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CONTROL OF SCABIES BY USE OF SOAP IMPREGNATED WITH **TETRA-ETHYLTHIURAM MONOSULPHIDE ("TETMOSOL")**

BY

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It is now generally recognized that scabies spreads from one individual to another by the transference of the mite causing the disease, and that this transference may be direct or indirect. Indirect transference is responsible for a minor proportion of infections, and may be efficiently controlled, when necessary, by disinfestation of fomites. In direct transference, which is responsible for the majority of infections, the more intimate the contact the greater the chances of spread; hence scabies is often spoken of as a venereal disease, though it would be more apt to call it a family disease, in which the highest proportion of infections are acquired between husband and wife, parent and child, and so on. Up to the present time the only method used to control the direct spread is by treatment of the infected individual, and, with the exception of Johnson's (1943) suggestion that persons likely to be in contact with cases of scabies should dip their hands in solutions of benzyl benzoate, we are not aware of any proposed method of prophylaxis which might be used by the individual to protect him against the disease.

The idea of controlling scabies by the use of soap impregnated with tetmosol originated in animal experiments with Notoëdres, the results of which have already been published (Davey, Gordon, and Unsworth, 1944). Since the publication of that paper we have extended our observations to include human cases caused by Sareoptes scabiei, and we here present the results of these investigations, together with some of our original observations.

In view of the high sarcopticidal activity of tetmosol in human and animal scabies (Gordon and Seaton, 1941; Percival, 1942; Jennings, 1942; Clayton, 1943) it appeared to us that, if the drug could be incorporated in soap and still retain its potency and non-irritative properties, it would then be available for prophylaxis and possibly for the treatment of mild infections without the necessity for medical supervision. In the Army, for instance, or in dealing with crowds of refugees, tetmosol-impregnated soap could be issued without the need for parades and disciplinary measures. Similarly, in an outbreak of scabies in factories, asylums, schools, and similar concentrations of people, it might be possible to control the infection by the provision of impregnated soap at the washbasins. Johnson (1943) has written: "It may be said . . . that if all the mites on the hands and wrists of all patients alone could be killed (e.g., by dipping in benzyl benzoate solution), then about 60% of all the parasites would be eliminated. This might have a progressive and great effect on the reduction of the disease." We doubt whether Johnson's suggested treat-

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ment would be carried out in the absence of supervision, but we believe that a tablet of tetmosol-impregnated soap of normal appearance would arouse no antipathy and would be used.

In order to ascertain whether such a soap could be employed to control scabies it was necessary to establish that tetmosol could be successfully combined with soap and remain stable This was accomplished by Imperial Chemical on storage. Industries, Ltd., in collaboration with Messrs. Unilever, Ltd., and the soap was found to remain chemically unaltered when tested at monthly intervals over a period of a year. There still remained the question whether the use of such a soap would result in dermatitis, and whether tetmosol would retain its sarcopticidal properties when used in this form.

Risk of Dermatitis from Tetmosol Soap

The risk of dermatitis from any drug will obviously be affected by the concentration of the drug, the idiosyncrasy of the individual, the period of time over which it is used, and the frequency of its application.

It is difficult to give a reliable average figure for the number of times the ordinary person washes during the course of the day, for the length of time he spends on the process, or for the degree of dilution of the soap applied to the skin. By studying the ablutions of a number of individuals, however, we found that they spend about 40 seconds in lathering either the face or the hands (in the case of a bath the whole body is lathered for about 60 seconds), and that if a drug is incorporated to the extent of 10% in soap its dilution when applied to the skin is in the region of 1.8%; further, we found that it is the common practice to wash off the soap with about six changes of water. On these observations our subsequent trials with the soap were based. The frequency of washing obviously varies according to the individual, but a rough idea of the extent to which soap is used in the Army was obtained by sending a questionary to 150 R.A.M.C. officers, whose replies suggested that almost 100% of the men wash the hands and face at least once a day and the body at least once a week, and that the majority probably do not use soap on the hands and face more than two or three times a day.

Evidence from the literature suggests that tetmosol, when applied to persons with dermal lesions due to scabies, only occasionally produces dermatitis (Percival, 1942; Clayton, 1943). Our own experiments with tetmosol soap confirm these findings: 242 patients suffering from proved scabies received three baths with 20% tetmosol soap during the course of six days; of these, four developed dermatitis; in three of these cases of dermatitis patch-tests showed that the reactions were not due to tetmosol; the remaining case was not tested. It follows, therefore, that only a low incidence of dermatitis is liable to occur after the use of tetmosol soap when applied for short periods to the skin, even when this has already been damaged by scabies. These results, however, did not directly

concern us in the present investigation, since the point to be established was whether or not tetmosol soap, when applied prophylactically for long periods to the normal skin, was apt to produce dermatitis. This must remain unanswered for the time being, since it can only be determined by a prolonged use of the soap by a large number of people. We have, however, certain evidence which is of some value. In our own experiments three volunteers in the laboratory have used soap containing 5% tetmosol twice daily on the face and hands, and once a week on the body, for two months without dermatitis resulting. Subsequently, one of the volunteers similarly used 10% tetmosol-impregnated soap for a further period of a year, and another used 20% tetmosol soap for a further period of six months, without ill effect in either case.

A further test over a shorter period was carried out by Major Kenneth Mellanby, R.A.M.C., who distributed two tablets of 10% tetmosol soap to each of 29 volunteers (conscientious objectors). All used the soap as long as it lasted, but the time varied with the care of the user; thus six men made it last only 14 to 18 days, but the remainder made it serve for as long as 63 days. The average for all users was 34 days. The following is quoted from Major Mellanby's report on "Skin Reaction":

"Six subjects observed no unusual sensations when they used the soap, but 23 of the 29 volunteers reported that some irritation of the skin occurred. In 12 cases this was very slight and transitory —generally just a slight stinging of tender areas after soaking in a hot bath; had these subjects not known that they were using a special soap they might not have noticed this symptom.

"Nine volunteers complained of more serious irritation, but this caused no erythema or other skin reaction. These volunteers continued to use the soap until it was finished, and mostly found that, if anything, the irritation was less severe towards the end of the exposure. There is nothing to suggest that there would have been any danger in these subjects continuing to use the soap for long periods; they agreed to continue for longer if necessary.

"Two subjects reacted more severely, and in the first instance they used the soap for only two and five days respectively. Brigadier R. M. B. MacKenna has examined both these patients, and reports that they are both individuals with unusually sensitive skins. One is genuinely sensitive (but only slightly) to tetmosol; in the other the impregnated soap acted apparently as a primary irritant. In both cases the skin recovered completely when the use of the soap was discontinued. It is obvious that these two volunteers would be unable to use tetmosol soap permanently; but, if the soap were issued to a large population, individuals of this type would discover that the soap disagreed with them before any damage had been done. It seems likely that the proportion of such individuals in Southern Europe and the Balkans (where the soap might be most useful) is considerably lower than in this country.

"The general conclusion seems to be that most people will not be harmed at all by the soap. A small minority will find it a skin irritant, but this fact will be easily detected before any harm is done. There is no evidence to suggest that anyone is highly sensitive to tetmosol soap."

Sarcopticidal Properties of Tetmosol Soap when Used Therapeutically

In Animal Infections due to Notoëdres

As already stated, observations on the washing habits of a number of individuals enabled an estimate to be made of the final dilution of the drug incorporated in soap when it reached the skin, and of the length of time during which the drug would be in contact with the skin. Infected rats were subjected to treatment similar to that which would be used by a person performing his ordinary ablutions. The infected area was washed for 40 seconds with a known dilution of soap lather. The soap was immediately washed off with six consecutive applications of clean swabs of cotton-wool dipped in clean warm water. Using this technique with soap containing 5% tetmosol (final dilution of the drug 0.9%) twice daily for periods of two to seven days, it was found that in only a few instances was the treatment followed by cure (8 animals treated, 1 cured)that is to say, by the complete destruction of all mites in the treated area; such treatment, however, invariably resulted in the destruction of a large number of mites. By increasing the concentration of tetmosol in the soap to 20% a greater proportion of mites were destroyed, although, as before, the majority of cases were not cured (6 animals treated, 1 cured). Further experiments were now carried out in which the rats

were treated in a manner corresponding to a person taking a weekly bath—i.e., the washing period was increased from 40 to 60 seconds, and instead of the operation being repeated twice daily it was performed once a week. Six rats were treated in this manner: in no instance did a complete cure result, and, although there was a considerable reduction in the mite population as compared with controls, this was not so marked as in the case of 20% or 5% tetmosol when used twice daily.

In Human Infections due to Sarcoptes scabiei

Having shown that tetmosol soap possessed curative properties in respect of animal infections due to *Notoëdres*, it remained to be shown whether it also possessed similar therapeutic effects in the case of human infections with *Sarcoptes scabiei*. Facilities for the investigation were obtained by arrangement with the War Office, soldiers suffering from scabies being sent to centres under our control. The total number of cases which received a full course of treatment was some 250, but owing to military exigencies only 110 were available for the entire subsequent observation period. In order to put the investigation on a scientific basis the following rules were rigidly adhered to and applied to all the cases recorded in this paper:

1. Every case recorded as positive was diagnosed by the finding of the live acarus.

2. All relapses were similarly diagnosed by the finding of the live acarus, any doubtful case being kept under observation until either a cure or a relapse had been definitely proved.

3. The bathing was supervised by a medical orderly, and the procedure was as follows: (i) The patient took a hot bath, using a tablet of 20% tetmosol soap. (ii) The patient stepped out of the bath and, assisted by an orderly, was thoroughly lathered all over (except for the face and neck), attention being given to such parts as the feet, which might otherwise have escaped the application of soap. (iii) The patient stepped into the bath, rinsing off the soap. (iv) Thorough lathering with tetmosol soap was then repeated out of the bath. (v) The soap was again rinsed off in the bath. (vi) The patient dried himself and dressed. (vii) Daily inspections were made, and any evidence of itching or skin reaction was recorded. In the case of treatment by six baths, these were given on successive days; in the case of treatment by three baths, some of the patient stepic their baths on the first, third, and fifth days.

4. After treatment was completed every case was kept under observation for a period of at least six weeks. So far as was possible, patients were recalled for observation at weekly intervals, and where such frequent attendance was not possible each case was examined by one of us at least twice during the six weeks, one of these examinations always occurring at the end of the observation period.

Results Obtained (a) After Six Baths.—The first six cases in which the acarus was found were given one tetmosol-soap bath on each of six consecutive days. All were observed for six weeks after the completion of treatment. All six cases were cured.

Results Obtained (b) After Three Baths.—A total of 110 cases were treated by means of three baths with 20% tetmosol soap and were subsequently observed at intervals over a period of six weeks. Of these 110 cases, 88 (80%) were cured. In practically every patient, including some of those who were not cured, treatment was attended by an immediate disappearance of irritation, the man often getting his first sound sleep for several nights.

Of the 110 cases treated by means of three baths with 20% tetmosol soap 22 (20%) relapsed. In the majority of relapses the irritation persisted after treatment, but in a small proportion it disappeared completely for periods varying up to three weeks, the renewal of the irritation being often associated with the finding of the acarus.

It must in fairness be stated that these figures, for reasons beyond our control, are biased in favour of relapse. In the first place, it is probable that a number of the cases recorded as failures were really reinfections, as there was ample opportunity for re-exposure, particularly in the case of men returning to infected families. In only four instances, however, was it possible to obtain clear evidence of re-exposure to infection; these four cases have been omitted. Secondly, cases which relapse are noted earlier than those which are cured, as the latter are recorded only at the end of six weeks and so are more likely to be lost to view than those which have relapsed. From the results recorded above it was clear that a high proportion of established cases of human scabies with wellmarked lesions were cured when thoroughly washed on three occasions with 20% tetmosol soap, and that tetmosol soap was much more effective in curing natural infections with *Sarcoptes* in man than with *Notoëdres* in rats.

The main object of our investigation, however, was to show whether tetmosol soap could be used as a prophylactic against the acquirement of the disease. The practical difficulties involved in a controlled experiment with human volunteers were found to be so considerable that this was not attempted. It was thought that, if it could be shown that the use of tetmosol soap protected rats against the acquirement of the disease when exposed to massive infection from their companions, this result, when considered in conjunction with the proved therapeutic value of the soap in human infections, would warrant its trial on a large scale in an infected human community.

Sarcopticidal Properties of Tetmosol Soap when Used Prophylactically

In order to test the prophylactic value of tetmosol incorporated in soap, white rats were confined in a large tank. Some of these received no treatment; others were washed over the entire surface of the tail with unmedicated soap, the soap, as before, being washed off with six fresh swabs dipped in warm clean water. The remaining rats were similarly treated, but tetmosol in various strengths was incorporated in the soap. After three days of treatment a number of rats suffering from severe *Notoëdres* infection were introduced into the tank containing the uninfected rats, the tail-washing of the uninfected rats being continued. From now on, the rats were examined daily for gross evidence of infection, but the burrows were not opened up until the end of the experiment, when the animal was killed, the tail removed, and a careful microscopical examination made of all papules.

Although it appeared to us unlikely that impregnated soap applied for a short period at relatively long intervals would prove effective as a prophylactic, our first experiments were designed to imitate a person taking a weekly bath with tetmosol soap, the soap not being used during the intervening period. A series of five experiments were carried out using the technique described above. The results are shown in Table I.

TABLE I.—Showing, in a colony of 20 clean rats in constant contact with 6 rats heavily infected with Notoëdres, the prophylactic effect of washing an area of skin (the tail) for 40 seconds once a week during three to five weeks with 5%, 10%, and 20% tetmosol soap

No. of Rats	Treatment	Period of Exposure to Infection in Days	Post-mortem Examination of the Treated Area (the Tail)		
			Average No. of Live Mites	Average No. of Eggs	
7	Unmedicated soap	18 (1) 22 (1) 23 (3) 25 (1) 30 (1)	57 115 195 131 190	313 640 980 747 648	
3	5% tetmosol soap	19 (1) 22 (2)	3 14	23 69	
7	10% tetmosol soap	24 (2) 25 (3) 30 (1) 31 (1)	24 47 17 91	82 160 67 185	
3	20% tetmosol soap	18 (1) 22 (2)	2 0	6 0	

It can be seen from Table I that neither 5 nor 10% tetmosolimpregnated soap, when used at weekly intervals, protected any of the rats from the disease. On the other hand, if the results following the use of the tetmosol-impregnated soaps are compared with those following the use of unmedicated soap it will be seen that in every instance the development of the disease had been controlled, so that fewer live mites and eggs were found in animals treated with impregnated soap than in those treated with ordinary soap. The table also shows that there is a tendency (which can be seen in almost all the series recorded) for the infection to become rapidly and progressively heavier with each day of exposure. This fact probably explains the apparent anomaly that a larger number of eggs and

live mites were found in rats treated with 10% tetmosol soap than in those treated with 5%, for the former series were exposed to massive infections for longer periods than the latter.

The results obtained by using 20% tetmosol soap were surprisingly good, considering the shortness of the application and the long interval between treatments; no mites or ova were found in the tails of the two rats which had four treatments in 22 days' exposure to infection; and in the remaining rat, which had 18 days' exposure to infection and three treatments, two mites and six ova only were found.

These experiments show that weekly treatment by washing with tetmosol soap of strengths varying from 5 to 20% did reduce the infection, in spite of the massive risk to which the rats were exposed. It is possible that weekly bathing with tetmosol soap might have greater value in the case of human beings than in the case of rats, for the risk of scabies infection in man is immensely less than among the rats recorded in these experiments. Even in a heavily infected person the number of mites present is relatively small in comparison with the enormous number found in such heavily infected rats as the carriers used in our experiments, and the same continuous and intimate contact does not exist between uninfected and infected human cases as it does in the rats in the above experiments. Moreover, it must be remembered that clean rats themselves rapidly became carriers, since untreated areas, such as the paws, nose, and ears, were soon heavily infected.

Having shown that a weekly bath with tetmosol soap protected only a small proportion of the rats exposed to infection with scabies, and reduced the intensity of the infection in the remainder, our next experiments were designed to ascertain whether daily washings with tetmosol soap would have a more marked prophylactic effect. They were planned in imitation of a person using 5% tetmosol soap for his daily ablutions, the technique used being the same as in the previous experiments. The results obtained are shown in Table II.

TABLE II.—Showing, in a colony of 18 clean rats in constant contact with 6 rats heavily infected with Notoëdres, the prophylactic effect of washing an area of skin (the tail) for 40 seconds twice daily with 5% tetmosol soap

No. of Rats	Treatment	Period of Exposure to Infection in Days	Post-mortem Examination of the Treated Area (the Tail)	
6	None	28 (1) 33 (2) 34 (2) 35 (1)	Live mites and ova +++	
6	Unmedicated soap	13 (1) 28 (1) 29 (1) 30 (2) 36 (1)	Live mites and ova +++	
6	5% tetmosol soap	25 (1) 28 (1) 29 (1) 30 (2) 36 (1)	No live mites, ova, or mite remains	

The results recorded in Table II show that washing the skin twice daily with unmedicated soap has no protective value against rat scabies, but that similar washing in which 5% tetmosol is incorporated gives complete protection among rats constantly exposed to heavy infection for a period of 25 to 36 days. It will be noted that no mite remains were found in the treated area. In spite of this, papules were present, which were presumably caused by invading mites. If this presumption is correct the action of tetmosol would appear to be not that of a repellant but rather that of a lethal agent which destroys the mites after they have penetrated the treated area of skin.

Conclusions and Summary

Tetraethylthiuram monosulphide (tetmosol) when combined with soap in 5, 10, and 20% dilutions has been shown to retain its sarcopticidal properties.

In cases of rat scabies due to *Notoëdres*, tetmosol soap was shown to produce a local therapeutic effect when used daily or weekly, the local infection being cured in some cases, the mite population being reduced in others.

In cases of human scabies six men suffering from Sarcoptes scabiei infection received five to six baths with 20% tetmosol soap on successive days; all were cured. A further series of 110 men received three baths with 20% tetmosol soap over a period of a week. All these cases remained under observation for at least six weeks, at the end of which period 88 (80%) were found to have been cured, and 22 (20%) to have relapsed.

Although it has been shown that the repeated use of tetmosol soap cures a high proportion (80%) of established cases of scabies, the soap is unlikely to supersede any of the standard methods employed which result in more than 90% cures. On the other hand, the simplicity of procedure involved in supplying the patient with a tablet of soap and instructing him to use it when bathing suggests the possible value of the soap if it is used therapeutically in communities which have become disorganized as a result of war, and in which it is not practicable to employ standard methods of treatment.

In the case of clean rats heavily exposed to Notoëdres infection from their companions, washing the tail once weekly with 5 and 10% tetmosol soap was followed by a marked reduction in the number of mites developing in the skin as compared with controls washed with unmedicated soap. When 20% tetmosol soap was similarly used once weekly the effect was more striking, two rats being completely protected against infection over 22 days, and the remaining rat developing only a very light infection.

In contrast to the partial protection provided by weekly washing with tetmosol soap, the regular use of 5% tetmosol soap twice daily on the tails of clean rats constantly in contact with companions suffering from severe Notoëdres infection gave complete protection to the treated area during periods of 25 to 36 days (the duration of the experiment). Little or no protective action followed the use of unmedicated soap.

It is considered that the results recorded justify the belief that the generalized use of tetmosol soap in an infected community would reduce the incidence of scabies by sterilizing some existing cases and by destroying the infection in freshly invaded persons. Such generalized use, however, will only be possible if it is found that a high incidence of dermatitis does not follow prolonged use of the soap. We have shown that the incidence of dermatitis following the use of the soap for short periods is low, and that it was low also among a small number of people tested over a prolonged period; but no estimate can be made of the risk of dermatitis until an extensive trial with a large number of individuals has been carried out.

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THE CARRIER STATE IN SONNE DYSENTERY

BY

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Since the discovery of B. dysenteriae Sonne in 1915 accounts have been published of many epidemic outbreaks of Sonne dysentery, but rarely has the original carrier in any single outbreak been traced. In fact, Bloch (1938) states: "It is generally accepted that symptomless chronic carriers of bacillary dysentery are rare"; while Buckle (1938), in the course of an investigation of an outbreak of Sonne dysentery in a mental hospital, says : "Tracing the cause appeared a hopeless task. . . . Proved persistent carriers of this organism are apparently rare, and . . . little investigation has been done to elucidate this point."

The appearance of Sonne dysentery in the Army in many places throughout the country, and particularly the large outbreak in a regiment which I propose to describe in some detail, have led me to search the literature for recorded outbreaks of this disease, especially noting whether or not an original carrier was found in each outbreak. The following table covers most of the recorded outbreaks in this country. It is seen that in only one outbreak-that reported by Thornton and Darmady (1938) -was an original carrier found.

In view of these facts and the suggestions that chronic carriers of Sonne dysentery are rare, the severe outbreak which occurred in an Artillery regiment in July-Aug., 1943, is of

special interest, since a chronic symptomless carrier who worked in the cook-house was traced as the originator.

Author	Place	No. of Cases	No. of Cases Bacterio- logically Positive	Cause	Remarks
Weisman (1927)	Glasgow	_	80	Milk	No carrier found
Laws (1936)	Mental hospital	113	75	No cause found	Suggested tha mild or symp tomless case were missed and they spread the infection
Parry and Peters (1936)	Mental hospital, Bristol	32	9	""	Case - to - case spread
Bloch (1938)	Institution, Glasgow		78	No evidence of spread by food, milk, or water	Origin not traced
Buckle (1938)	Mental hospital	115	74	No cause found	Six positive among staff nurses, and porters, but no cooks
Savage (1938)	Somerset	130	?	Ice-cream	No carrier o specific source of infection ascertained
Thornton and Darmady (1938)	Mental colony	-	30	Two sympto one a dish-	mless carriers
Cruickshank and Swyer (1940)	-	32	29	No carrier found	Suggested case to-case spread
Graham (1942)	School	52	Only 5 tested, who were positive	No carrier or infecting agent found	All kitchen staf examined, bu negative
Irvine (1942)	Leicester village	73	17	No carrier found	Suggested case to-case spread
Green and Macleod (1943)	Somerset	About 400	• ?	Water	No carrier found Eight water works employ ees examined all negative

The Outbreak

An Artillery regiment, consisting of three batteries and with a total strength of about 900 men, was at a practice camp in Wales when an outbreak of diarrhoea occurred. This started about July 20, 1943, and appears to have been at its height about Aug. 1, but no examination of faeces was done until Aug. 3. However, from this date every soldier with a history of diarrhoea since the start of the outbreak had specimens of faeces examined. Those with a positive result were admitted to isolation hospital immediately, while negatives had further examinations of faeces until three specimens had been found negative. Altogether there were 292 cases of diarrhoea (32.5% of the total strength), of which 81 were positive for B. dysenteriae Sonne. It is probable that the infection had died out in many of the remaining 200-odd cases before the stools were examined, as the attack of diarrhoea in some cases had been two to three weeks previously. Treatment in isolation hospital with sulphaguanidine resulted in the rapid cure of all cases, including the carrier.

This outbreak occurred in what was virtually a closed community, since the camp was isolated and outside amenities were few. The water supply was satisfactory, and was regularly examined bacteriologically. The general lay-out of the camp and the sanitary arrangements were also satisfactory. There was no fly nuisance; food-storage facilities were good; and both larders and cook-houses were clean and well kept. Food for the whole camp was drawn from a single central store. There were four main cook-houses in the camp, one of which served the permanent staff of the camp, while the other three were staffed by and served the visiting regiment.

No cases arose among the permanent staff, and no evidence of diarrhoea was found among the cooks of the staff cookhouse. Cases, however, occurred among men served from all the cook-houses used by the visiting regiment. All the cooks and orderlies in each cook-house were paraded and questioned carefully whether they had had diarrhoea during the last 12 months. Twelve gave a history of diarrhoea within the period of the outbreak, and, in addition, one in June, one in May, one in Feb., 1943, and one in Aug., 1942. These men were all excluded from the cook-house immediately and their stools