

CLINICAL TRIAL OF THIOSEMICARBAZONE

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The policy of this colony during the two years that I have been in charge has been not to emphasize how much medicine we can give each week, but how little we can give to realize maximum average improvement with minimum complications. It is also our purpose to test drugs and methods of treatment so as to determine their feasibility for use in outside units, called "preventive leprosy villages," of which we have over 20. The necessity of such trials is obvious: ninety per cent or more of all leprosy cases here actually live in country village areas. To lower the incidence of leprosy in a given area we must treat the patients where they are, even in most primitive conditions.

METHOD

In the trial of thiacetazone here reported,¹ to meet the conditions described we made a plan to treat two equal groups, one in the colony as a control and one in an outside unit which would include the entire village. In doing experimental work of this nature we are between two desires: first, to produce results in a hurry, so that the findings may be used quickly; second, to comply with the now known fact that any medicine used in the treatment of leprosy requires two to five years for fair and true evaluation. It is our plan, therefore, to use any drug to be tested for a period of at least two years before drawing any conclusions. In the case of thiacetazone, because the results are falling into a rather evident pattern, we are making this summary report at the end of one and one-half years. Our results are in line with those reported by other workers.

In this experiment we wished to end up with at least 100 patients having taken the drug for the full time, so we started with 120 patients. Sixty of them were in the central colony, and the other 60 were in the complete village of Jaum Tong, situated 57 km. from the home base. All types of leprosy and both sexes were included, distributed according to the incidence as the cases come to us. Thus there were included some 15 patients who belonged to the burnt-out class, in which no marked success could be expected. On the other hand, any unfavorable development in these burnt-out cases would be blamed on the new medicine, although it may have had no relationship to their leprosy. The patients were officially checked three

¹ Through the courtesy of the Boots Drug Company a sufficient amount of their brand of thiacetazone, "newstab," was supplied us for the purpose.

times during the experiment, but any complications were noted on their charts as they occurred.

The patients were further divided into two groups. It was intended that one group should receive 75 mgm. of thiacetazone daily, and the other group 150 mgm., and that was done at the colony. Every fourth week the medicine was stopped completely. Ferrous carbonate was given three times daily, 5 grains per dose. It was supposed at the time the experiment was started that this was essential for all patients receiving sulfone drugs. Since then we have learned from published reports and from our own experience that this is not necessary. Iron is no longer given except to those who show marked anemia, and then only for periods of one or two months.

RESULTS

The results obtained are shown in Table 1.

TABLE 1.—*The results of thiacetazone treatment in colony and village.*

Group	Number of patients	Dosage (mgm.)	Reactions	Improvement		
				Total	Marked	None
Colony	17	150	7	11	6	0
Colony	29	75	14	23	6	0
Village	55	25-150	6	54	0	1
Total	101		27	88	12	1

The Central Colony.—Forty-six patients here continued the course to the end. Twelve were much improved. Those taking 75 mgm. and those taking 150 mgm. daily were carefully compared as to the amount of improvement and the number developing leprosy reactions.

Of the patients taking 150 mgm., 17 finished the course. Six were markedly improved; 7 developed one or more reactions. Of the patients taking 75 mgm., 29 finished the course. Six were markedly improved; 14 developed one or more reactions.

Outside village.—Fifty-five patients here finished the course. Six had one or more reactions. Five complained of dimness of vision while taking the medicine. When the medicine was stopped for a month the eye dimness disappeared, only to return when the drug was again administered. These patients, however, felt so much better while taking the medicine that they continued to do so in spite of the dimness of vision. One woman (an advanced burnt-out case) claimed no benefit; all of the other patients were loud in their praise of the drug.

For unknown reasons the drug seemed better tolerated, with fewer reactions, in the outside village than at the colony. All

recorded reactions were leprosy reactions, and not allergic reactions to the drug. Cases favorable for marked improvement were not as many in the outside village as in the main colony.

COMMENTS

Although it might seem that the patients taking six tablets a day (150 mgm.) had the best record for markedly improved cases, actually after taking various factors into account the difference is not felt to be important. Analysis of the dosages given in the outside village revealed that in spite of the instructions laid down some patients were given 25, some 50, some 75, some 100, and some 150 mgm. daily. This is due to the type of mind that we meet in all villages. In general we are convinced that those on 75 mgm. daily do as well as those on twice that amount. On the other hand, reactions do not occur any more frequently with the larger doses than with smaller ones. There was one death in the outside village, apparently due to a severe type of leprosy reaction, but this was not confirmed by a trained observer.

Skin smears were made twice, nine months apart. As the findings follow the pattern being reported by careful observers of patients on DDS—i.e., no marked tendency to negative smears within one year, and evidence of granulation and change in the morphology of the bacilli—nothing further would be expected from more frequent examinations.

The results in the village proved to those doing the work that thiosemicarbazone can be used in relatively small dosage of 75 mgm. per day. The entire routine of its administration can be safely entrusted to any villager of average intelligence. The larger dose used (150 mgm.) did no harm, and therefore the danger of overdosage will be small. It is feasible to use this drug in a public health program reaching into large undeveloped areas.

COMPARISON WITH DDS

A comparison was made of the results of this treatment with those obtained with DDS treatment of a similar group within the main colony, taken at random as they were admitted. Of 98 patients taking 100 mgm. of DDS daily for three weeks and resting every fourth week, there were 27 who had one or more reactions during the 18-month period in question. Of 10 patients taking 200 mgm. of DDS daily for the same period 5 had reactions, but this group is too small to permit any real deductions. However, the assistants who administer the drugs

are all convinced that there are many less reactions with thiacetazone than with DDS.

Except for the 5 patients taking thiacetazone in the outside village who complained of dimness of vision, there were fewer side effects with that drug than with others. General improvement was satisfactory. Thiacetazone is of special value for use in cases in which DDS cannot be tolerated. The greatest drawback in using this drug with large groups is the expense, the cost being about four times that of DDS.

SUMMARY

The work here reported was done to try out the value of thiosemicarbazone in leprosy as would be used in a public health program in country areas. For this purpose two groups of 60 patients each were treated, one in the central colony as a control group, the other in a preventive leprosy village outside. Each group was further divided into two sections, one section supposed to receive 75 mgm. daily, the other group 150 mgm. All types of leprosy were treated. All patients except one showed some degree of improvement. Smears showed the same changes as seen in DDS treatment, changes in the morphology of the bacilli but no negative smears at the end of the 1½ years of observation. The smaller dosage produced the same degree of improvement as the larger. There were fewer leprosy reactions than in cases under treatment with DDS. There were no allergic reactions. Five patients in the village complained of dimness of vision, but did not have to stop the medicine. Except for the cost, which is about four times that of DDS, thiosemicarbazone is an excellent drug to use with large groups in undeveloped areas.

RESÚMEN

Se trató de evaluar el thiosemicarbozone en el tratamiento de la lepra tal y como se usaría en un programa de salud pública rural. Se usaron dos grupos de 60 pacientes, uno tratado en la colonia central como testigo del otro grupo tratado en una aldea preventiva en las afueras. Cada grupo se dividió en dos secciones, una que recibió 75 mgm. diarios, la otra 150 mgm. Todos los tipos de lepra fueron tratados. Todos los pacientes a excepción de uno, mejoran algo. Frotis demostraron cambios similares a los que ocurren bajo tratamiento con DDS, cambios en la morfología de los bacilos pero no negatividad al finalizar 1½ años de observación. Ambas dosis produjeron resultados similares. Hubo menos reacciones leprosas que bajo el tratamiento con DDS. No hubo reacciones alérgicas. Cinco pacientes en la aldea se quejaron de turbidez visual, pero no tuvieron que discontinuar el tratamiento. Excepto por el costo, casi 4 veces el de DDS, thiosemicarbozone es una droga excelente para el uso en grandes grupos en regiones rurales.