stimulus was only a half. In many instances the malignant cell appeared to be completely refractory to such stimuli. Of course the importance of this finding depends on how far it reflects an essential difference between the malignant cell and its normal prototype. The effects of local carcinogen treatment do, however, strongly suggest that the resistance of the fully developed cancer cell is acquired very early in neoplasia and gradually becomes a permanent property of the cell.

Although such a resistance to normal growth-regulating agents has often been postulated as a property of the cancer cell, and in fact is vaguely included in one definition—that is, “autonomous new growth”—the property has never been precisely demonstrated experimentally. It may be that this work not only reveals the existence of such a property but offers an approach to an elucidation of its nature. If, as we think (Green and Bullough, 1950; Green and Ghadially, 1951), these antimitotic agents act on the normal cell by interfering at one or more stages in carbohydrate utilization, the work of the Sheffield Traumatic Shock Team on carbohydrate metabolism in shock may prove to have some bearing not only on the mechanism of this general bodily reaction but also, somewhat surprisingly, on the intimate changes in cell metabolism, which in themselves reflect, or constitute, the essential nature of neoplastic transformation.

Summary

A short period of painting of the ear with the carcinogen 9:10-dimethyl-1:2-benzanthracene renders the epidermis relatively refractory to the antimitotic action of shock or of cortisone.

Various transplanted malignant neoplasms are also relatively insensitive to the same stimuli.

Whether these findings have a bearing on the essential nature of the neoplastic change is briefly discussed.

We are indebted to the Medical Research Council Committee on A.C.T.H., Cortisone, and Related Substances for supplying the cortisone; to Mr. R. F. Wrighton, of the Department of Social Medicine, Sheffield University, for his valuable statistical help; and to Dr. W. S. Bullough for his expert collaboration in one experiment.

REFERENCES

- Bullough, W. S. (1948). *Proc. roy. Soc. B*, **135**, 212.
 Green, H. N. (1949). *Rep., Brit. Emp. Cancer Campgn.*, **27**, 172.
 — (1950). *Proc. Fifth Congrès International du Cancer*, Paris. *Acta Un. int. Cancer*, **7**. In press.
 — and Bullough, W. S. (1950). *Brit. J. exp. Path.*, **31**, 175.
 — and Ghadially, F. N. (1951). *British Medical Journal*, **1**, 496.
 — and Stoner, H. B. (1950). *Biological Actions of the Adenine Nucleotides*. Lewis, London.
 Pearson, O. H., and Eliel, L. P. (1950). *J. Amer. med. Ass.*, **144**, 1349.

How the honey-bee discovers the first, newly opened flowers of a crop was discussed in a paper read to the Royal Society on March 8 by Dr. C. G. Butler, of Rothamsted Experimental Station, Harpenden. It has been known for a long time that bees possess good colour vision, though they can see into the ultra-violet where the human eye is blind and are insensitive to red—whence, it is suggested, arises the scarcity of pure red flowers. More recently Professor Karl von Frisch has described the amazing dance a scout bee performs on returning to the hive to let its worker colleagues know where it has found a new group of open flowers with pollen and nectar ready. But how does the scout discover the new flowers in the first instance—by sight or smell? Dr. Butler reported that colour is the chief attractive factor, though a really strong perfume acts in the same way. The scent of an individual flower is, however, often weak, and it serves only to induce the honey-bee to enter the corolla once the colour has done its work. If the scent is masked, the bee hesitates to enter on the first or subsequent visits.

CHEMOTHERAPY IN CHOLERA

BY

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Really effective chemotherapy in cholera has hitherto proved to be a baffling problem. However, good results have been claimed for a few of the newer compounds. Among these, sulphaguanidine has been extensively used for the past few years, but opinions regarding its efficacy in this disease have not been uniform (Chopra *et al.*, 1941; Carruthers, 1942; Lahiri, 1945, 1948). In another series of observations (Lahiri, 1949; Lahiri and Dutta, 1949) thiodiamine was tried. This is derived from the decomposition product of the bark of *Crataeva roxburghii* and also of *Moringa pterygosperma*. *In vitro* it prevented the growth of *Vibrio cholerae* (both Ogawa and Inaba types) even in a concentration of 0.5 mg. in 10 ml. of media. On clinical trial in 30 bacteriologically positive cases the stool became free of vibrio in three to five days in all the 23 cases systematically observed, but the death rate was not materially lowered.

Bhatnagar *et al.* (1948) had remarkably good results with another compound—a condensation product of sulphathiazole and formaldehyde. Out of 85 patients treated with this drug in a part of the Madras Presidency during an epidemic in 1947 only three died (3.53%); the case mortality rate had been about 60% in epidemics during the previous seven years. Saline transfusion was not given to any of these patients, and there was no nursing and general medical care or adjuvant treatment, though 57 patients (67.06%) were in a critical condition with anuria, marked dehydration, “semi-comatose condition, algidity, imperceptible pulse, and body cramps.” Stools became free from vibrio in all the cases within six days. The prophylactic value of this drug has also been emphasized. Bose (1949), in experiments *in vitro* with different condensation products of formaldehyde and sulphonamides, found that formosulphacetamide and formosulphabenzamide exerted better bactericidal effect on *V. cholerae* than formosulphathiazole and other similar compounds.

A clinical trial of some of the above compounds—for example, sulphaguanidine, formosulphathiazole, and formosulphacetamide—was undertaken in cholera cases admitted into the cholera ward of the Chittaranjan Hospital, Calcutta, during the last epidemic (1950). The findings are discussed below.

Clinical Investigation

The period of observation of the cases discussed here was from May to July, 1950. The total number of patients admitted during this period was 377, and there were 122 deaths (32.35%). Many of these patients were refugees in a bad state of nutrition and with lowered vitality. Consequently the death rate was high. A total of 268 patients were under clinical observation for the present study. All these patients presented typical symptoms of cholera, with profuse rice-water stools, vomiting, and dehydration with anuria, prostration, and high specific gravity of blood. At the time of admission 133 patients (49.62%) were in a very bad state of collapse, with imperceptible radial pulse and the specific gravity of blood varying between 1068 and 1072.

Powdered sulphaguanidine, formosulphathiazole, and formosulphacetamide were given orally to successive patients in cyclic order according to their admission into the ward, the fourth one admitted receiving no chemotherapeutic drug, and thus serving as a control. But this order could not always be strictly maintained owing to irregular supply of drugs and other difficulties. Of the 268 patients, 72 received sulphaguanidine, 64 formosulphathiazole, 61 formosulphacetamide, and 71 were controls. All received adjuvant treatment.

Dosage.—The dosage was the same for all three compounds—4 g. initially, followed by 2 g. every four hours throughout the day and night for an adult, till the symptoms subsided or the stool became vibrio-free. Children received proportionately lower doses according to age. During the first few days of the investigation the dosage for both formosulphathiazole and formosulphacetamide was 2 g. initially, followed by 1 g. every four hours, but this was subsequently increased for want of any beneficial response with this dosage schedule. Adjuvant treatments were given to all the patients when necessary.

Adjuvant Treatments.—All patients received saline transfusion (hypertonic, isotonic, and alkaline) till the specific gravity of the blood came down to normal level. Atropine sulphate, 1/100 gr. (0.65 mg.) hypodermically, was given to all adult patients on admission, and was repeated after 8 to 12 hours as necessary. All the patients received glucose intravenously either in the form of 25% solution, 50 ml. every eight hours, or with normal saline in 5% solution as transfusion, children receiving a proportionately less quantity. As an analeptic nikethamide was extensively used, intravenously in grave cases, and intramuscularly otherwise, and also extract of suprarenal cortex when available (Lahiri, 1945). Compounds of theophyllin were used intravenously in many cases to stimulate urination. To combat the persistent collapse a number of patients belonging to all the four groups received plasma or Knox special intravenous 6% gelatin solution intravenously. The result of the latter observation is being published elsewhere.

Examination of Stools

Stool was collected by a sterile rubber catheter direct from the rectum of the patient into a test-tube containing alkali-peptone media solution, and sent to the laboratory. The first sample was taken before giving any chemotherapeutic drugs. Subsequent samples were taken on successive days, in the same way, to study the bactericidal effect of the drug used or as controls. Altogether 745 samples of stools were cultured in this series.

Results

V. cholerae was found in the stools of 197 cases (73.5%) (Table I). These were all typical *V. cholerae* belonging to Heiberg's group 1 category. Serological investigation with monospecific sera showed initially:

TABLE I.—Results of Treatment

	No. of Cases	Deaths	
		No.	%
Investigated	268	78	29.1
Vibrio-positive (V+)	197	54	27.41
Ogawa cases	142	39	27.46
Inaba cases	51	11	21.56
Admitted with imperceptible radial pulse (P-)	133	57	42.85
Vibrio-positive, admitted with imperceptible radial pulse (V+, P-)	109	45	41.28
Vibrio-negative (V-)	71	24	33.8
Vibrio-negative, admitted with imperceptible radial pulse (V-, P-)	24	12	50.0

(a) type Ogawa in 142 samples (72.08%), (b) type Inaba in 51 samples (25.88%), and (c) four were not investigated. In 29 cases (14.72%) culture of the first sample of stool failed to reveal any vibrio, though subsequent examinations demonstrated the vibrio.

The effects of sulphaguanidine, formosulphathiazole, and formosulphacetamide therapy, and also of control with no chemotherapeutic drugs, were studied in this series in 72, 64, 61, and 71 patients respectively, the respective case mortality rates being 30.55%, 34.37%, 34.43%, and 18.31% (Table II). In severe cases admitted with imperceptible radial pulse, death rates

TABLE II.—Analysis of Results of Treatment

Cases	Sulphaguanidine			Formosulphathiazole			Formosulphacetamide			Nil		
	No.	Deaths		No.	Deaths		No.	Deaths		No.	Deaths	
		No.	%		No.	%		No.	%		No.	%
V+	51	15	29.41	50	17	34.0	44	12	27.27	52	10	19.23
Ogawa	34	10	29.41	42	15	35.71	29	7	24.14	37	7	18.92
Inaba	15	3	20.0	8	2	25.0	13	3	23.07	15	3	20.0
V-	21	7	33.33	14	5	35.71	17	9	52.94	19	3	15.78
P-	31	14	45.16	41	20	48.75	30	13	43.33	31	10	32.26
V+P-	28	12	42.86	34	16	42.66	23	9	39.13	24	8	33.33
Total	72	22	30.55	64	22	34.37	61	21	34.43	71	13	18.31

V+ = *V. cholerae* present in stool. V- = *V. cholerae* absent in stool. P- = Admitted with imperceptible radial pulse. V+P- = Vibrio-positive cases admitted with imperceptible pulse.

TABLE III.—Analysis of Results According to Age Group

Age in Years	Sulphaguanidine				Formosulphathiazole				Formosulphacetamide				Nil			
	No.	No. P-	Deaths		No.	No. P-	Deaths		No.	No. P-	Deaths		No.	No. P-	Deaths	
			No.	%			No.	%			No.	%			No.	%
0-4	9	3	3	33.33	1	1	1	100.0	0	—	—	—	3	0	0	0.0
5-9	5	3	2	40.0	2	0	0	0.0	3	2	3	100.0	0	—	—	—
10-19	12	6	2	16.66	13	9	5	37.46	10	3	2	20.0	18	5	1	5.5
20-39	36	17	12	33.33	38	24	9	23.68	41	19	12	29.27	40	20	9	21.9
40-49	5	1	3	60.0	5	4	1	20.0	3	3	3	100.0	4	4	0	0.0
50-59	3	0	0	0.0	5	3	3	60.0	2	2	1	50.0	4	1	1	25.0
60+	2	1	0	0.0	0	—	—	—	2	1	0	0.0	2	1	2	100.0

were 45.16%, 48.75%, 43.33%, and 32.26% respectively, respective numbers of cases being 31, 41, 30, and 31. In the studies of age groups (Table III) the lowest mortality rates were also obtained in the control group. This was true both for vibrio-positive and vibrio-negative patients. Among those receiving formaldehyde condensation products the mortality was a little higher than among those receiving sulphaguanidine.

Table IV reveals that the largest percentages of deaths in all the groups were due to peripheral circulatory failure. In these patients the systolic blood pressure

TABLE IV.—*Causes of Death (Clinical)*

Treatment	No. of Deaths	Causes of Death					
		Peripheral Circulatory Failure		Uraemia		Other Causes	
		No.	%	No.	%	No.	%
Sg ..	22	12	54.54	5	22.72	5	22.72
FST ..	22	11	50.0	11	50.0	0	0.0
FSA ..	21	10	47.61	7	33.33	4	19.04
Nil ..	13	9	69.23	3	23.07	1	7.69
Total	78	42	53.84	26	33.33	10	12.82

failed to rise above 70–80 mm. Hg, or it dropped down again after a slight temporary rise, though the specific gravity of the blood was brought down to normal level by rapid intravenous saline transfusion, followed by the continuous slow-drip method as long as required. The next most frequent cause of death was uraemia, the formol compound groups recording higher percentages than the other two groups.

Effects on *V. cholerae* in the Stool

This was studied in 130 cases. The stools from 33 patients taking sulphaguanidine, 34 taking formosulphathiazole, 27 taking formosulphacetamide, and

36 having no chemotherapeutic drugs were examined systematically from day to day to study the effects of these drugs on *V. cholerae* (Table V). On the eighth day from the onset vibrio disappeared from the stool in 32 patients (96.93%) in the first group, 32 (94.11%) in the second group, 26 (96.29%) in the third group, and 30 (83.3%) in the control group. All the stools became vibrio-negative by the ninth day in the first group, by the tenth day in the third group, and by the twelfth day in the control group. In the formosulphathiazole group, one patient, who still had *V. cholerae* in the stool on the tenth day, after taking 72 g. of the drug, became symptom-free and left hospital.

The average amount of these drugs received before the stools became vibrio-negative was not at all uniform, larger total quantities being taken as a matter of course as the number of days increased. In some cases the stools became vibrio-negative one or two days after the drugs were discontinued, though they were positive all the time the drugs were being taken. In 18 patients in the whole series, distributed in all the four groups, it was noticed that the vibrio, while present in the stool on one day, was absent again for one or more days, and then reappeared, though the respective treatments were being continued. The longest interval observed was four days in a patient in the control group.

Another interesting fact observed was the alteration of the serological types of the *V. cholerae* *in vivo*. This occurred in 24 patients, and was not influenced by chemotherapy. Though the question of chance contamination cannot be entirely ruled out in all the cases in this series, in some cases a particular serological type was the only one of its kind isolated that day. A few examples of mutation are given in Table VI.

TABLE V.—*Analysis of Results of Treatment on V. Cholerae in Human Stool*

Day When Vibrio-Free	Sulphaguanidine					Formosulphathiazole					Formosulphacetamide					Nil				
	Total Cases Freed				Av. Quantity Drug Required (g.)	Total Cases Freed				Av. Quantity Drug Required (g.)	Total Cases Freed				Av. Quantity Drug Required (g.)	Total Cases Freed				Av. Quantity Drug Required (g.)
	Ogawa	Inaba	V+	%		Ogawa	Inaba	V+	%		Ogawa	Inaba	V+	%		Ogawa	Inaba	V+	%	
2nd ..	0	1	1	3.03	10.0	0	1	1	2.94	9.0	1	0	1	3.7	6.0	2	0	2	5.5	0
3rd ..	2	2	4	12.12	18.25	5	1	6	17.64	14.6	5	1	6	22.2	18.5	3	1	4	11.1	0
4th ..	6	4	10	30.3	22.16	7	1	8	23.52	25.2	3	3	6	22.2	22.0	7	4	11	30.5	0
5th ..	1	0	1	3.03	25.0	4	3	7	20.58	35.6	6	3	9	33.3	20.0	6	1	7	19.4	0
6th ..	10	3	13	39.39	32.07	3	0	3	8.82	36.4	0	1	1	3.7	6.0	2	1	3	8.3	0
7th ..	1	1	2	6.06	28.5	3	0	3	8.82	32.6	3	0	3	11.1	33.3	1	0	1	2.7	0
8th ..	1	0	1	3.03	21.0	4	0	4	12.35	50.5	0	0	—	—	—	1	1	2	5.5	0
9th ..	1	0	1	3.03	50.0	0	0	—	—	27.0	0	0	—	—	—	2	0	2	5.5	0
10th ..	—	—	—	—	—	0	1	1	2.94	27.0	0	1	1	3.7	13.0	1	1	2	5.5	0
11th ..	—	—	—	—	—	1*	0	1	2.95	72.0	—	—	—	—	—	—	—	—	—	—
12th ..	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	1	2	5.5	0
Total V+ studied			33					34					27					36		

* This patient, though still showing *V. cholerae* (Ogawa) in the stool on the tenth day after 72 g. of formosulphathiazole, became symptom-free and left hospital.

TABLE VI.—*Example of Alteration of Serological Types of V. Cholerae During Treatment*

Case No.	Treatment	Amount Used before V—	Examinations								Remarks
			1st	2nd	3rd	4th	5th	6th	7th	8th	
A ..	Sg	50 g.	Ogawa	Nil	Ogawa	*Ogawa	Inaba	Nil	Nil	Nil	*Ogawa + after 50 g.; drug stopped; then Inaba; then nil. Out of 415 strains serologically tested Hikojima was present in only one sample
B ..	FST	40 g.	Inaba	Ogawa	Inaba	Inaba	Hikojima	Nil	Nil	Nil	
C ..	FSA	26 g.	Inaba	Inaba	Ogawa	Nil	Nil	Nil	Nil	Nil	
D ..	Nil		Inaba	Inaba	Inaba	Inaba	Inaba + Ogawa	Inaba + Ogawa	Inaba	Nil	

Blood Concentration of the Drugs

Systemic absorption of the different chemotherapeutic drugs used in this series was studied by estimating their concentration in the blood, in terms of free and total sulphonamide (Table VII). This was estimated in

TABLE VII.—Serum Concentration of Sulphaguanidine (Sg), Formosulphathiazole (FST), and Formosulphacetamide (FSA) in Terms of Sulphonamide in mg. per 100 ml.

Case No.	Treatment	Total Quantity and in Days	Sulphonamide Concentration mg./100 ml.		Urinary History
			Free	Total	
1	Sg	26 g. 3 days	2.1	2.9	1st urine after 24 hours, then free
	Sg	50 g. 6 days	1.4	1.5	Free urine
2	Sg	58 g. 6 days	2.1	2.2	1st urine after 12 hours, then free
3	Sg	36 g. 4 days	12.5	13.9	1st urine after 48 hours; then scanty for two days, then free
4	FST	13 g. 2 days	0.64	1.4	No urination; died
5	FST	64 g. 6 days	0.75	1.5	Urine showed sulphanilamide (free 12.5, total 13.5 mg. per 100 ml.)
6	FST	72 g. 8 days	0.4	1.2	1st urine after 21 hours, then free
7	FST	56 g. 9 days	2.5	4.2	1st urine after 53 hours, then free
8	FST	52 g. 5 days	Not detectable	Not detectable	Free urine, after 12 hours
9	FST	32 g. 3 days	2.1	2.2	1st urine after 30 hours, then free
	FST	54 g. 6 days	0.46	0.6	Free urine
10	FST	23 g. 4 days	0.87	1.1	1st urine after 24 hours, then free; cured
11	FST	14 g. 3 days	0.60	1.1	1st urine after 48 hours, followed by anuria; died
12	FST	44 g. 7 days	0.35	0.54	1st urine after 12 hours, then free; cured
13	FST	19 g. 6 days	0.37	0.63	1st urine after 24 hours, then free; cured
14	FSA	24 g. 3 days	6.0	14.4	No urination; died
15	FSA	24 g. 2 days	2.4	2.6	1st urine after 18 hours, then free
	FSA	53 hrs., after 36 g.	0.71	0.87	Free urine
16	FSA	30 g. 4 days	2.1	2.96	1st urine in 24 hours, then free
17	FSA	8 g. 1 day	0.8	1.1	No marked anuria
18	FSA	17 g. 2 days	2.0	5.5	1st urine after 28 hours, then free; cured
19	FSA	18 g. 6 days	1.7	4.5	No urine; died
20	FSA	36 g. 4 days	3.7	5.7	1st urine after 24 hours, then free; cured

three patients having sulphaguanidine, ten patients having formosulphathiazole, and seven patients having formosulphacetamide. The average blood sulphonamide concentration for formosulphacetamide was free 2.42 mg. and total 4.7 mg., and for formosulphathiazole free 0.82 mg. and total 1.31 mg. per 100 ml. of blood; the respective total quantities of drugs received were 24.12 g. and 40.27 g. in four and five days respectively.

One patient having sulphaguanidine, with prolonged anuria followed by scanty urination, showed a high blood concentration (free 12.5 mg. and total 13.9 mg. per 100 ml.). Except for this case formosulphathiazole showed the lowest and formosulphacetamide the highest blood concentrations. In several instances the importance of free urination in keeping the blood concentration low was apparent. A sample of urine from a patient having formosulphathiazole showed fairly high excretion figures (12.5 and 13.5 mg. per 100 ml.). Formosulphacetamide was detectable in the blood of one patient examined 53 hours after discontinuation of the drug.

Discussion

In the present series sulphaguanidine, formosulphathiazole, or formosulphacetamide did not reduce the mortality rate of cholera patients, the rate being lowest in the group that did not receive chemotherapy. This latter fact was noticeable not only in vibrio-negative but also in vibrio-positive cases, and even in patients admitted in a serious condition with no perceptible radial pulse. On an analysis of the causes of death it was noticed that the highest mortality was due to peripheral circulatory failure in all the groups. The next most frequent cause was uraemia, which was more apparent in patients getting the formaldehyde compounds.

The failure of chemotherapy in cholera is not altogether unexpected from the nature of the disease itself, with its sudden onset and profuse vomiting and purging, which rapidly produce a condition of marked dehydration and serious systemic biochemical changes. There also occurs a great fall in the systolic blood pressure, resembling shock. It is not only the loss of systemic fluid but also the absence of sufficient filtration pressure in the glomeruli of the kidneys that produces the anuria. In many cases a quick supply of fluid and salt rapidly improved both dehydration and the low blood pressure, but in others, especially in late cases, circulatory collapse becomes irreversible. Chemotherapy cannot be expected to influence the above condition except possibly by way of prevention of the development of the disease initially. Once the disease is fully developed the most important factor in its treatment is undoubtedly an adequate supply of fluid and salt, and efforts should be made to prevent collapse becoming irreversible.

Analysis of the effects of the different chemotherapeutic compounds on *V. cholerae* in human stool in this series does not show any appreciable vibriocidal result *in vivo* when compared with the control group having no chemotherapy. In day-to-day observations regarding the numbers of persons becoming vibrio-free, from the second day onward the control group showed practically the same results as the groups having chemotherapeutic treatment, slight differences being negligible. If the vibrio disappears from the stool at practically the same rate without chemotherapy as with it, then the sulphonamides used in this series cannot be of much practical value.

In some patients it was observed that the vibrio continued to be present in the stool so long as the drug was being administered, but disappeared one or two days afterwards. This fact also demonstrates that time is more important for the disappearance of the vibrio from the stool than the quantity of chemotherapeutic drugs given. In the absence of any appreciable vibriocidal effects of these drugs *in vivo*, their prophylactic value cannot be of any significance. Another point noted was that, once the symptoms of cholera developed, the death rate was also high among patients who showed no *V. cholerae* in their stools.

Estimation of blood sulphonamide concentration showed that all the drugs used in this series were absorbable even at the height of the disease, though least absorption occurred with formosulphathiazole. A sulphonamide may be an additional burden on the already dysfunctioning excretory system, especially if associated with irritant compounds like formaldehyde, as may be seen in increased mortality figures for uraemia in persons receiving the latter drug. On serological typing it was found that most positive cases were

infected with the Ogawa type of organism. The death rate was also higher in that type. Mutations of the serological types are little-understood phenomena. These were not abolished by chemotherapy.

Conclusion

Sulphaguanidine, formosulphathiazole, and formosulphacetamide given orally did not reduce the mortality rate in cholera patients, and results in these cases compared unfavourably with those in cases where no chemotherapy was given; other treatment remained the same. No special vibriocidal effect of these compounds was apparent *in vivo*, the *V. cholerae* disappearing from the stools practically at the same rate, both in those who had chemotherapy and in those who had none. In assessing the value of the vibriocidal effect of any drug in this disease *in vivo*, it is important to note that the *V. cholerae* disappears from the human stool automatically at a fairly quick rate. This disease characteristically comes on and passes off like a storm, and once it is fully developed the most important part of treatment is undoubtedly to replace quickly the fluid and salt lost and to prevent the development of the irreversible condition of circulatory collapse. This peripheral circulatory failure is an important cause of persistent anuria occurring as a result of failure of adequate glomerular filtration pressure, which ultimately leads to complete renal failure. Chemotherapeutic drugs, to be of any real value in cholera, must have a quicker action than any of the sulphonamides tested in this series, and also should not be toxic.

My thanks are due to Mr. P. N. Sen Gupta, of Bengal Immunity Research Institute, for bacteriological work; to Dr. A. N. Bose, of the same institute, for estimating the blood sulphonamides; and to the Director of the Institute, Dr. U. P. Basu, for supplying free of cost the sulphacetamide used and for allowing the investigations to be carried out there. Thanks are also due to Messrs. Ciba Pharma Ltd. for supply free of cost the formosulphathiazole, in the form of "formocibazole." I am grateful to my house-physicians and nursing staff, but for whose untiring co-operation during an epidemic this work would not have been possible.

REFERENCES

- Bhatnagar, S. S., *et al.* (1948). *British Medical Journal*, **1**, 719.
Bose, A. N. (1949). *Ann. Biochem. exp. Med.*, **9**, 201.
Carruthers, L. B. (1942). *Trans. R. Soc. trop. Med. Hyg.*, **36**, 89.
Chopra, R. N., *et al.* (1941). *Indian med. Gaz.*, **76**, 712.
Lahiri, S. C. (1945). *J. Indian med. Ass.*, **14**, 113.
— (1948). *Indian med. Gaz.*, **83**, 24.
— (1949). *J. Indian med. Ass.*, **18**, 155.
— and Dutta, S. K. (1949). *Ibid.*, **19**, 1.

The Tavistock Clinic, as an out-patient hospital dealing with psychological problems of individuals and families, has been absorbed in the National Health Service, but a branch of it known as the Tavistock Institute of Human Relations has been incorporated as a separate social research organization concerned with the psychology of relations between human beings in domestic, industrial, and civic groups. It is governed by a council of eight, four of whom are medical, and the council is responsible to an association of 50 members elected on a basis of professional activity or interest in applied social research. In a small brochure recently issued from 2, Beaumont Street, W.1, an account is given of four years' work. About 70 projects of different kinds have been undertaken, some of them for government departments or local authorities, others for industrial concerns or voluntary organizations interested in community and family affairs. To name a few: a study of some aspects of resettlement in the British zone of Germany; the design of a medical statistics service in a local health authority; the job analysis of nursing auxiliary roles in a hospital group; the development of a new type of family case-work agency; the assessment of safety education films for children.

THE INCIDENCE AND PREVENTION OF TETANUS AMONG CIVILIANS

BY

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Tetanus is not a notifiable disease in England and Wales, and the only useful indication of its general incidence is that obtainable from the mortality statistics of the General Register Office.

Recent Trend of Mortality

Table I gives the numbers of registered deaths and the death rates from 1931 to 1948, and the latter are illustrated in Fig. 1. (See footnote to Table I regarding

TABLE I.—Deaths From Tetanus and Death Rates Per Million Living by Sex. England and Wales, 1931–48

Year	Males		Females	
	No. of Deaths	Rate per Million Living	No. of Deaths	Rate per Million Living
1931	92	4.8	25	1.2
1932	93	4.8	21	1.0
1933	74	3.8	28	1.3
1934	85	4.4	26	1.2
1935	98	5.0	28	1.3
1936	86	4.4	29	1.4
1937	85	4.3	22	1.0
1938	72	3.6	17	0.8
1939	62	3.1	23	1.1
1940	91	5.0	18	0.8
1941	79	4.6	20	0.9
1942	66	3.9	29	1.4
1943	61	3.7	24	1.1
1944	55	3.4	33	1.5
1945	55	3.4	24	1.1
1946	41	2.2	22	1.0
1947	49	2.5	22	1.0
1948	48	2.4	21	0.9

Note.—This and subsequent tables exclude non-civilian males on and after September 3, 1939, and non-civilian females on and after June 1, 1941.

FIG. 1.—Annual death rates from tetanus per million living at all ages. England and Wales, 1931–48.

exclusion of non-civilians.) The male death rate has recently shown a definite tendency to decline, and the rates during 1946–8 were about half of those recorded between 1931 and 1940. Female rates, on the other hand, remained fairly steady, declining only very slightly during the period.