

## TREATMENT OF TROPHIC ULCERS OF LEPROSY WITH RONIACOL

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The problem of the trophic ulcer in the various types of leprosy is one that is frequently met, especially in advanced cases and those with extensive nerve damage. It is often the sole cause of disability in cases which are bacteriologically negative and which could otherwise be released from institutional care. The anesthesia that the patient has, and the relative unimportance to him of these lesions compared with some of his complications, tend to bring about disregard and carelessness of them so that they may not be reported to the leprologist until progression is advanced. These cases habitually account for a large proportion of the beds in the hospital or infirmary sections of leprosaria, and consume material portions of budgets devoted to nursing care, feeding, laundry, etc., and result in loss of production time from institutional jobs.

Treatment of these lesions is diversified, according to the circumstances at the time and the judgment of the physician. In general, conservative therapy seems to be preferred and revolves around bed rest, elevation, Buerger's exercises, plaster casts, relief from pressure and trauma, and applications designed to stimulate granulation and epithelialization. The surgical approaches of curettage, sequestrectomy, amputation, etc., are of course necessary at times for proper results.

During my service as medical director of the Kalaupapa Settlement, Molokai, I was impressed by the role of circulatory changes of the damaged extremities in delaying closure time of trophic ulcers. Feet and hands subjected to disuse during years of neuropathy and muscular atrophy usually present a waxy, smooth skin with pallor and progressive sclerosis of connective tissues, accompanied by extreme hyperkeratosis of the normal friction- and weight-bearing surfaces. It is also often observed that there is a minimum of bleeding from incisions made into these areas.

It is suggested that the sclerosis and fibrosis of the extremities leads to extravascular compression and narrowing of blood vessels, which would naturally prolong healing time of trophic ulcers because of the impaired blood flow. For this reason vasodilator drugs have often been used as an adjunct to conservative treatment of these ulcers.

In an attempt to evaluate the actual worth of these drugs in such cases a brief study of the clinical effects of a simple vasodilator drug was made. Sympathetic blocking agents were rejected because the nerve damage of the limbs was an obviating factor. Roniacol tartrate<sup>1</sup> was chosen as an agent which acts directly on the arterial musculature to

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<sup>1</sup> A supply of this drug was provided by the Hoffmann-La Roche Co.

produce dilatation. This drug is beta-pyridyl carbinol, the alcohol conforming to nicotinic acid, and its action resembles that of nicotinic acid but is more prolonged and has less tendency to cause flushing.

The study was a double-blind experiment, neither the patient nor the observer knowing which cases received the placebo and which were actual treatment cases. Cases were selected on the criteria of (1) simple trophic ulcers of the feet, (2) previous episodes for comparison of treatment time and (3) absence of complicating conditions affecting the status of the ulcer (uremia, diabetes, etc.) All were under some form of sulfone therapy at the time, and two of the cases were bacteriologically negative.

Blood pressure records were kept t. i. d., and the areas of the ulcers were measured. Any side reactions were noted. In all cases the treatments were limited to simple cleansing of ulcers, bed rest, and administration of Roniacol, 50 mgm. t. i. d. orally. No antibiotics or special ointments were used, and there was no surgical intervention. When the patient was discharged with a healed ulcer or with maximum healing, the total treatment time was compared to the treatment time on bed rest alone or on cast treatment alone.

CASE 1. T. Y. Treatment begun June 27, 1952. Previous history of ulcers: repeated multiple plantar ulcers over the heads of the metatarsals, and absorption of bones; patient walks on sponge-rubber sandals. Previous treatment and healing times: in 1950, right foot in cast (ambulatory), 33 days healing; and left foot in cast (also ambulatory), 30 days; bed rest and cast in 1951 for fewer ulcers than now, healing 65 days. Hoffman amputation, head of right second metatarsal, November 1951; good results in this area. Blood picture: chronic aplastic anemia. Area of ulcer, initially (6/27/52), 50.2 mm<sup>2</sup>; at end of course (7/31/52), 0. Blood pressure record: occasional drops to 98/66. Side reactions: gastritis (?), flushing of face.

Remarks and evaluation: A multiple-ulcer case with much previous treatment, local rest with casts and surgery. The healing time of 33 days seems superior to the previous bed-rest time of 65 days, but not to the plaster-cast time of 33 and 30 days on two occasions.

CASE 2. S. M. Treatment begun July 1, 1952. Previous history of ulcers: recurrent ulcer of the plantar surface, left great toe. X-ray shows spur of bone at base of distal phalanx. Previous treatment and healing time: from November 3, 1947 to January 19, 1948 (76 days) the patient was on bed rest for lesions of the same location, both feet; sulfone treatment continuing. Curretment of ulcer in 1950. Blood picture: normal. Area of ulcer, initially (7/1/52), 28.2 mm<sup>2</sup>; at end of course (7/30/52), 0. Blood pressure record: satisfactory. Side reactions: hot feeling in face.

Remarks and evaluation: There was maceration and hyperkeratosis of the dorsal surface of the toes; no fungi found. The healing time of 30 days compared with 76 days previously suggests that the patient derived benefit from the treatment.

CASE 3. J. W. Treatment begun June 30, 1952. Previous history of ulcers: plantar ulcer over the third metatarsal, July 9-21, 1951. Present ulcer over the second metatarsal. Previous treatment and healing time: 12 days on bed rest. All toes amputated. Blood picture: normal. Area of ulcer, initially (6/30/52), 201 mm<sup>2</sup>; at end of course (7/10/52), 0. Blood pressure record: 132/90 on July 1. Side reactions: none.

Remarks and evaluation: This ulcer was not strictly trophic, but may have

been due to an old tendon abscess. The healing time of 11 days seems to have no advantage of the previous bed-rest time of 12 days.

CASE 4. J. K. Treatment begun July 1, 1952. Previous history of ulcers: on right foot, August 29 to September 6, 1950, incompletely healed; January 5 to February 4, 1951; August 2 to September 22, 1951; December 13, 1951 to February 28, 1952 (Priscoline treatment). Curretment in August 1951. Average time of healing, 52 days on three occasions of bed rest and antibiotics, with complete healing. Blood picture: normal. Area of ulcer, initially (7/1/52), 658 mm<sup>2</sup>; at end of course (9/11/52), 100 mm<sup>2</sup>. Blood pressure record: satisfactory. Side reactions: none.

Remarks and evaluation: Present treatment, 71 days, with incomplete healing, compared with average of 52 days on conservative treatment previously. No apparent benefit.

#### DISCUSSION

Although this group of only four cases is much too small to warrant the drawing of any conclusions, certain general impressions were gained. In the first place, it is to be said that at the end of the double-blind period it was found that Case 1 had been given the placebo, while the other three cases had received Roniacol. Case 1, on the placebo, derived no benefit over previous forms of treatment. Case 2 showed a definite advantage over previous episodes of bed rest and curretment. Case 3 showed no significant difference from other forms of treatment. Case 4 definitely did not benefit from the addition of Roniacol to bed rest, and after prolonged use of that drug the patient was discharged with the ulcer incompletely healed. The possible inferences are that this was a true study without the influence of biased enthusiasm of the observer, and that some benefit may at times be derived from the use of vasodilators.

The factors against benefit from the drug used are: (1) Vasoconstriction is not the original, basic cause of trophic lesions, and consequently the production of vasodilation may not always help. (2) Occlusion of blood vessels is principally due to fibrosis of the perivascular connective tissue, accompanied by marked hyperkeratosis, and a vasodilator drug is powerless against that condition.

The factors favoring use of this drug are: (1) Where collateral fibrosis is not too severe, it may be effective. (2) Explanation of the mechanisms, plus the subjective warming of the affected extremities, induces the patient's self-interest in following a bed-rest regimen to its conclusion even though it be prolonged and tedious.

#### SUMMARY AND CONCLUSIONS

1. A double-blind study of the use of Roniacol, a vasodilator, with respect to its effect on the healing time of plantar trophic ulcers, was made in four cases.
2. The drug is a harmless adjunct to other methods of therapy.
3. In some cases there may be benefit from its use, either subjectively or objectively, if collateral conditions of excessive fibrosis do not interfere with augmented circulation.

## RESUMEN

1. En cuatro casos, se hizo un estudio del uso de Roniacol, un vasodilatador, con respecto a su efecto sobre el tiempo de cicatrización de las úlceras tróficas de la planta del pie.
2. La droga es un coadyuvante inocuo de otros métodos terapéuticos.
3. En algunos casos, puede derivarse beneficio, ya subjetiva u objetivamente, de su empleo, si las condiciones colaterales de excesiva fibrosis no impiden el aumento de la circulación.