 90 g. over 6 days and the response of symptoms to treatment occurred as in the cured cases. Sulphaguanidine was stopped on the day stools became normal. These cases continued to improve for a few days and then suffered a relapse, although not of a very acute nature. Stools became loose, 4 to 10 daily, with blood and mucus. There was some return of colic and abdominal tenderness. In all cases sigmoidoscopy showed moderate hyperaemia and granulation of the mucosa, accompanied by a variable degree of oedema, induration, and bleeding from actual induration. Subsequent treatment with colonic wash-outs produced complete healing in from 2 to 4 weeks. As both the very severe cases were Shiga infections they are here described separately:

Case 16.—Sulphaguanidine was stopped owing to a shortage of supply after 136 g. had been given over 7 days. The response to treatment was quite satisfactory, with the disappearance of symptoms and the return of faeces to the stools. The latter, however, still contained mucus with very slight traces of blood the day treatment had to be suspended. No further improvement was seen and the case became chronic, with up to 6 loose stools daily containing blood and mucus. Shiga's bacillus was again isolated from the stools, and sigmoidoscopy showed much induration and oedema of the bowel wall, with a coarsely granular hyperaemic surface, nodular in places and covered by mucus which was expressed from pockets by passage of the instrument. Colonic wash-outs effected a temporary improvement only, and after 5 weeks a further course of sulphaguanidine—175 g. over 10 days—was given. Subsequent sigmoidoscopy revealed a healed mucosa.

Case 23 showed an initial response which was not sustained: although blood disappeared on the sixth day the stools remained as frequent as 20 or more a day. Malaise and toxæmia, with abdominal colic and tenderness, were marked. Sulphaguanidine was continued until 350 g. had been given over 20 days, but without improvement in the patient's condition. Repeated sigmoidoscopy showed an oedematous and injected mucosa without ulceration. Shiga's bacillus was again isolated after 100 g. of sulphaguanidine had been given.

Case Reports (Acute Cases)

Case 10.—This is an example of the very severe cases that were cured. Dec. 1: Gradual onset of symptoms; no treatment was received, and the condition had steadily increased in severity until admission to hospital on Dec. 11. Admitted very weak, pale, exhausted, and in a collapsed condition. Temperature 97.4°; pulse 120; abdominal pain very severe. Stools showed almost continual passage of blood and mucus. Morphine 1/4 gr. was given; hot blankets, water-bottles, etc. Some hours later temperature was 102° and pulse 110; treatment with

sulphaguanidine was begun. Treatment of the case continued as follows:

Day of Dis.	P.M. Temp. & Pulse	General Condition	Stools		Abdom. Tender	Colic	Sulphaguanidine
			No.	Nature			
10	102°/110	As above	+++	B. & M. only +++	+++	+++	7 g. stat. 3.5 g. after 2 hrs. + 3.5 g. ditto
11	101°/90	Slight improv.	20	B. & M. only ++	+++	++	3.5 g. × 6
12	100°/90	I.S.Q.	8	B. & M. only ++	++	++	3.5 g. × 6
13	99.2°/90	"	+6	B. & M. only ++	++	++	3.5 g. × 6
14	99.4°/90	"	+6	B. & M. only ++	+	++	3.5 g. × 6
15	99.2°/85	Still much malaise and toxæmia	+4	Slightly faecal, mostly B. & M. only +. 3 faecal B. ++ M. ++	Slight	+	3.5 g. × 6
16	99°/85	"	4	1 B. & M. only	Slight	+	3.5 g. × 6
17	N.	Marked improv.	3	Semi-solid. B. & M. ++	0	0	3.5 g. × 4
18	N.	Improv. contd.	2	Semi-solid. M. ++	0	0	3.5 g. × 4
19	N.	"	1	Solid. Slight M.	0	0	3.5 g. × 3
20	N.	"	1	Solid. Slight M.	0	0	3.5 g. × 3

Adjuvant treatment was as follows: 10th day—morphine gr. 1/4 × 2; anti-Shiga serum, 30,000 units; mist. bism. cret., 1 oz. q.h. 11th to 14th days—mist bism., tinct. opii η 10 × 4. Adjuvants were then stopped.

The stools remained normal except for a slight excess of mucus, and sigmoidoscopy showed a healed mucosa with an occasional submucous haemorrhage. The urine was normal throughout. A final blood count after treatment showed: Hb 96%, R.B.C. 4,910,000, W.B.C. 5,300, with normal differential count.

Case 11.—This case illustrates the quick response to early treatment in comparison with Case 10. In the early morning of Sept. 28 the patient was taken with sudden diarrhoea and abdominal colic, blood appearing in the stools after a few hours. Marked vomiting and tenesmus were present. Sixteen hours after onset admitted to hospital collapsed, with severe abdominal colic. Tongue furred and dry; abdomen showing marked tenderness; stools slightly faecal, with much blood and mucus. The severity of the symptoms suggested a Shiga infection, and 30,000 units of antiserum were given, although the report received 2 days later indicated a typical Flexner bacillus.

Day of Dis.	P.M. Temp. & Pulse	General Condition	Stools		Abdom. Tender	Colic	Sulphaguanidine
			No.	Nature			
1	101°/100	As above	+15	First faecal, becoming B. & M. only	+++	+++	7 g. stat.
2	99.4°/80	Marked improv. at end of day	+5	Occ. faecal. B. & M. only ++	++	++	3.5 g. × 6
3	N.	—	3	Fluid. Faecal. B. + M. +	0	0	3.5 g. × 6
4	N.	—	3	Semi-solid. M. +	0	0	3.5 g. × 4
5	N.	—	1	" "	0	0	3.5 g. × 4

Adjuvant treatment given was: 1st day—morphine gr. 1/4, mist. bism. cret. 1 oz.; antiserum 30,000 units q.h.; 2nd day—tinct. opii η 10 × 2.

The stools remained normal and sigmoidoscopy showed a healed mucosa. Urine normal. Blood count normal.

The Chronic Series

These patients had been suffering from chronic dysentery for from a few weeks to many months, and all had received various periods of routine treatments.

Dosage.—Indications as to dosage were again purely arbitrary and, as in the acute series, the nature of the stools passed was taken as a guide, sulphaguanidine being continued until 2 days after the stools had become normal. Of 20 cases so treated, 9 were not cured. In these, symptoms returned and sigmoidoscopy showed that although the stools were microscopically normal the mucosa had not healed. It was evident that this plan of dosage, although satisfactory in acute cases, when used in the chronic cases resulted in too small a total dosage and too short a period of treatment. Accordingly a new scheme was adopted whereby all the cases were treated for a minimum of 8 days, 3.5 g. of sulphaguanidine being given at 4-hourly intervals, omitting the 2 a.m. dose. The total daily dose was therefore 17.5 g. The number of days under treatment was increased in cases of more than average severity, where such was indicated by the degree of toxæmia of the patient, sigmoidoscopic appearances, and length of illness.

Treatment and Routine

Preliminary to Sulphaguanidine.—Most cases gave a history of previous treatment with sodium sulphate and fluid diet. Cases 6, 23, 25, 26, and 51 had received from 30 to 80 g. of sulphaguanidine in the acute phase (i.e., during their evacuation), but treatment had not been continued until the stools were normal. 19 cases received a period of treatment (after admission here) with colonic wash-outs while on a low-residue diet. Sigmoidoscopy sometimes showed temporary improvement, but complete healing did not take place.

With Sulphaguanidine.—During the first few days the patient's general condition was observed, nature of stools noted, and sigmoidoscopy carried out, material being removed for microscopic examination and plating. The sigmoidoscopic appearances are illustrated in case notes given below. Diet was the same as in the acute cases. The urine was tested daily, and a blood count done at the end of treatment.

Description of Chronic Cases

Of the 51 chronic cases treated, 20 were Shiga infections, 14 Flexner, and 17 unidentified. They are described in two groups: Group A, in which the original plan of dosage was used, and Group B, in which the modified plan was used. Table IV shows both groups in descending order of dosage.

Group A.—This consisted of the first 20 cases treated, and the average total dose was 90 g. over 6 days. All responded to treatment, and in from 3 to 6 days the stools had become normal, abdominal tenderness and colic had disappeared, and the patients' general condition had greatly improved. Yet only 11 (55%) cases showed complete healing on sigmoidoscopy. In the other 9 granular hyperaemic areas with some induration and oedema remained. There was some return of symptoms, and complete healing took several weeks, during which period the patients remained on a low-residue diet and received daily colonic wash-outs.

Group B.—This series consisted of the subsequent 31 cases, and the average total dose was 160 g. over 10 days. Symptoms responded to treatment as in Group A, but the final results were much better in that 24 (77%) cases showed complete healing on sigmoidoscopy and 5 complete healing except for granular hyperaemic patches limited to the lower part of the rectum. These had disappeared after one week's treatment with rectal wash-outs, during which time the patient was given liquid paraffin to soften the stools. Two cases (Nos. 33 and 45) which appeared to respond quite well suffered a subacute relapse when treatment was suspended. Sigmoidoscopy showed a return of ulceration on an oedematous indurated hyperaemic mucosa. Treatment with colonic wash-outs was tried again, but the lesions did not heal completely. A further course of sulphaguanidine—189 g. and 175 g. respectively—resulted in cure.

Table III (including both groups) shows the average day, the earliest day, and the latest day on which recovery occurred.

TABLE III

	Average Day	Earliest Day	Latest Day
Marked general improvement	3rd	2nd	7th
No abdominal tenderness ..	4th	3rd	7th
No abdominal colic ..	4th	2nd	9th
Normal stools ..	4th	3rd	10th

Case Reports (Chronic Cases)

Case 13.—This case was from Group A and was treated according to the original scheme of dosage without complete cure. In the acute phase of an attack of dysentery in Sept., 1941, after 4 months in the Middle East, the routine saline treatment was given for 10 days with improvement, but the stools never became normal. When admitted here a month later (Oct. 3) he was pale, thin, and toxic, with temperature 99° to 100° and pulse 80 to 110. There was marked tenderness over sigmoid, ascending colon, and caecum. The stools, about four daily, contained much bloody mucus. Sigmoidoscopy showed numerous irregular ulcers with overhanging edges covered by yellowish muco-pus, which on removal left a bleeding granular floor. Some ulcers had become confluent, and the intervening mucosa was granular, slightly indurated, and oedematous. The exudate was bacillary in type, but culture from swabs proved negative. From Oct. 17 to 27 treatment was carried out with colonic irrigation. The patient's condition would improve for a few days and then relapse. Stools continued to contain blood and mucus. Sigmoidoscopy now showed much increase in the oedema and induration of the bowel wall, and instrumentation was impossible beyond 10 cm. The ulcers had not healed. Culture from a swab again proved negative. Therapy with sulphaguanidine was started on Nov. 3, and was continued as follows, 70 g. in all being given:

Day of Dis.	P.M. Temp. & Pulse	General Condition	Stools		Abdom. Tender	Colic	Sulphaguanidine
			No.	Nature			
52	100°/90	As above	4	S-S. B. + M. ++	+	+	7 g. stat. + 3.5 g. × 5
53	99°/90		1	S-S. B. + M. ++	+	0	3.5 g. × 5
54	98.4°/90	Slight improv.	0	—	+	0	3.5 g. × 4
55	N./85	Marked improv.	0	—	0	0	3.5 g. × 4
56	N./N.	Improv. contd.	1	S. M.	0	0	3.5 g. × 3

After a few days stools were again loose, with occasional blood-streaked mucus. Sigmoidoscopy showed a great improvement, but indurated, oedematous, bleeding granular areas remained. From Nov. 13 to 28 treatment was continued by colonic irrigation, and sigmoidoscopy one week later showed a healed mucosa.

Case 28.—This was a severe case from Group B, and was treated according to the revised scheme, with complete cure. At the onset of an acute attack of Shiga dysentery in Nov., 1941, after 3 months in the Middle East, routine saline treatment was given with initial improvement but subsequent acute relapse; on Dec. 1, when admitted here, saline treatment was repeated, and was followed by colonic irrigation. On Dec. 28, 2 months after the onset, stools were about 5 daily, and contained much blood-stained mucus; chronic toxæmia was gradually worsening the patient's condition. Sigmoidoscopy showed numerous irregular-shaped ulcers covered with blood-stained mucus-pus. The rest of the mucosa was granular and haemorrhagic, and in some places nodular. Pus was expressed from between the nodules by the passage of the instrument. Oedema and induration of the bowel wall became so great that instrumentation was impossible beyond 12 cm. Treatment with sulphaguanidine was started on Dec. 29—the 55th day of disease—and continued as follows (total dosage, 175 g.):

Day of Dis.	P.M. Temp. & Pulse	General Condition	Stools		Abdom. Tender	Colic	Sulphaguanidine
			No.	Nature			
55	99.8°/90	As above	5	S-S. B. + M. +++	++	+	7 g. + 3.5 g. × 3
56	99.8°/90		2	S-S. B. + M. ++	+	+	3.5 g. × 5
57	99.2°/90		1	S-S. B. M. ++	+	Occ.	3.5 g. × 5
58	N./90	Marked improv.	2	S-S. M. +	+	Occ.	3.5 g. × 5
59	N./85	Improv. contd.	1	S. M. +	0	0	3.5 g. × 5
60	N./N.	"	2	S-S.	0	0	3.5 g. × 5
61	N./N.	"	1	S.	0	0	3.5 g. × 5
62	N./N.	"	1	S.	0	0	3.5 g. × 5
63	N./N.	"	1	S.	0	0	3.5 g. × 5
64	N./N.	"	1	S.	0	0	3.5 g. × 5

Stools remained normal, and sigmoidoscopy one week after treatment showed a completely healed mucosa.

Case 47.—A moderate case from Group B showing complete healing but some residual proctitis. At the onset of an acute attack of dysentery on Dec. 4 routine saline treatment was given. Admitted here on Dec. 14 much improved, but still with loose faecal stools containing blood and mucus. Sigmoidoscopy showed a granular hyperaemic mucosa, covered by blood-stained mucus-pus, with moderate oedema and induration of the bowel wall. Culture was negative. From Dec. 20 to 30 colonic irrigation and low-residue diet. On Jan. 6 stools were still loose, with blood and mucus. Sigmoidoscopy showed no healing. Treatment with sulphaguanidine was started on Jan. 7—the 33rd day of disease—and was continued as shown, the total amount given being 140 g.:

Day of Dis.	P.M. Temp. & Pulse	General Condition	Stools		Abdom. Tender	Colic	Sulphaguanidine
			No.	Nature			
33	99.2°/85	Malaise and toxæmia +	3	S-S. B. + M. +	+	+	7 g. + 3.5 g. × 3
34	98.6°/N.	"	0	—	+	+	3.5 g. × 5
35	N./N.	Marked improv.	1	S. M. +	0	0	3.5 g. × 5
36	N./N.	"	0	—	0	0	3.5 g. × 5
37	N./N.	Improv. contd.	0	—	0	0	3.5 g. × 5
38	N./N.	Slight toxic effects here—malaise, anorexia, erythema [N.B. Bowels confined]	1	S. M. +	0	0	3.5 g. × 5
39	N./N.	—	1	S.	0	0	3.5 g. × 5
40	N./N.	Rash gone. [N.B. Bowels open]	2	S-S. M.	0	0	3.5 g. × 5
41	N./N.	"	2	S-S.	0	0	3.5 g. × 5

Sigmoidoscopy showed a healed mucosa except for hyperaemic granular patches with slight oedema and induration in the rectum. Stools were loose for 4 to 5 days, with flecks of blood-stained mucus. Treatment was continued with rectal wash-outs and liquid paraffin for 10 days. On Jan. 27 sigmoidoscopy showed the rectal lesions to have healed, and stools were quite normal, with patient fit and well.

TABLE IV.—Chronic Cases

Case	Previous Treatment	Day of Disease	Bacteriology	No. Days Treated	Total Dosage SG	Day of Marked General Improv.	Day No. Abdom. Tender.	Day No. Abdom. Colic	Day No. Stools	Sigmoidoscopic Findings and Results One Week after Treatment
GROUP A										
15 S		24	Flexner	9	126	4	4	4	6	Healed
1 S		21	" I	7	98	4	4	4	3	Improved after treat. CI
11 S		42	"	6	91	3	3	3	4	Healed. Sequel: tachycardia
17 S		30	"	6	84	3	3	3	3	Healed
8 S		22	"	5	73	3	3	3	3	"
6 S	SG 30 g.	31	"	5	70	3	3	3	3	Improved after treat. CI
3 S		30	" II	5	66.5	3	3	2	3	Healed
4 S		25	Shiga	8	101.5	5	5	3	7	Improved after treat. CI
5 S		26	"	6	77	3	3	3	3	Healed
10 S		24	"	5	63	3	3	2	4	Improved after treat. CI
7 S	CI	37	Unidentified	6	91.5	3	3	3	3	Healed
12 S		?	"	6	87	4	4	2	3	"
19 S		34	"	6	80.5	3	3	—	3	"
2 S		16	"	5	80.5	2	3	3	4	Improved after treat. CI
9 S		31	"	5	77	3	3	3	4	Healed
16 S		21	"	6	77	3	3	3	2	"
13 S	CI	52	"	5	70	3	3	2	4	Improved after treat. CI
20 S	CI	30	"	5	70	3	3	2	3	"
18 S	CI	21	"	5	63	3	3	2	2	"
14 S	CI	32	"	4	53	3	3	3	4	Slightly imp.*
GROUP B										
51 S	SG 50 g.	39	Shiga	12	224	4	9	9	9	Healed
45 S	CI	39	"	12	210	—	9	9	4	Subacute relapse
	Re-treated			10	175	7	5	8	4	Improved and finally healed
31 S		30	"	13	206.5	7	7	5	3	Healed
24 S	SG 50 g.	21	"	12	191	7	6	9	10	Healed but for rectal patches
22 S	CI SG 50 g.	—	"	11	183.5	5	5	5	5	"
26 S		31	"	10	175	3	4	4	2	"
27 S		—	"	10	175	6	7	5	4	"
28 S		50	"	10	175	4	5	5	4	Healed
37 S	CI	—	"	10	175	4	4	4	4	"
38 S		43	"	10	175	4	4	4	4	"
39 S		41	"	10	175	4	3	3	5	"
41 S		67	"	10	175	6	6	6	7	"
42 S		38	"	10	175	4	4	5	6	"
46 S		23	"	10	175	5	5	5	6	"
49 S	CI	50	"	10	175	5	4	4	4	"
34 S		40	"	9	157.5	3	2	6	6	"
48 S	CI	70	"	8	140	3	3	3	5	"
30 ?		—	Flexner	9	151.5	3	3	3	3	"
21 S		18	"	9	143.5	4	4	2	4	"
25 S	SG 82 g.	38	"	8	143.5	4	4	4	4	"
23 S	CI	21	"	8	140	3	4	4	4	"
29 S	CI	21	"	8	140	4	4	2	4	"
32 S	CI	39	"	8	131	3	3	3	3	"
43 S	CI	66	"	8	130	3	3	3	3	"
36 S	—	—	Unidentified	10	175	4	3	4	4	"
50 S		25	"	10	175	6	6	2	5	"
35 S	CI	—	"	9	157.5	3	3	2	4	"
40 S	CI	46	"	8	140	3	3	3	3	"
47 S	CI	23	"	8	140	3	3	3	3	Healed but for rectal patches
44 S	CI	63	"	8	130	5	3	3	4	Healed
33 S	CI	33	"	6	108	4	4	3	4	Subacute relapse*
	Re-treated after 3 weeks			11	189	3	3	5	4	Healed

* Supply of sulphaguanidine ran short.

S=Saline. CI=Colonic irrigation. SG=Sulphaguanidine.

Toxicity of Sulphaguanidine in Chronic Series

Toxic symptoms were rare, occurring in only 9 patients out of 51 chronic cases treated. (No toxic symptoms occurred in the acute cases.) They comprised rashes, nausea, headache, tachycardia, and fever (see Table V). It will be seen that in all but 2 cases a dose of at least 100 g. had been given, and it was noted that all patients with toxic symptoms were relatively constipated—i.e., one stool in 2 or 3 days. It is therefore reasonable to assume that the concentration of sulphaguanidine in the bowel was unusually high and that this may have led to increased absorption into the blood stream.

TABLE V.—Toxic Symptoms

Case	Day of Treatment	Dosage Given (g.)	Symptoms	
			Duration	Nature
51	12th	224	3 days	Macular red rash on trunk; headache and tachycardia
34	9th	157.5	2 "	Slight fever; tachycardia; headache; nausea
23	8th	140	2 "	" " " "
29	8th	140	2 "	" " " "
46	8th	140	4 "	Maculo-papular rash; headache; nausea
48	7th	122.5	3 "	Generalized erythema; headache; slight fever
47	6th	105	3 "	" " " "
19	2 days after 4th	80.5	4 "	Maculo-papular red rash
6	4th	4	2 "	Slight fever; headache; nausea

Conclusions**Acute Cases**

In all, 26 acute cases of bacillary dysentery were treated with sulphaguanidine. 19 cases were completely cured in from 14 to 21 days; 6 cases relieved, 1 of which became chronic; and 1 case hardly affected. The chronic case was subsequently cured by further treatment with sulphaguanidine.

Sulphaguanidine, like other sulphonamides, would appear to be bacteriostatic, the dysentery bacilli dying only slowly. Hence an efficient concentration of the drug must be maintained for some time after the active infective process has been inhibited. Such a stage is evidently reached when the stools are almost normal, and the failure to continue the sulphaguanidine makes a relapse likely. Cases 1, 2, 3, 4, and 5 were the first treated, and sulphaguanidine was stopped when the faecal stools had a consistency and showed no blood. The fact that these cases relapsed after a few days would appear to stress the importance of continuing treatment for 2 to 3 days after the stools are normal and while the final stages of healing are taking place. Further evidence in support of this is given by Cases 6, 23, 25, 26, and 51 of the chronic series, which received up to 80 g. in the acute phase but subsequently became chronic. Treatment had not been continued until the stools were normal.

The early acute infections showed a very quick response to treatment, and the longer the interval between the onset of the disease and the beginning of treatment, the longer was treatment necessary.

The more frequent and looser the stools the less the concentration of sulphaguanidine in the bowel (*Trop. Dis. Bull.*, 1942, 39, 34), and in the initial stages of treatment adjuvants such as tinct. opii, bismuth and chalk, and kaolin were used to lessen the frequency and increase the consistency. In the one case which failed to respond the stools remained fluid and frequent in spite of all treatment.

The feeling of well-being as toxæmia is overcome and the early fall in the frequency of the stools greatly reduced the exhaustion and dehydration of the patient. Fluid can be made up adequately by mouth, and the patient's early desire for food as his condition quickly improves allows his strength to be built up while the infective process is overcome.

Chronic Cases

A series of 51 cases of chronic bacillary dysentery were treated with sulphaguanidine. All showed an early and marked response to treatment. In the first 20 cases, as in the acute series, the nature of the stools governed the dosage given, and the average total dose was about 90 g. over 6 days. Only 11 (55%) cases were completely healed, without relapse. In the subsequent 31 cases a minimum dosage of 17.5 g. for 8 days was given, and the advent of normal stools was not taken as an indication for reducing or stopping treatment. The average total dose was 160 g. over 10 days. 24 (77%) cases showed complete healing, and 5 complete healing but for granular patches in the rectum; 2 responded but relapsed after treatment.

Stool examination and the general examination of the patient are inadequate as a means of gauging the state of the lesions in the bowel, and sigmoidoscopy is essential. It would seem that passage of normal stools and disappearance of symptoms in chronic cases indicate only that the active infective process has been inhibited and not that healing of the mucosa has taken place. If sulphaguanidine is not continued the infective

process may again become active, delaying healing for some weeks. A full daily dose of 17.5 g. for at least 8 days, and longer in cases showing other than moderate severity, would appear to afford adequate protection against this delay in healing. Nine cases of the chronic series showed mild toxic symptoms from the sulphaguanidine.

Summary

In all, 77 cases of bacillary dysentery were treated—26 acute, 51 chronic. Of the 26 acute cases 16 were Shiga infections, 6 Flexner, and 4 unidentified. Of the 51 chronic cases 20 were Shiga and 14 Flexner infections; in 17 the organism was undetermined.

Patients were put to bed, rested and warmed. The frequency and character of stools were noted, and specimens plated and examined microscopically. Diet was limited to fluid in the first 24 hours. A large fluid intake by mouth was encouraged in the early stages to replace fluid loss. No intravenous fluid was necessary.

Adjuvant treatment was given, cases of Shiga infection receiving 30,000 units of antiserum.

Acute cases received an initial dose of 7 g. of sulphaguanidine, followed by 3.5 g. at 4-hourly intervals. In very severe cases 3.5 g. was given 2 hours after the initial dose, followed in 2 hours by a further 3.5 g. In the main, sulphaguanidine was given until 2 days after the stools had become normal.

Chronic cases received 17.5 g. of sulphaguanidine daily, in 5 doses, for a minimum of 8 days, the length of treatment being increased in the severer cases. A preliminary period of treatment with colonic wash-outs while on a low-residue diet was carried out in 19 cases.

In chronic cases sulphaguanidine must be given until healing of the mucosa has taken place: to gauge this, sigmoidoscopy is essential.

Complete cure was obtained in 19 (73%) acute cases, in 11 (55%) chronic cases receiving 90 g. over 6 days, and in 24 (77%) chronic cases receiving an average dose of 160 g. over 10 days.

Toxic symptoms occurred in only 9 of the 51 chronic cases; there were none in the acute series.

Illustrative cases, showing the scheme of treatment, are recorded.

PROBABLE TETANUS DESPITE INOCULATION WITH TOXOID

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Preliminary reports upon battle casualties previously protected with tetanus toxoid seem to vindicate both its use and the administration of two doses at a six-weekly interval. In the B.E.F. in France and Flanders no tetanus occurred in the wounded who had been so inoculated (Perry, 1940), and the third dose after a six-months interval, which is now the standard method advocated by Boyd (1938) and in practice in the British and Indian Armies, should further raise the antitoxin level. The following is a probable case in a subject who had been protected by two doses at a six-weekly interval.

Case History

A sepoy aged 20 received 1 c.cm. of tetanus toxoid subcutaneously on April 25, 1941, and again on June 7 (as recorded in his pay-book). He was admitted to this hospital on Dec. 4 with a history of stiffness in the dorsal thoracic muscles and the muscles of the back of the neck for two days. Slight stiffness of the jaws and dysphagia appeared first on the day of admission. His only injuries were a wound on the left thenar eminence and one on the palmar surface of the left middle finger, each about 3/4 in. long, incised, superficial, and at the time of admission quite healed, with only the edges of the most superficial horny layer very slightly gaping. He had received them on Nov. 18 while serving on the Red Sea Littoral.

Moderate risus sardonicus and trismus were present, the jaws opening 1/2 in. There was marked stiffness of the back and neck. One could just pass the flat of the hand between the