Treatment should be instituted at the earliest possible moment, particularly in view of the noteworthy absence of complications in cases so treated.

In face of failure to respond within a week, or of early relapse, persistence with M & B 693, even in repeated courses, has proved ineffective. In the interests of the patient, in such circumstances, resort should be made to some other form of therapy.

In our experience M & B 693 has proved the most effective therapeutic agent yet introduced in the treatment of gonorrhoea.

We wish to thank Dr. John Smith, director of the City Hospital Laboratory, Aberdeen, for his co-operation in this investigation. We desire also to express our thanks to Pharmaceutical Specialities (May & Baker) Ltd. for generous supplies of M & B 693 over the trial period of this study.

REFERENCES

- Batchelor, R. C. L., Lees, R., Murrell, M., and Braine, G. I. H. (1938). *British Medical Journal*, 2, 1142.
Bowie, F. J. T. (1938). *Ibid.*, 2, 283.
Lloyd, V. E., Erskine, D., and Johnson, A. G. (1938a). *Lancet*, 1, 1305.
— (1938b). *Ibid.*, 2, 1160.
McGregor-Robertson, J. G. (1938). *Ibid.*, 2, 1463.
Prebble, E. E. (1938). *Ibid.*, 2, 1163.
Whitby, L. E. H. (1938a). *Ibid.*, 1, 1210.
— (1938b). *Ibid.*, 2, 1095.

SULPHANILAMIDE IN THE TREATMENT OF MEASLES*

BY

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There is now a considerable literature regarding the value of sulphanilamide in the prevention and treatment of certain streptococcal infections. The investigation of its value in the treatment of measles, in which many of the complications are of streptococcal origin, is therefore important, and such an investigation was carried out during the 1937-8 epidemic in Glasgow. A ward in Ruchill Hospital was allocated for the purpose, and this report is based on the cases admitted to that ward between December, 1937, and March, 1938. There was no selection of patients, the ward taking its normal part in the reception of such cases of measles as were admitted to hospital. The material may therefore be regarded as representative of the disease in this district during the period reviewed. There is, of course, some selection of cases outside of hospital, so that a high proportion of complicated cases is admitted. The patients were under my own control throughout.

Plan of Investigation

The cases were allocated, in order of admission, alternately, to two groups. The first, or control group, received the usual nursing and expectant medical treatment; the second group received in addition sulphanilamide (para-aminobenzenesulphonamide). The dosage of the drug was varied with the age of the patient: under 5 years, 0.25 gramme was administered at four-hourly intervals for a

period of ten days, followed by 0.25 gramme thrice daily until dismissal; those over 5 years received 0.5 gramme at the same intervals and for a like period. (This dosage was similar to that which had been used with benefit in cases of erysipelas. While no serious ill effects were noted from the use of the drug, five cases showed moderate cyanosis and one case drug fever.) Apart from this the two groups received strictly comparable treatment. All cases were given on admission 4,000 units of diphtheria antitoxin as a prophylactic procedure. The control group numbered sixty-two, and those treated with sulphanilamide sixty-three, a total of 125 cases. The additional case in the treated group is explained by the removal from the control group of a case in which the diagnosis of measles was not confirmed.

Method of Assessment

Each case was examined on admission and a note made of the presence of any complication. It was decided that information regarding the value of the drug would be best obtained by comparing the two groups with respect to the following criteria: (i) the duration, in days, of primary pyrexia; (ii) the duration, in days, till clinical cure of complications noted on admission; (iii) the incidence and nature of complications arising in hospital; (iv) the duration, in days, till clinical cure of complications arising in hospital; (v) the duration, in days, of residence in hospital. All cases were therefore reviewed and examined daily and notes were made of their progress, with special reference to the above points. For the purpose of the experiment the day on which the rash appeared was regarded as the first day of the disease.

Before recording the results it is necessary to compare the two groups with respect to factors which might influence them. The most important of these are: (1) the age and sex distribution, (2) the duration of the disease before admission to hospital, and (3) the incidence of complications noted on admission. Tables I, II, and III show that the two groups were fairly evenly balanced in these respects, except that the cases receiving sulphanilamide treatment showed a slightly higher incidence of complications on admission.

Measles

TABLE I.—Age and Sex Distribution

Age Group (Years)	Control Group		Sulphanilamide Group	
	Males	Females	Males	Females
0-1	4	5	8	7
1-2	13	9	9	8
2-3	7	4	8	2
3-4	2	3	5	4
4-5	3	4	2	1
Over 5	1	7	3	6
Totals	30	32	35	28

TABLE II.—Duration of Illness (in Days) before Admission

Days:	0	1	2	3	4	5	6	7	8-14	Over 14
Control Group	3	12	7	9	3	8	4	4	9	3
Sulphanilamide Group	7	11	12	5	6	4	4	3	9	2

* A report to the Therapeutic Trials Committee of the Medical Research Council.

TABLE III.—Complications Present on Admission

	Control Group	Sulphanilamide Group
Conjunctivitis	29	29
Blepharitis	3	3
Otitis media	3	3
Rhinitis	19	31
Tonsillitis	1	2
Stomatitis	0	4
Laryngitis	2	3
Bronchitis	43	42
Bronchopneumonia	13	16
Empyema (pneumococcus Group IV) ..	0	1
Resolving pneumonia	1	0
Gastro-enteritis	13	12
Cervical adenitis	0	3
Burn of skin	1	1
Impetigo	1	2
Totals	129	152

Results of Treatment

TABLE IV.—Duration (in Days) of Primary Pyrexia

Days :	0	1	2	3	4	5	6	7	8-14	Over 14	Mean Duration
Control Group ..	9	11	11	11	2	4	4	1	6	3	3.92
Sulphanilamide Group	8	14	13	7	7	4	3	1	5	1	3.43

Table IV indicates that sulphanilamide has little effect in shortening the febrile period after admission to hospital. There is a slight reduction in the mean duration in the sulphanilamide-treated cases.

DURATION OF COMPLICATIONS NOTED ON ADMISSION

Table V shows the maximum, minimum, and average duration, in days, of some of the principal complications.

TABLE V

	Control Group Duration in Days			Sulphanilamide Group Duration in Days		
	Maximum	Minimum	Average	Maximum	Minimum	Average
Conjunctivitis ..	11	1	3.5	8	1	3.7
Otitis media ..	82	22	42.0	25	6	14.0
Rhinitis ..	10	1	4.1	12	1	6.0
Bronchitis ..	30	2	6.8	11	2	6.0
Bronchopneumonia	24	3	13.2	16	3	8.3
Gastro-enteritis ..	11	1	5.0	20	3	6.4

These figures do not suggest that sulphanilamide is of great value in hastening the cure of the major complications of measles. In the case of otitis media, the numbers (three in each group) are too small to admit of comparison. The duration of bronchopneumonia, however, is materially less in those cases which received sulphanilamide treatment. The figures have been analysed statistically, and the difference is regarded as significant.

COMPLICATIONS ARISING IN HOSPITAL

In the control group thirty cases developed a total of forty-seven complications, while in the sulphanilamide group twenty-two cases developed twenty-three complications (Table VI). It must be remembered that the cases

receiving sulphanilamide had a higher proportion of complications on admission, and might therefore be expected to develop fewer complications in hospital. But in the control group there were fifteen cases of those complications usually associated with streptococcal infection (tonsillitis and adenitis, and otitis media), while in the sulphanilamide-treated group only three such cases were noted. A χ^2 test has been applied to these figures, and the difference is regarded as significant ($P = 0.01$).

TABLE VI

	Control Group	Sulphanilamide Group
Otitis media	7	3
Otitis externa	—	1
Rhinitis	3	1
Tonsillitis and adenitis	8	—
Laryngitis	—	1
Bronchitis	3	1
Bronchopneumonia	3	3
Sterile pleural effusion	1	—
Empyema (pneumococcus Group IV) ..	—	1
Gastro-enteritis	12	5
Acute dermatitis	2	2
Subcutaneous abscesses (<i>Staphylococcus aureus</i>) ..	2	—
Paronychia	2	1
Hordeolum	4	3
Furuncle	—	1

With regard to the duration of these complications, however, no material difference was noted between the two groups, except in the case of otitis media, the averages here being: control group, 13 days; sulphanilamide group, 6.3 days.

DURATION OF STAY IN HOSPITAL

Table VII shows the residence in hospital of the two groups. The average in the control group was 26.5 days; in the sulphanilamide group, 25.6 days. No beneficial effect from the use of sulphanilamide was noted.

TABLE VII

Days :	Under 14	15-21	22-28	29-35	36-42	Over 42
Control Group	3(a)	27	16	4	4	8
Sulphanilamide Group	2(b)	35	17(c)	4	2	3

(a) One death. (b) Two deaths. (c) One death.

Four deaths occurred in the series (3.2 per cent.)—one in the control group and three in the sulphanilamide group.

Discussion

The series is a small one, and conclusions must be drawn with caution. It is felt, however, that the following factors are of importance in evaluating the results.

(a) All cases were under the clinical care of one person. Individual variations in assessment or diagnosis are thus overcome.

(b) All cases were treated in the same open-type ward under the supervision of the same sister and nursing staff. Differences in nursing technique therefore do not arise. Again, the practice in some hospitals of segregating severely complicated cases into certain wards may make combined figures difficult to assess. The work of Okell and Elliott (1936) and Allison and Brown (1937) with regard to the epidemiology of strepto-

coccal infections in open wards indicates that the accumulation of figures from different wards might give rise to fallacies—for example, due to differences of bed-spacing, incidence of infective cases, etc.—for which it would be difficult to make allowance.

(c) Finally, the two groups were evenly balanced in respect of such factors as age, sex, and duration of illness before admission. The incidence of complications noted on admission was greater in those cases receiving sulphanilamide.

The figures suggest that sulphanilamide is of some value in shortening the duration of bronchopneumonia, but that it has little effect upon the course of the other main complications of measles, with the possible exception of otitis media (see below).

Certain complications—namely, those usually associated with streptococcal infection—were of less frequent occurrence during the period in hospital in the cases receiving sulphanilamide. With regard to otitis media, it may be noted that there was in the control group a total of ten cases with an average duration of 21.7 days; while in the cases receiving sulphanilamide there was a total of six cases with an average duration of 10.1 days. These differences suggest a therapeutic benefit, and indicate that sulphanilamide has a place in the treatment of measles cases in open-type hospital wards. The complications prevented are largely those which might arise from ward "cross-infection."

Summary

A series of 125 cases of measles admitted to hospital between December, 1937, and March, 1938, was investigated to determine the value of sulphanilamide in treatment.

The cases were divided into two groups without selection, one group being treated with sulphanilamide, the other acting as controls.

Comparison is made between the two groups with respect to complications before and after admission, and length of stay in hospital.

The conclusions to be drawn from the survey are given.

I have to thank Dr. W. M. Elliott, physician-superintendent, Ruchill Fever Hospital, for permission to carry out the investigation. I am indebted to Dr. P. L. McKinlay, Department of Health for Scotland, who was kind enough to read the paper and carry out the statistical analyses.

The preparation of sulphanilamide used in these tests was "sulphonamide-P," of which supplies were generously placed at my disposal by Messrs. Burroughs Wellcome and Co. through the Therapeutic Trials Committee of the Medical Research Council.

REFERENCES

- Allison, V. D., and Brown, W. A. (1937). *J. Hyg., Camb.*, **37**, 153.
Okell, C. C., and Elliott, S. D. (1936). *Lancet*, **2**, 836.

The annual report for 1938 of the British Red Cross Society Clinic for Rheumatism states that the financial position of this institution has not improved and that the year's working shows a considerable deficit. There were 88,671 attendances with 135,760 treatments in the general department; 7,881 attendances and 10,698 treatments in the private patients' department. It is gratifying to note the attendance of a greater proportion of patients suffering from the earlier manifestations of rheumatism, although the number of advanced cases, for whom treatments must necessarily be palliative and prolonged, is still all too large. Close collaboration is maintained with the various specialist departments. The pathologist carried out 1,756 examinations; 1,695 patients were radiographed; seventy-eight patients, several of whom were found to require operative treatment, were referred to the gynaecologist and sixty-six to the dental department. Investigations are proceeding on the relation between pathological dental conditions and rheumatism.

PARA-BENZYLAMINO BENZENESULPHONAMIDE IN THE PREVENTION OF MEASLES COMPLICATIONS

BY

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Although the causal virus of measles may rarely be responsible for death in the very early stage of the disease, much the greater part of the mortality is due to complications, the most fatal being bronchopneumonia (Parsons and Barling, 1933; Stimson, 1936; Ellison, 1931). Besides having a high mortality the complications of measles may seriously curtail health and capacity in later life by leaving grave sequelae such as lung fibrosis and chronic middle-ear disease. The bacteriology of the complications of measles has received much study and, while it is recognized that a general inflammation of mucous membranes is associated with the viral phase of the disease, it is accepted that complications are due to the invasion of this suitably prepared soil by a secondary organism, of which much the most common is the haemolytic streptococcus (Okell and Elliott, 1936; Williams, 1935; Layton, 1937; Keevil and Camps, 1937; Allison and Gunn, 1932; Banks, 1938). Occurring with much less frequency are the pneumococcus and *Haemophilus influenzae*. In addition the convalescent measles patient is susceptible in varying degree to secondary diseases such as diphtheria, scarlet fever, Sonne dysentery, and other enteric infections of childhood. Attempts to control the invading power of the haemolytic streptococcus in measles by anti-streptococcal serum having been quite unsuccessful, an adequately controlled experiment with chemotherapy was clearly indicated. A suitable opportunity arose during the winter of 1937-8, when measles assumed epidemic proportions in London.

The prontosil derivative which I decided to use was para-benzylaminobenzenesulphonamide (proseptasine). Although my experience with this preparation in the treatment of scarlet fever had been disappointing (Hogarth, 1937), I was now quite convinced, from results obtained in erysipelas and other streptococcal diseases, that this derivative is active against most strains of haemolytic streptococci. Another important point in favour of proseptasine, as judged from my previous experience, was its comparative lack of toxicity—a matter of some moment when dealing with young children, many of whom might be extremely ill.

The Present Investigation

It has been the practice for some time at this hospital to administer a combined prophylactic injection of scarlet fever and diphtheria antitoxin to all measles cases on admission. This procedure has amply justified itself in a sharp reduction in the incidence of scarlet fever in measles wards and in the virtual disappearance of the serious and occasionally lethal attacks of diphtheria to which the measles patient is particularly prone. All the cases in the present investigation received passive immunization in this way.

Classification of Severity.—The 329 cases of measles which formed the subject of this investigation were graded according to severity on admission. All received the usual routine treatment such as fresh air and simple drugs when indicated, in addition to the prophylactic dose of antitoxin described above. Approximately half of these cases received para-benzylaminobenzenesulphonamide in