TREATMENT OF SCABIES BY T.E.T.M.S.

BY

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Gordon and Seaton (1942) drew attention to a new preparation [(tetraethylthiuram monosulphide)—T.E.T.M.S.] which they suggested was worthy of clinical trial, and their experiments on rats infested with itch-mites of the genus *Notoedres* gave reasonable grounds for assuming that this sarcopticide may give even better results in the treatment of human scabies than either dimethylthianthrene or benzyl benzoate preparations. Percival (1942) has demonstrated that a 5% solution was curative in 50 consecutive hospitalized or ambulatory cases, but that in 0.25% strength the results were much less satisfactory.

The preparation used in the following series of cases was one kindly supplied by Messrs. Imperial Chemical Industries Ltd., and had the following formula: T.E.T.M.S., 25%; polyglycerol ricinoleate, 10%; industrial methylated spirit, 65%. The solution was of a dark yellowish-brown colour and at temperatures below that of the body there was a tendency for crystals of a distinctive yellow colour to form, which, however, were easily redissolved with moderate increase in temperature. The makers recommend that one part of the preparation be added to four parts of water immediately before use and applied twice daily for three days. Force of circumstances, however, compelled deviation from this advice in my original series of cases, so that the 25% emulsion was used in concentrated form, but the results of treatment lead me to assume that a useful purpose was served. About one ounce of the emulsion was sufficient to cover the body surface of an average-sized adult, and it was easy of application, not unpleasant to handle, and without objectionable odour.

Since, at this time, no records were available as to the propensity of the preparation to produce a dermatitis it was

several days' observation—nor was there anything detrimental except that the solution stained the clothing. The stain, however, was easily removed.

After a preliminary test on 4 scabietic patients it was decided to proceed to full-scale treatment of a series of cases with the 25% solution, and in order to give the preparation a stringent trial, patients with severe scabies or severe complicated scabies were chosen. In each case the entire body, with the exception of head and upper neck, was subjected to a uniform method of washing with soft soap and warm water, while a loofah was used for friction in preference to a scrubbing-brush. (The fact that scrubbing-brushes are used in the treatment of scabies seems, in my experience, to deter many of the public from accepting treatment, and I agree with Morris (1908) that "vigour must not be pushed to the length of violence" and am satisfied that such drastic measures are unnecessary in the majority of cases.) The patient was then quickly dried and the monosulphide solution was rubbed thoroughly over the body, particular attention being reserved for the sites most severely affected. In addition, raw or grossly septic areas were dressed with white lint wrung out of the solution. The treatments were for convenience carried out at three- and four-daily intervals by a specially instructed staff of volunteers derived from the personnel attached to a first-aid post where decontamination facilities were available. The patients were requested to bring a clean change of underclothing for use after the final treatment and were advised to sterilize their "cast-offs" and bed-linen by suitable methods. (My experience, however, leads me to the conclusion, like Hebra (1868), Dixon (1941), Mellanby (1941, 1942), and Monro (1942), and unlike Lydon (1941) and MacCormac and Small (1917), that clothing is of decidedly minor importance in the transmission of scabies as opposed to actual and prolonged bodily contact.)

In all cases so treated the results were most heartening, and in some, indeed, remarkable. On presenting themselves for the second treatment several patients or parents made such spontaneous remarks as: "The treatment is marvellous," or "She had the first good night's sleep in weeks." Itching was relieved at once, and the general well-being of the patients improved almost immediately.

TABLE I.—Details of 14 Patients treated with 25% T.E.T.M.S.

Case	Sex	Age (years)	Severity of Scabies	Severity of Septic Concomitants	Sites of Maximum Severity	No. of Applications of 25% T.E.T.M.S.	Date of Last Application	Date of Follow-up	No. of Occupants in House	No. of Occupants Affected	No. of Cases Concealed in House	Remarks
1	F	17	++	Nil	Back and buttocks	3	July 6	Aug. 27	6	4	3	Recurrence; probable familial reinfection
2	F	13	+	++	Buttocks	3	" 8	" 24	10	6	—	Cure
3	F	23	+++	+	Abdomen	3	" 8	" 24	3	2	—	"
4	F	3	++	+	Abdomen and buttocks	3	" 8	" 24	7	6	—	"
5	M	5	++	++	Generalized (usual sites)	3	" 8	" 24	7	6	—	"
6	F	12	++	+	Hands	3	" 13	" 24	2	1	—	"
7	M	5/12	++	++++	Right arm, back, palms, legs, and feet	4	" 28	" 24	4	4	—	"
8	F	16	++	+++	Legs and feet, elbows	4	" 28	" 24	4	4	—	"
9	F	16	+++	++++	Arms and hands, legs and feet	5	" 28	" 24	4	4	3	" (Later mid-October recurrence)
10	F	4	++	+++	Lumbar region and buttocks	3	" 27	" 18	6	4	—	Recurrence; probable reinfection from neighbours
11	M	8	++	+	Generalized (usual sites)	3	" 27	" 18	6	4	—	"
12	F	6	+++	+++	Arms and hands, legs and feet	4	" 28	" 24	3	3	—	Cure
13	M	4	++	+++	Feet	3	" 17	" 24	3	3	—	"
14	F	5	++	++	Generalized (usual sites)	3	Aug. 11	" 31	3	3	2	" (Early October recurrence)

+ Slight. ++ Moderately severe. +++ Severe. ++++ Very severe.

considered an advisable preliminary to test the solution, in full strength (25%), on 15 volunteers and as follows:

The flexor surface of a forearm in each volunteer was vigorously rubbed with warm water and soft soap for three minutes, dried with a towel, and the solution rubbed into the prepared area for a further three minutes and then allowed to dry under atmospheric conditions. This procedure was repeated on three consecutive days, and the volunteers were asked to record any immediate or remote observations. In 2 cases out of 15 a moderate degree of frictional erythema was noted (one a female particularly liable to severe dermatitis on the application of iodine); but this gradually disappeared, and in no case was there the remotest sign of a localized dermatitis during

In the limited series of 14 cases detailed in Table I it will be noticed that younger patients predominate, yet, in spite of several applications, no sign of dermatitis developed on these supposedly tender skins. Moreover, it was apparent that some of the secondary pyodermitic concomitants of scabies appeared to be very favourably influenced by the monosulphide dressings. It was also noted that there was a tendency for the preparation to sting on contact with some of the more exposed lesions.

A follow-up of patients in from three to six and a half weeks after treatment showed three cases of apparent reinfection, since in Case 1 there was deliberate concealment of infestation in

TABLE II.—Details of 93 Patients treated with 5% T.E.T.M.S.

	Sex	Age (years)	No. of Applications of 5% T.E.T.M.S.	Date of Last Application of Mono-sulphide	Date of First Follow-up	Date of Second Follow-up	Re-infection	No. of Occupants in House	No. Affected in House	B.P. = Affected Bed-partner S = Sleeps by Self	Cases Concealed in House	No. of Rooms in House	Bath-room in House	Remarks
1	F	4	1	1/10/42	27/11/42	5/1/43	—	7	3	B.P.	—	5	+	Cure
2	F	4	1	"	"	"	—	7	3	B.P.	—	5	+	Cure
3	F	10	3	5/10/42	14/12/42	1/1/43	—	4	1	S.	—	3	+	Cure
4	F	7	2	"	27/11/42	5/1/43	—	8	7	B.P.	—	4	+	Cure
5	F	4	2	"	"	"	—	8	7	B.P.	—	4	+	Cure
6	M	10	3	"	14/12/42	4/1/43	—	3	1	S.	—	4	+	Cure
7	F	6	3	"	27/11/42	5/1/43	—	7	3	B.P.	—	5	+	Cure
8	F	7	3	"	"	"	—	5	3	B.P.	—	3	—	Cure
9	M	6	3	"	7/12/43	24/1/43	—	3	1	S.	—	3	+	Cure
10	F	5	1	2/10/42	14/12/42	26/1/43	—	3	3	B.P.	—	2	—	Cure. Previous reinfection, Table I, No. 14—Parents concealed
11	M	17	2	9/10/42	27/11/42	29/1/43	—	10	3	B.P.	—	5	+	Cure
12	M	15	4	"	"	"	—	10	3	B.P.	—	5	+	Cure
13	M	12	4	10/10/42	"	"	—	10	3	B.P.	—	5	+	Cure. Slight dermatitis, chest
14	M	14	1	14/10/42	7/12/42	5/1/43	—	6	6	B.P.	—	4	+	Cure. Father concealed
15	M	9	3	19/10/42	"	"	—	6	6	B.P.	1	4	+	Cure. Slight dermatitis, abdomen, chest
16	M	13	4	"	"	"	—	6	6	B.P.	1	4	+	Cure. Father concealed
17	F	35	2	"	"	"	+	6	6	B.P.	1	4	+	Cure. Husband "
18	M	11	5	22/10/42	"	"	+	6	6	B.P.	1	4	+	Cure. Father "
19	M	51	1	17/10/42	27/11/42	"	—	4	4	B.P.	—	4	+	Cure. Previous concealed case
20	M	14	8	18/12/42	"	"	—	4	4	B.P.	—	4	+	Cure
21	F	16	4	20/10/42	"	"	—	4	4	B.P.	—	4	+	Cure. Reinfection (Table I, No. 9)
22	F	44	4	22/10/42	"	"	—	4	4	B.P.	—	4	+	Cure. Previous concealed case
23	F	6	1	20/10/42	"	"	—	3	2	B.P.	—	2	—	Cure
24	M	4	1	"	"	"	—	3	2	B.P.	—	2	—	Cure
25	F	17	4	19/10/42	2/12/42	6/1/43	—	6	4	B.P.	—	4	+	Cure. Slight dermatitis, chest and abdomen
26	F	38	3	"	14/12/42	"	—	6	4	B.P.	—	4	+	Cure
27	M	1	4	21/10/42	"	"	—	6	4	B.P.	—	4	+	Cure
28	M	3	5	"	"	"	—	6	4	B.P.	—	4	+	Cure
29	M	12	4	19/10/42	29/12/42	22/1/43	—	4	2	B.P.	—	4	—	Cure
30	F	9	3	21/10/42	"	"	—	4	2	B.P.	—	4	—	Cure
31	F	28	2	20/10/42	14/12/42	26/1/43	—	4	4	B.P.	—	2	—	Cure
32	F	2	2	"	"	"	—	4	4	B.P.	—	2	—	Cure
33	F	3	5	21/10/42	27/11/42	5/1/43	—	7	7	B.P.	—	5	—	Cure. Slight dermatitis, chest
34	F	7	6	"	"	"	—	7	7	B.P.	—	5	—	Cure. Slight dermatitis, chest and shoulders
35	F	13	6	"	"	"	—	7	7	B.P.	—	5	—	Cure
36	F	27	4	30/10/42	7/12/42	2/1/43	—	5	3	B.P.	—	4	+	Cure. Slight dermatitis, buttocks
37	F	16	4	26/10/42	"	"	—	5	3	B.P.	—	4	+	Cure
38	F	50	3	"	"	"	—	5	3	B.P.	—	4	+	Cure
39	M	8	1	"	14/12/42	24/1/43	—	5	2	B.P.	—	3	—	Cure
40	F	12	5	"	2/1/43	22/1/43	—	8	6	B.P.	—	6	—	Cure
41	M	4	2	"	7/12/42	24/1/43	—	7	6	B.P.	1	4	+	Cure
42	F	2	2	"	"	"	+	7	6	B.P.	1	4	+	Cure. Mother previously denied scabies—later admitted.
43	F	8	3	29/10/42	"	"	—	7	6	B.P.	1	4	+	Cure. Elder sister—inefficient home treatment—still affected
44	F	7	3	"	"	"	+	7	6	B.P.	1	4	+	Cure
45	F	45	2	"	14/12/42	6/1/43	—	6	5	B.P.	—	5	+	Cure
46	F	9	3	30/10/42	"	"	—	6	5	B.P.	—	5	+	Cure
47	F	8	3	"	"	"	—	6	5	B.P.	—	5	+	Cure
48	M	1	2	29/10/42	"	"	—	6	5	B.P.	—	5	+	Cure
49	M	10	4	30/10/42	"	5/1/43	—	11	7	B.P.	—	6	+	Cure
50	M	7	4	"	"	"	—	11	7	B.P.	—	6	+	Cure
51	M	11	4	"	"	"	—	11	7	B.P.	—	6	+	Cure
52	F	13	5	"	"	"	—	11	7	B.P.	—	6	+	Cure
53	F	5	4	"	"	"	—	11	7	B.P.	—	6	+	Cure
54	M	9	5	"	2/1/43	21/1/43	—	6	2	B.P.	—	3	—	Cure. Slight dermatitis, chest and shoulders
55	F	12	4	"	"	"	—	6	2	B.P.	—	3	—	Cure
56	F	5	3	"	"	"	—	5	2	B.P.	—	4	—	Cure
57	F	9	5	"	"	"	—	5	2	B.P.	—	4	—	Cure
58	F	10	3	"	8/12/42	6/1/43	—	5	3	B.P.	—	3	—	Cure
59	F	9	3	"	"	"	—	5	3	B.P.	—	3	—	Cure
60	M	4	3	"	"	"	—	5	3	B.P.	—	3	—	Cure
61	F	10	5	"	30/11/42	4/1/43	—	6	4	B.P.	—	3	—	Cure
62	M	14	1	4/11/42	"	"	—	6	4	B.P.	—	3	—	Cure
63	F	9/12	6	6/11/42	"	"	—	6	4	B.P.	—	3	—	Cure
64	F	36	7	"	"	"	—	6	4	B.P.	—	3	—	Cure
65	F	41	4	4/11/42	14/12/42	21/1/43	—	5	4	B.P.	—	3	—	Cure
66	M	9	7	9/11/42	"	"	—	5	4	B.P.	—	3	—	Cure
67	F	11	6	31/10/42	"	5/1/43	—	4	2	S.	—	4	—	Cure
68	M	6	2	30/10/42	"	24/1/43	—	5	4	B.P.	—	3	—	Cure
69	F	19	2	12/11/42	"	4/1/43	—	3	3	B.P.	—	3	—	Cure
70	F	1	2	"	"	"	—	3	3	B.P.	—	3	—	Cure
71	M	14	2	11/11/42	4/1/43	24/1/43	—	8	5	B.P.	—	4	+	Cure
72	M	13	2	13/11/42	14/12/42	"	—	8	8	B.P.	—	3	+	Cure
73	F	19	4	27/11/42	"	"	—	5	2	B.P.	—	5	—	Cure
74	M	13	4	"	"	"	—	6	3	B.P.	—	4	+	Cure
75	F	11	3	30/11/42	6/1/43	"	+	3	3	B.P.	2	5	—	Cure. Foster parents at first denied and later admitted original infection
76	F	12	2	29/11/42	29/12/42	4/1/43	—	4	4	S.	—	4	+	Cure
77	F	25	4	7/12/42	"	24/1/43	—	4	3	B.P.	1	4	+	Cure
78	F	13	3	"	"	"	+	4	3	B.P.	1	4	+	Cure. Father admitted an infection previously denied
79	F	8	4	30/12/42	22/1/43	4/2/43	—	4	4	B.P.	—	4	—	Cure
80	F	45	2	7/1/43	"	"	—	4	4	B.P.	—	4	—	Cure
81	M	43	3	6/1/43	"	"	—	4	4	B.P.	—	4	—	Cure
82	F	19	4	8/1/43	"	"	—	4	4	B.P.	—	4	—	Cure
83	M	12	3	18/12/42	4/1/43	24/1/43	—	9	5	B.P.	—	3	—	Cure
84	M	8	2	11/12/42	"	"	—	8	4	B.P.	—	4	+	Cure
85	M	14	3	"	"	"	—	8	4	B.P.	—	4	+	Cure
86	F	5	3	14/12/42	"	"	—	8	4	B.P.	—	4	+	Cure
87	F	12	3	"	"	"	—	8	4	B.P.	—	4	+	Cure
88	M	12	3	21/12/42	7/1/43	24/1/43	—	8	8	B.P.	—	3	+	Cure
89	M	11	3	"	"	"	—	8	8	B.P.	—	3	+	Cure
90	F	6	3	"	"	"	—	8	8	B.P.	—	3	+	Cure
91	F	15	4	2/1/43	24/1/43	3/2/43	—	8	8	B.P.	—	3	+	Cure
92	F	37	4	"	"	"	—	8	8	B.P.	—	3	+	Cure
93	F	36	3	"	"	"	—	2	1	B.P.	—	3	—	Cure

other adult members of the family, while Cases 10 and 11 were probably reinfected from next-door neighbours, whose infestation had not then come to notice. It will be noted that in two other cases (Nos. 9 and 14) in which there was concealment recurrences occurred at a much later date.

From Aug., 1942, onwards a second series of scabietic cases were treated with a 5% aqueous preparation of the 25% emulsion. On the addition of water an interesting bright-yellow suspension was formed, and it was found that not only was it essential to prepare the medicament immediately before use but that warm water as a diluent was superior to cold water, since the sediment which invariably formed upon the bottom of the vessel was less bulky. Such a 5% preparation, allowed to stand overnight, produced a substantial gritty deposit and rendered the solution unsuitable for application to the skin. In the series of 93 cases treatment was in some instances performed daily and in others every other day, whilst a similar method of routine was practised as before.

So far as could be ascertained, none of the cases treated had received prior medication; neither were directions given by me regarding the desirability of sterilizing or fumigating clothing and bedding during or after treatment. Table II shows the relevant details.

Analysis of Table II

Of 93 cases treated and subsequently visited on the first of two "follow-ups" (74 not less than one month and 19 in from two to four weeks after the last application of T.E.T.M.S.) none showed any sign of recurrent scabies. A second "follow-up" not less than one month after the last application showed 6 cases suffering from early scabies (Nos. 17, 18, 42, 44, 75, and 78), and of these only one case (No. 78, who showed a few minute papules and vesicles on one hand) had received her first "follow-up" under one month—i.e., 22 days. Since Munro (1919) has indicated that the life-cycle of the parasite, egg-to-egg stage, varies between 9 and 15 days (and there is much extraneous support for his findings), it is reasonable to conclude that none of the 6 recalcitrant cases could have been recurrences in the true sense, but rather reinfections. It can therefore be stated with some degree of certainty that the entire series of 93 cases were cured, but that 6 were reinfected from a concealed familial source. Further points which appear from the analysis are:

(a) An approximate average of 3 applications were needed, although in some cases 6, 7, and 8 applications were deemed necessary. From 6 of the later cases, acting as a small test group, active female itch-mites were extracted before treatment with 5% T.E.T.M.S. Twenty-four hours later further samples were extracted, and in 4 cases the parasites were found to be dead, while a further application had killed additional specimens taken from the remaining 2 cases twenty-four hours later still.

(b) From 227 occupants in the houses concerned 154 (67.8%) cases of scabies were discovered.

(c) Of 93 patients treated 88 slept with infested bed-partners, while the remaining 5 were of school age and associates of scabietics or living in the same house with them.

(d) Out of the 93 patients 55 lived in houses having a slipper bath with an adequate hot and cold water supply.

(e) Of the 93 cases 7 produced a mild erythematous dermatitis, which was found to be of little moment and quickly subsided on discontinuing the treatment. The rash was usually most obvious on the upper chest and shoulders. It is of interest to note that in the first series treated with the 25% emulsion no sign of dermatitis was apparent, and this would seem to be due to the oily and more penetrating character of the soluble T.E.T.M.S., as opposed to the watery 5% suspension.

From these results, and in my experience generally, routine fumigation and sterilization of clothing and bedding have limited value, besides being expensive. Reasonable cleanliness of person, clothing, and household is calculated to give equally good results.

Comment

It is stressed that the original cases were on the whole, and of their type, severe and responded extremely well to treatment. It is suggested that the application of the 25% emulsion, though seemingly wasteful, may be found both useful and time-saving, especially in severe and complicated cases for which hospitalization is considered necessary and when available beds are at a premium. Furthermore, it is admitted that in the

first series of cases treatment erred on the generous side, and experience may show that the number of applications of the 25% emulsion may be reduced without detrimental effects. Alternatively, it is suggested that a similar emulsion with a smaller percentage of combined T.E.T.M.S. may perhaps give comparatively good results.

In 5% aqueous solution the preparation was less spectacular, though of considerable potency, and the dermatitis recorded in 7 cases was of a mild order. My observations, bearing in mind the limitations of the series, stimulate a cautious yet hopeful opinion that T.E.T.M.S., used under adequate supervisory control, may prove a potent and convenient acaricide and be preferred to other sulphur compounds. In conclusion, I would stress that it has not been my intention to detract from the merits of benzyl benzoate, for which I have high regard.

Summary

T.E.T.M.S. in 25% emulsion has been found to be curative in 11 out of 14 cases of severe and complicated scabies, the remaining 3 cases being probable reinfections.

In 15 volunteers and 18 patients the emulsion failed to produce dermatitis or irritation beyond a preliminary smarting in some severe cases.

It would appear to have extremely beneficial results upon some of the secondary concomitants of scabies.

In 5% aqueous solution it has proved curative in 93 consecutive cases and produced only mild dermatitis in 7 patients.

It has proved to be a sarcotocid of potency against the human itch-mite and is worthy of extended trial.

Thanks are extended to Messrs. Imperial Chemical Industries Ltd. for generous supplies of tetraethylthiuram monosulphide and, in particular, to Dr. C. M. Scott, whose kind co-operation was much appreciated.

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ON THE VALUE OF VITAMIN B₁ IN PREVENTION OF TOXAEMIA OF PREGNANCY

BY

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This experiment was suggested by perusal of the last (1940) Annual Clinical Report of the Department of Obstetrics and Gynaecology of the University of Hong Kong, in which Gordon King reported 155 cases of avitaminosis B₁ (beriberi) complicating pregnancy and labour, 117 (75%) of which had a blood pressure of 140/90 or over, including 16 cases of eclampsia. Assuming that the usual incidence of eclampsia is 1 in 500, it is apparent that its incidence in beriberi is increased about 50 times. Other observations pointed in the same direction, though less definitely. Siddall (1938), impressed by the high incidence of pre-eclampsic toxæmia and eclampsia in Canton, where beriberi is endemic, believes that B₁ deficiency in pregnancy leads to a malignant hyperfunction of the pituitary, with disturbed carbohydrate metabolism, oedema, and raised blood pressure. Nixon, Wright, and Fieller (1942) investigated the vitamin B₁ content of the urine, and in certain cases also of the placenta, in 46 clinically normal and 60 abnormal pregnant women whose disabilities were as