PROMIZOLE TREATMENT OF LEPROSY*

A Preliminary Report[1]

by

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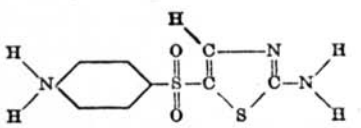
Promizole is the trade name for 2, 4'-diamino-5-thiasolylphenyl sulfone, which has the following structure:



It was synthesized[2] primarily for the treatment of mycobacterial diseases, since promin had been found too toxic for continuous oral administration in these diseases. In preliminary experimental and clinical tuberculosis, promizole did not produce sufficiently encouraging results to warrant further investigation; however, good results were obtained in tuberculosis of the skin (1). For this reason and because of its relative nontoxicity by mouth and its close resemblance to promin and diasone, which had been used with some success in the treatment of leprosy (2), (3), (4), (5), it was considered feasible to test the possible therapeutic effect of promizole on leprosy at the National Leprosarium.[3] The present preliminary report is published because clinical improvement in patients under treatment for leprosy seems to appear in some cases more rapidly with promizole than with either promin or diasone. Past experiments with other sulfa drugs given orally, particularly sulfanilamide (6), have proved unsuccessful in this institution.

At present 7 of the original group of 11 patients have been under treatment with promizole for approximately 1 year. These patients were started on doses of 0.5 gm. three times daily, dosage being gradually increased to 2 gm. three times daily, over a period of several weeks.

In 2 of the original 11 patients it was necessary to discontinue the drug because of toxic reactions — general malaise in 1 patient, and repeated febrile episodes in the other. Discontinuance of med-

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[1]From the U. S. Marine Hospital (National Leprosarium), Carville, La.

[2]By Parke Davis & Co.

[3]The promizole used in this experimental study was supplied gratis by Parke Davis & Co. through the courtesy of Dr. E. A. Sharp, Director of Experimental Research.

ication in the other 2 patients was not incidental to the drug; 1 absconded from the institution, and the other died of a cerebrovascular accident.

After 6 months of treatment, objective clinical improvement was observed in some of the patients. Because of these encouraging results, 8 more patients were started on the promizole treatment, making a total of 15 under treatment at the present time. Others will be added when more of the drug becomes available. Some of the last 8 patients started on this treatment have already shown benefits (figs. 1 and 2), but for the most part it is as yet too early to evaluate the therapeutic effects of the drug in this latter group.

This report is, therefore, based primarily upon the effects of promizole in the group of seven patients who have undergone treatment for a period of at least 1 year. All of these patients have tolerated the drug well in doses up to 6 gm. daily. Brief clinical abstracts of these seven cases are included below.

CASE REPORT

Case 1: Registered No. 1452.—Mexican male, 35 years of age, had fairly early active mixed type of leprosy at beginning of treatment with promizole. The disease was of about 6 years' standing. Prior to April 1945, when promizole was begun, he had received only 11 intramuscular injections of chaulmoogra oil with benzocaine in 1941 and 16 in 1942 and chaulmoogra oil by mouth in doses of 25 minims three times per diem regularly from 1942 to the beginning of 1945. Promin had then been given intravenously for a period of 3 months but was discontinued because of the patient's dread of the needle. During this period his leprous lesions had not improved. When promizole was begun, the clinical findings were as follows: Discrete eruption of brown nodules over the face, ears, limbs, and body, becoming confluent in some areas over face and ears; and some areas of anesthesia over feet, ankles, and lower third of legs. Nasal and skin smears were positive for *Mycobacterium leprae.*

Promizole was administered in doses of 6 gm. daily after the first 3 months for a period of 11 months. Improvement was noted in the shrinking of all nodules. The patient was bacterioscopically negative in November and December 1945, and continues negative in the April 1946 test, no test having been made in the 3 months' interim.

Case 2: Registered No. 271.—White male, 50 years of age, with advanced mixed type leprosy of about 25 years' duration. Clinical manifestations were total blindness; leprous laryngitis; nodules scattered over arms, legs and face; and many ulcerations on legs and plantar trophic ulcers. No improvement had been noted with oral and intramuscular injections of chaulmoogra over many years. Skin tests were positive for *M. leprae.*

Promizole was started in March 1945. There is definite improvement after 1 year of treatment. Voice is normal, all ulcerations are healed, and all nodules are considerably flattened, but bacterioscopy remains positive.

Case 3: Registered No. 1691.—White male, 28 years of age, wtih early mixed type of leprosy, of about 3 years' duration. Clinical manifestations were nodules of both ears; diffuse thickening of skin over face; and anesthesia in both legs and arms in scattered areas. He had taken no previous treatment. Skin smears were positive for *M. leprae.*

Promizole was given in doses increasing from 1.5 to 6 gm. daily for 1 year. There is slight evidence of flattening of nodules on ears, and skin over face is less thickened. Bacterioscopy remains positive.

Case 4: Registered No. 1445.—Filipino male, 42 years of age, with advanced mixed type of leprosy of about 10 years' duration. Clinical manifestations were many scattered nodules varying in size and occurring over face, limbs, and body; diffuse thickening of skin over face, brow, ears, hands, feet, and legs; extensive areas of anesthesia over legs and arms; small ulcers over lips and around nose; and atrophy of interosseous muscles of both hands. No improvement had been noted with oral or intramuscular injections of chaulmoogra oil. Skin and nasal smears always positive for *M. leprae.*

Promizole was given in doses increasing from 1.5 gm. to 6 gm. daily for 1 year. There is a definite flattening of nodules, and ulcerations have healed. Bacterioscopy is still positive.

Case 5: Registered No. 277.—Colored male, 37 years of age, with advanced lepromatous leprosy of about 24 years' duration. Clinical manifestations were total blindness; much scarring over face and upper and lower extremities from old ulcerating nodules and trophic ulcers; scattered large nodular lesions of neck; and diffused infiltration of extremities. He had many different treatments during past years without benefit except from sulfathiazole, 1.5 gm. daily, which had resulted in healing of all ulcerations but had not affected nodular lesions or leprous infiltrations. At the time promizole was begun, all ulcerations had been healed. Skin smears were positive for *M. leprae.*

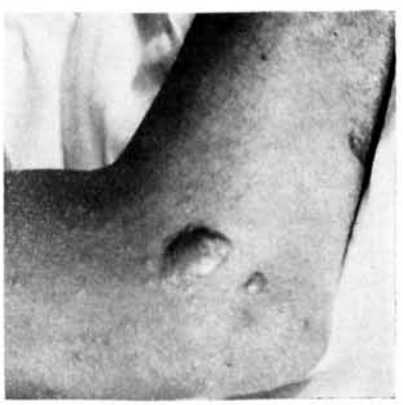
Promizole was given in daily doses increasing from 1.5 gm. to 6 gm. for 1 year. Nodular lesions have become smaller and flattened. Skin smears continue positive for *M. leprae.*

Case 6: Registered No. 1690. — Mexican male, 26 years of age, with early mixed type of leprosy of about 4 years' duration. Clinical manifestations were nodules over ears; a few scattered nodules over legs and arms; anesthesia in areas over legs and arms; a superficial ulcer on dorsum of right hand, and another, 2 x 3 cm., over left Achilles tendon. Skin smears were positive. He had taken no other treatment.

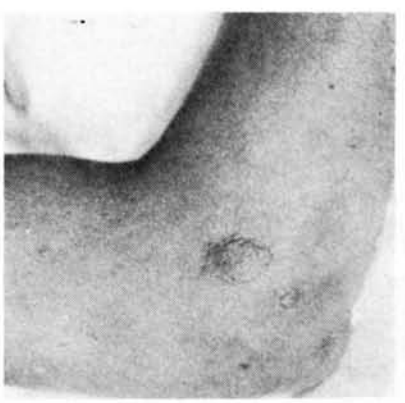
Promizole, starting with 1.5 gm. and increasing to 6 gm., was given daily for 1 year. Ulcers have healed, and there is a shrinking of nodules over ears, legs, and arms but skin smears remain positive.

Case 7: Registered No. 1498.—White male, 68 years of age, with moderately advanced lepromatous leprosy of about 7 years' duration. Clinical manifestations were many discrete nodules over ears, on arms to shoulders, and on both legs from knees to toes and thighs to hips. Some were slightly flattened. There was also some thickening of skin over face, nose, forehead, hands, and arms. There were no ulcerations. Skin and nasal smears were positive for *M. leprae.*

PLATE I

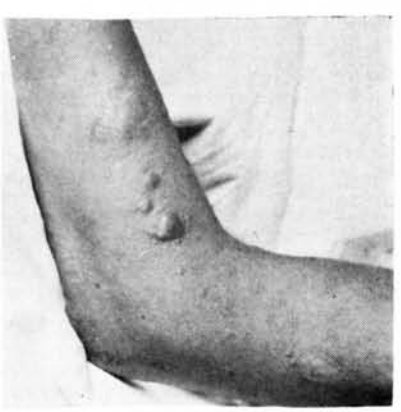


October 1945.
(Before treatment.)

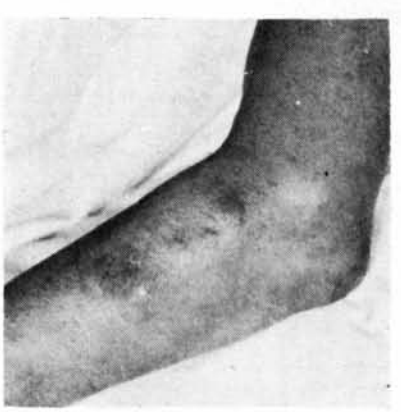


January 1946.
(After treatment.)

Right arm.



October 1945.
(Before treatment.)



January 1946.
(After treatment.)

Left arm.

FIGURE 1.—Case No. 1285, illustrating rapid changes in lepromatous lesions after only 3 months of treatment with promizole.

Promizole was given in increasing doses from 1.5 gm. to 6 gm. daily for 1 year. Condition appears stationary. Possibly, thickening of skin over face is slightly improved. Bacterioscopy remains positive.

CONCLUSION

No claim is made in regard to the ultimate value of promizole given orally in doses of 6 gm. daily in the treatment of leprosy. Attention is called to the fact that promizole is well tolerated by patients with leprosy and that clinical improvement occasionally can be demonstrated more quickly with promizole than with similar sulfones, such as promin and diasone. It is felt that the therapeutic results thus far obtained are sufficiently encouraging to warrant further clinical study, which will be necessary before a final evaluation of promizole in the treatment of leprosy can be given.

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