SULPHAMIDO-CHRYSOIDINE, SULPHANILAMIDE, AND BENZYL SULPHANILAMIDE IN THE TREATMENT OF ERYSIPELAS

A CONTROLLED SERIES OF 242 CASES

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We have recently published two reports to the Therapeutic Trials Committee of the Medical Research Council on the treatment of erysipelas (Snodgrass and Anderson, 1937a, 1937b). In our first report we showed in a controlled series of 312 cases that prontosil "red" (sulphamido-chrysoidine) was more effective than ultra-violet light in that the cases which received sulphamido-chrysoidine gave better results in respect of the curtailment of (1) the duration of the spread of the local lesion; (2) the duration of primary pyrexia; (3) the duration of toxæmia. The evidence supporting these statements was assessed statistically.

In our second report, dealing with a controlled series of 270 cases of erysipelas, we investigated the action of the derivative of sulphamido-chrysoidine termed *p*-aminobenzenesulphonamide, and commonly called sulphanilamide. Ultra-violet light was again used as the method of treatment for the control series of cases. We once more came to the conclusion that the use of sulphanilamide was better than the use of ultra-violet light in respect of the same criteria as in our first report. This evidence was also assessed statistically. The question of the optimum dosage was not determined, but it was found that an effective method of treatment was to give 1 gramme of sulphanilamide by mouth at four-hourly intervals until the cessation of primary pyrexia, and thereafter 0.75 gramme by mouth thrice daily until final cure was determined.

Toxic symptoms in this second series, in which large doses of sulphanilamide were used, were common, amounting to 35.5 per cent. in 270 cases. Cyanosis was the most frequent manifestation, and occurred in 29.6 per cent. of cases. It was considered, therefore, that further work was necessary in an attempt to settle a minimum adequate dosage, for the incidence of cyanosis rapidly increased with an increase in dosage. In our first series, employing sulphamido-chrysoidine, there were only two cases of cyanosis, but the average case dosage was 5 grammes and the maximum case dosage 15 grammes. In the second series, employing sulphanilamide, the average case dosage was 41.6 grammes and in the first two days 14.64 grammes, while cyanosis, as already stated, occurred in 29.6 per cent. of all cases. Thirty-nine cases in our second series received more than 6 grammes of sulphanilamide a day during their initial stages of treatment, and in this small group the incidence of cyanosis

rose to 48.7 per cent. Sulphamido-chrysoidine and sulphanilamide are not chemically equivalent drugs, nor were they employed in equivalent dosage. It was therefore difficult to compare their therapeutic efficiency as exhibited in our two series of cases. It was thought desirable to undertake a third series of controlled cases with a view to determining this, and, further, it was considered desirable to investigate the anti-streptococcal activity in erysipelas of yet another derivative of this group of anti-bacterial compounds, and so *p*-benzylaminobenzenesulphonamide was employed. The objects of this third report are therefore: (1) To investigate the comparative therapeutic activities of (a) sulphamido-chrysoidine (the preparation used was prontosil red, Messrs. Bayer, Ltd.); (b) *p*-aminobenzenesulphonamide, commonly termed sulphanilamide (the preparation used was streptocide, Messrs. Evans Sons Lescher and Webb); (c) *p*-benzylaminobenzenesulphonamide, hereafter referred to as benzylsulphanilamide (the preparation used was propeptasine, Messrs. May and Baker Ltd.). (2) To determine an optimum dosage, taking into account the question of drug intolerance.

The material consists of all patients over 5 years of age whose case was diagnosed as erysipelas after admission to Ruchill Hospital, Glasgow, from November, 1937, to March, 1938. Again our material was thoroughly representative of the incidence of the disease in this district during the period under review. All patients were under the clinical control of T. A. and J. L. R.

Plan of Investigation and Details of Treatment

Part I: 122 Cases.—There were four treatment groups:

- A. Benzylsulphanilamide, 1 gramme four-hourly.
- B. Benzylsulphanilamide, 2 grammes four-hourly.
- C. Sulphanilamide, 1 gramme four-hourly.
- D. Sulphanilamide, 2 grammes four-hourly.

For each group fifteen male patients and fifteen female patients were gathered—the cases being allocated strictly in order of admission. (In each ward, male and female, one extra case was taken on at the end of the investigation and was retained in the series.)

These cases were admitted during the months of November and December, 1937, and early in January, 1938.

Part II: 120 Cases.—There were four treatment groups:

- A. Sulphamido-chrysoidine, 1 gramme four-hourly.
- B. Sulphamido-chrysoidine, 2 grammes four-hourly.
- C. Sulphanilamide, 0.5 gramme four-hourly.
- D. Sulphanilamide, 0.75 gramme four-hourly.

Again each group comprised fifteen male patients and fifteen female patients taken in rotation according to the order of admission. These cases were admitted during the months of January, February, and March, 1938.

The specific treatment noted above was continued until the temperature of the patient became normal. Thereafter all cases in groups A, B, C, and D, Part I, and groups A and B, Part II, received 1 gramme of the drug originally given thrice daily till dismissal from hospital. In respect of groups C and D, Part II, the original dosage of the drug chosen, 0.5 gramme and 0.75 gramme, was administered thrice daily.

No local treatment was given, and all cases, as before, were treated under strictly comparable conditions. Full

details of diet and laxatives will be found in our second paper (Snodgrass and Anderson, 1937b), which also recorded the data used to obtain our records of results. In a word, this series of cases, apart from specific treatment, has been subjected to the same controls and to the same analyses as the preceding series.

Assessment of Results

1. The distribution of the individual cases in the two treatment groups must be considered in respect of certain factors known to influence the course of the disease. Those regarded as being of greatest importance are: (a) the duration of the disease before admission to hospital; (b) the age of the patient; (c) the severity of the infection; (d) associated diseases. Tables constructed to show the relation of these factors to the types of treatment indicate an even distribution. A statistician who has examined them is satisfied that there was no weighting of any one line of treatment by any of these factors.

2. The question when "cure" is achieved has to be determined. The fatality rate in erysipelas is so low that it cannot be used in a small series of cases to assess the value of a therapeutic measure. There is no single clinical feature which can be regarded as a satisfactory criterion of recovery. Cases are seen where the lesion continues to spread after the temperature has become normal; and, again, it is not uncommon for the local lesion to cease spreading while the temperature is still elevated and the patient continues in a toxic condition. In order to arrive at a conclusion in this series of cases, attention was paid to the following points from the beginning of treatment: (i) the duration in days of the spread of the local lesion; (ii) the duration in days of the primary pyrexia; (iii) the time in days which elapsed until the patient was free from toxic symptoms. These are the criteria which were used in our previous reports.

Results of Treatment

There were five deaths. Four of these have been excluded from the following tables.* All deaths will be dealt with later in this report. The corrected and rearranged numbers for each subsection are therefore:

Sulphamido-chrysoidine	1 gramme	four-hourly	30 cases
"	2 grammes	"	28 "
Sulphanilamide	0.5 gramme	"	30 "
"	0.75 "	"	30 "
"	1 "	"	31 "
"	2 grammes	"	31 "
Benzylsulphanilamide	1 gramme	"	29 "
"	2 grammes	"	29 "

Total .. 238 cases

Table I shows that out of fifty-eight cases receiving sulphamido-chrysoidine 86.2 per cent. had no further spread of lesion after twenty-four hours; out of 120 cases receiving sulphanilamide the equivalent percentage was 88.3; while out of fifty-eight cases receiving benzylsulphanilamide the percentage was only 68.9. The difference between this last percentage and either of the others is more than twice the standard errors of the differences, and is considered significant. This reflects unfavourably on the effect of benzylsulphanilamide. With regard to the various subgroups receiving sulphanil-

amide little can be said: there is a slightly better outcome during the first day for those cases receiving the larger dosages, but the difference is small and cannot be deemed significant.

TABLE I.—*Spread of Lesion*

Method of Treatment		Duration in Days				Total Cases
		0	1	2	3	
Sulphamido-chrysoidine	1 gm.	13 (43.3)	11 (36.7)	6 (20.0)	0	30
	2 gm.	11 (39.3)	15 (53.6)	2 (7.1)	0	28
Sulphanilamide	0.5 gm.	13 (43.3)	10 (33.3)	7 (23.3)	0	30
	0.75 gm.	14 (46.7)	12 (40.0)	3 (10.0)	1 (3.3)	30
Sulphanilamide	1 gm.	17 (54.8)	11 (35.5)	3 (9.7)	0	31
	2 gm.	18 (58.1)	11 (35.5)	2 (6.5)	0	31
Benzylsulphanilamide	1 gm.	16 (55.2)	4 (13.8)	7 (24.1)	2 (6.9)	29
	2 gm.	16 (55.2)	4 (13.8)	8 (27.6)	1 (3.5)	29
Totals		118 (49.6)	78 (32.8)	38 (16.0)	4 (1.7)	238

Table II shows that there is no significant difference between the various results. After forty-eight hours, pyrexia had ceased in 77.6 per cent. of the cases receiving sulphamido-chrysoidine, in 72.1 per cent. of the cases receiving sulphanilamide, and in 74.1 per cent. of the cases receiving benzylsulphanilamide.

TABLE II.—*Primary Pyrexia*

Method of Treatment		Duration in Days								Total Cases
		0	1	2	3	4	5	6	Over 6	
Sulphamido-chrysoidine	1 gm.	1 (3.3)	11 (36.7)	14 (46.7)	3 (10.0)	1 (3.3)	0	0	0	30
	2 gm.	4 (14.3)	8 (28.6)	7 (25.0)	6 (21.4)	1 (3.6)	0	2 (7.1)	0	28
Sulphanilamide	0.5 gm.	5 (16.7)	8 (26.7)	12 (40.0)	4 (13.3)	1 (3.3)	0	0	0	30
	0.75 gm.	0	11 (36.7)	11 (36.7)	5 (16.7)	2 (6.7)	0	0	1* (3.3)	30
Sulphanilamide	1 gm.	0	11 (35.5)	10 (32.3)	9 (29.0)	0 (3.2)	1 (3.2)	0	0	31
	2 gm.	0	8 (25.8)	12 (38.7)	3 (9.7)	7 (22.6)	1 (3.2)	0	0	31
Benzylsulphanilamide	1 gm.	1 (3.5)	9 (31.0)	12 (41.4)	5 (17.2)	0	2 (6.9)	0	0	29
	2 gm.	0	9 (31.0)	12 (41.4)	7 (24.1)	0	0	1 (3.5)	0	29
Totals		11 (4.6)	75 (31.5)	90 (37.8)	42 (17.6)	12 (5.0)	4 (1.7)	3 (1.3)	1 (0.4)	238

* The delay here was due to drug fever.

Table III shows that out of fifty-eight cases receiving sulphamido-chrysoidine the percentage having no toxæmia after the third day was 65.6. Out of 122 cases receiving sulphanilamide the equivalent percentage was 59.0. Out of fifty-eight cases receiving benzylsulphanilamide the percentage was 29.3. These percentages reflect unfavourably upon the action of benzylsulphanilamide.

* One patient died during convalescence, and as the local lesion was at the time of death completely cured the case has been retained in the statistical tables.

TABLE III.—Toxaemia

Method of Treatment		Duration in Days								Total Cases
		0	1	2	3	4	5	6	Over 6	
Sulphamido-chrysoidine	1 gm.	0	0	7 (23.3)	13 (43.3)	9 (30.0)	0	1 (3.3)	0	30
	2 gm.	1 (3.4)	2 (6.8)	3 (10.2)	12 (40.8)	9 (30.6)	0	1 (3.4)	0	28
Sulphanilamide	0.5 gm.	0	4 (13.3)	4 (13.3)	11 (36.7)	8 (26.7)	2 (6.7)	1 (3.3)	0	30
	0.75 gm.	1 (3.3)	0	7 (23.1)	12 (39.6)	8 (26.4)	1 (3.3)	1 (3.3)	0	30
	1 gm.	0	0	3 (9.7)	15 (48.4)	10 (32.3)	2 (6.5)	1 (3.2)	0	31
	2 gm.	0	0	3 (9.7)	12 (38.7)	12 (38.7)	2 (6.5)	2 (6.5)	0	31
Benzylsulphanilamide	1 gm.	0	0	2 (6.9)	7 (24.1)	11 (37.9)	6 (20.7)	2 (6.9)	1* (3.5)	29
	2 gm.	0	1 (3.5)	0	7 (24.1)	10 (34.5)	8 (27.6)	3 (10.4)	0	29
Totals		2 (0.8)	7 (2.9)	29 (12.2)	89 (37.4)	77 (32.3)	21 (8.8)	12 (5.0)	1 (0.4)	238

* Very severe case with scalp abscess.

Recurrence

No recurrence took place in any case during the period of stay in hospital, nor has any patient been readmitted with a recurrence one month after the closing of the records. This is rather a remarkable result. In our first series of 312 cases there were twenty-seven cases of recurrence, an incidence of 8.65 per cent. In our second series of 270 cases the percentage incidence was 3.7. As half the cases in the two preceding series were not treated with any preparation of sulphanilamide, and as all cases in this third series received some form of sulphanilamide, the absence of recurrence may be adduced as a further strong argument in favour of treatment by some form of sulphanilamide.

Complications

Here are included the septic complications directly attributable to infection with erysipelas. Among such conditions are abscess formation, septicaemia, thrombosis, and nephritis.

The percentage incidence was 13.8 in those cases receiving sulphamido-chrysoidine, 6.6 in the cases receiving sulphanilamide, and 13.8 in the cases treated with benzylsulphanilamide. The number of complicated cases is so small that no significance is attached to the slight differences in the three percentages.

Deaths

The number of deaths was five out of 242, a percentage of 2.06. This is low if compared with the annual fatality rate given for Ruchill Hospital in the medical officer of health's annual returns. The percentages there for the past few years are: 1935, 7.5; 1934, 7.6; 1933, 9.3; 1932, 9.6; 1931, 7.7. Four of the patients who died have been excluded from Tables I, II, and III for obvious reasons, but one is included because the erysipelas was completely cured and the patient, a male aged 72, who suffered from chronic myocarditis, collapsed and died on being allowed up on the ninth day after admission to hospital. In this case the duration of spread of the lesion was two days, of primary pyrexia three days, and of toxaemia four days. The data relevant to these fatal cases are given in Table IV.

TABLE IV.—Details of Fatal Cases

Case No.	Method of Treatment	Sex and Age	Site	Days Ill before Admission	Dose of Drug in Gms.	Duration of Treatment in Days	Days in Hospital	Remarks
581	Sulphamido-chrysoidine	M. 75	Facial	2	6	1	1	Large rodent ulcer of face. Acute nephritis on admission. Developed cavernous sinus thrombosis
1214	Sulphamido-chrysoidine	F. 58	"	2	24	2	2	Carbuncle of neck. Diabetes mellitus. Died in coma
*716	Sulphanilamide	M. 72	"	1	11	3.5	9	Chronic myocarditis. Allowed up on ninth day in hospital—collapsed and died
95	Benzylsulphanilamide	M. 64	"	3	36	3	8	Lesion had subsided at death. Chronic drinker of meth. spirit. ? due to cerebral atheroma. P.m. refused
6011	Benzylsulphanilamide	F. 77	Leg	10	30	5	45	Developed subcutaneous abscesses of legs which would not heal. Senile: hypostatic pneumonia terminal event

* This patient was completely cured at time of death, and death had no relation to erysipelas.

It is to be noted from Table IV that none of these deaths occurred in uncomplicated cases of erysipelas. It is quite apparent that no definite conclusions can be drawn from fatality rates in this disease as to the relative merits of different types of treatment, since there will always be a proportion of patients suffering from associated disease in whom erysipelas is merely one of the terminal events.

Toxicity

Table V gives the total observed incidence of toxic manifestations.

TABLE V.—Toxic Effects

Type of Toxic Reaction	Sulphamido-chrysoidine		Sulphanilamide				Benzylsulphanilamide	
	1 gm.	2 gm.	0.5 gm.	0.75 gm.	1 gm.	2 gm.	1 gm.	2 gm.
Moderate cyanosis	—	—	—	—	1	6	—	—
Slight cyanosis ..	7	2	14	12	13	13	2	3
Pyrexia	—	—	—	2	1	3	1	1
Rash	—	1	2	—	—	—	1	1
Vomiting or severe nausea	2	2	—	1	1	2	1	—
Delirium	1	1	—	1	—	—	—	—
*Jaundice (?) ..	—	—	—	—	1	—	—	—
Complaint of severe drowsiness	—	—	—	1	—	1	—	—
Total cases showing toxic effects	10 (33.3)	6 (21.7)	16 (53.3)	17 (54.8)	17 (54.8)	25 (80.1)	5 (17.2)	5 (17.2)

* This case left hospital against advice on day jaundice was noted—twelfth day

The occurrence of some degree of cyanosis was the most commonly observed toxic effect. Irrespective of drug or dosage, the total incidence was 30.7 per cent. In no case could the appearance of cyanosis be considered dramatic; it was never of long duration and there was little constitutional disturbance. No spectroscopic examinations were made, but none of the cases exhibited the severe degree of cyanosis that had been previously noted by us in patients with proved sulphaemoglobinaemia. No patient received any form of sulphur while under treatment. Twenty-nine per cent. of the patients, however, gave a history of taking "salts" before admission to hospital. The routine which is adopted in the hospital when such a history is obtained is to administer a soap-and-water enema on admission, repeat it in twelve hours, and delay treatment with the drugs until after the second enema. Cyanosis developed in 32.8 per cent. of those who gave a history of taking "salts," while in those who had no such antecedent history the incidence of cyanosis was 29 per cent. It has been suggested that there is a causal relation between premedication with saline purgatives containing sulphur and the occurrence of cyanosis (Paton and Eaton, 1937; Discombe, 1937). The close equivalence of the percentages in the two groups in this series and the absence of severe cyanosis rather suggests that the enemata may have some preventive action on the occurrence of cyanosis.

At no time did cyanosis give cause for alarm, and while in some cases the drug was stopped on its appearance, in the majority the drug was continued with no apparent ill effect. When comparison is made between the drugs used, it is found that the incidence of cyanosis was less in those cases which received sulphamido-chrysoidine or benzylsulphanilamide, and that, as we had previously suggested, cyanosis increased in incidence with the larger doses of sulphanilamide.

Toxic effects other than cyanosis were noted in 11.8 per cent. of the cases. These (see Table V) were transient in nature, rapidly ceased after stoppage of the drug, and did not give rise to prolonged illness or unpleasant sequelae. The occurrence of these secondary toxic effects cannot be correlated with any particular type of drug used, and whether they are an expression of idiosyncrasy or of some factor still undetected cannot yet be stated. While routine blood examinations have not been carried out, no case has been observed in which there was any clinical suggestion of blood dyscrasia.

One further observation should be made regarding toxic effects. Reference to Table II shows that when 1 gramme of sulphanilamide was given four-hourly only 3.2 per cent. of cases remained pyrexial after three days in hospital, while with a dosage of 2 grammes four-hourly the equivalent percentage was 25.8. When the other criteria of cure are examined in these two groups it is seen that if 2 grammes of sulphanilamide are given four-hourly the duration of the spread of the lesion and of toxæmia closely corresponds to the results obtained with 1 gramme of sulphanilamide given at four-hourly intervals. If this is taken in association with the later occurrence of drug fever as a toxic sign it would seem that larger doses of sulphanilamide may have a direct effect in the prolongation of fever.

Discussion

Table VI summarizes the results obtained with the different drugs used in the combined series, irrespective of dosage employed. Percentages only are given.

TABLE VI

Drug Employed	No Spread after 24 Hours in Hospital	No Pyrexia after 48 Hours in Hospital	No Toxaemia after 3 Days in Hospital	Toxic Effect of Drug	No. of Cases
Sulphamido-chrysoidine	86.2	77.6	65.5	27.5	58
Sulphanilamide	88.3	72.1	59.0	61.4	122
Benzylsulphanilamide	68.9	74.1	29.3	17.2	58

It would appear that in respect of its effect on the duration of spread and toxæmia the action of benzylsulphanilamide is slower than that of either of the other drugs. The incidence of toxic effects from this drug is the lowest, but on the other hand, as has been stated earlier, the occurrence of these toxic phenomena seems to have no harmful sequelae, provided that the drugs are used in proper dosage and under careful clinical supervision. On these grounds, therefore, and after careful study of Tables I, II, and III, we feel that benzylsulphanilamide is not the drug of choice in the treatment of erysipelas.

The figures in Table VI indicate that there is little to choose between sulphamido-chrysoidine and sulphanilamide. In Table VI, however, the varied dosage of the two drugs employed is not taken into account. One of the purposes of this paper is to attempt to ascertain a dosage which will have the optimal clinical effect. After careful scrutiny of Tables I, II, and III it is thought that the best results have been obtained with the employment of sulphamido-chrysoidine in 1 and 2 gramme doses and sulphanilamide in 0.75 and 1 gramme doses. The effects of these are summarized, therefore, in Table VII, using the same criteria for assessment and again expressing the results as percentages.

TABLE VII

Drug and Dosage Employed	No Spread after 24 Hours' Treatment	No Pyrexia after 48 Hours' Treatment	No Toxaemia after 3 Days' Treatment	Toxic Effects of Drug	No. of Cases in Group
Sulphamido-chrysoidine: 1 gramme	80	86.7	66.7	33.3	30
2 grammes	92.9	67.9	66.7	21.7	28
Sulphanilamide: 0.75 gramme	86.7	73.3	65.5	54.8	30
1 gramme	90.3	67.7	58.1	54.8	30

Analysis of Table VII suggests the following conclusions:

(a) *Duration of Spread.*—The percentage differences are small and not statistically significant. The fact that with each drug better percentage results are obtained when the larger doses are employed is, however, suggestive of increased therapeutic effect.

(b) *Duration of Primary Pyrexia.*—We again note a slight lag in the fall of temperature when the larger doses are employed. As already stated, we feel that the drugs may have a direct pyrexial effect in the larger quantities.

(c) *Duration of Toxaemia.*—No difference is observed between the two drugs or their varied dosage.

(d) *Toxic Effects.*—The occurrence of toxic effects is slightly less when sulphamido-chrysoidine is used.

(e) *Dosage.*—The percentages indicate that the therapeutic results obtained with a dosage of 2 grammes of sulphamido-chrysoidine and 1 gramme of sulphanilamide

closely correspond. In other words, the sulphanilamide radical, weight for weight, is clinically more effective than the original sulphamido-chrysoidine.

We are, however, of the opinion, from the above figures, that the choice of drug to be employed can be left to individual preference. The method of administration to an adult patient should be: (i) Sulphamido-chrysoidine: 1.5 grammes every four hours—that is, 9 grammes a day—until cure is established; thereafter 1 gramme three times daily for a further period of fourteen days. (ii) Sulphanilamide: 1 gramme every four hours—that is, 6 grammes a day—until cure is established; thereafter 1 gramme three times daily for a further period of fourteen days.

All other drugs must be avoided during the period of specific treatment: a list of suitable purgatives should be given to the patient, the use of enemata explained, and explicit instructions given regarding diet along the lines laid down in our previous paper (Snodgrass and Anderson, 1937b). Toxic effects should be reduced to a minimum if these suggestions are followed.

We wish to thank Dr. W. M. Elliott, physician-superintendent of Ruchill Fever Hospital, for permission to conduct the investigation. We would also record our thanks to Mr. Victor Goode, registrar, for careful assistance in the collection of the figures.

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LATE RESULTS OF SURGICAL TREATMENT IN PERFORATED PEPTIC ULCER

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Upon the late results of surgical treatment in cases of perforated peptic ulcer there appears to be a considerable diversity of opinion. Thus Thompson, Miles, and Wilkie (1931) state that "the successful closure of a perforation is in many cases followed by freedom from digestive trouble," though they add that this is not so "in a number of cases." Sherren (1932) considers that if the ulcer which perforates is acute and situated on the anterior surface of the stomach no further symptoms will develop in most cases. Walton (1934), commenting on the different views held, says that a close follow-up does not confirm the opinion that the majority of cases have no further symptoms after recovery from operation. Romanis and Mitchiner (1937) consider that successful recovery from a perforation is nearly always followed by a period of relief from symptoms that may last from six to eighteen months before the recurrence, which they seem to regard as a common event.

The present investigation was carried out at the Wellington Hospital, New Zealand, with a view to ascertaining the late results of simple closure of a perforated peptic ulcer. No attempt was made to divide the cases into groups in which the ulcer was thought to be acute or chronic. The findings are compared with the results obtained from the treatment of a group of cases of unperforated peptic ulceration by medical methods.

There were forty-one cases of perforated peptic ulcer treated by simple closure, this figure comprising fourteen cases of gastric ulcer, twenty-five cases of duodenal ulcer, and one case each of jejunal and gastro-jejunal ulceration. The time elapsing between the occurrence of perforation and operation varied considerably, being in some cases as short as one hour and in others as long as two days. That the period was often longer than is usually the case in Great Britain is due in large measure to geographical considerations and lack of transport facilities, and is reflected in the high mortality, for of the forty-one patients submitted to operation twelve died. The site of the ulcer in the latter was duodenal in eight cases, gastric in three, and jejunal in one case.

A careful follow-up was made at a period after the operation varying from six months to three and a half years. Of the twenty-nine surviving patients five were not traced, leaving twenty-four cases to be assessed. The cases were divided into four groups according to their condition at this examination. (1) Classed "excellent": the patient can eat anything without symptoms. (2) Classed "good": the patient remains free from symptoms while keeping to some dietary restrictions. (3) Classed "fair": symptoms troublesome even on dietary restrictions, but have not obliged the patient to lie up or to stop work. (4) Classed "poor": where the symptoms have required further treatment or have prevented the patient from working. The results according to this classification are shown in Table I.

TABLE I

	No. of Cases	Percentage of Cases Traced
Excellent	2	8
Good	6	25
Fair	6	25
Poor	10	42

Of the ten cases classed as poor, four have required surgical treatment, from which two patients died, while two others have since died from gross haemorrhage. Two more have been readmitted to hospital; one of these was found to have some pyloric stenosis, and would have received surgical treatment had he not been considered too poor a risk on account of his age and general health. Thus of the forty-one patients admitted for treatment of a perforated ulcer sixteen (39 per cent.) are known to have died as a direct result of the ulcer, while six others (15 per cent.) are in a state of chronic invalidism, and only eight cases (19.5 per cent.) could be grouped together as good or excellent results.

Comparison with Medical Treatment

These results may be compared with those obtained from treating a group of cases of peptic ulcer medically. The diagnosis in this group was made clinically and was confirmed from radiographs, a definite crater being the criterion.

The mode of treatment was the usual dietary restriction and alkaline powders, with rest in bed for a minimum of three weeks. This treatment was carried out thoroughly for approximately three weeks in hospital, but at the end of that time in some cases the later treatment was not so strict as is now the rule. It was considered that this lack of strictness was the principal reason for the somewhat unsatisfactory results of medical treatment, and consequently a prolonged and thorough regimen as advo-