

PENICILLIN USED UNSUCCESSFULLY IN TREATMENT OF  
LEPROSY\*

By

G. H. FAGET

*Senior Surgeon, U. S. Public Health Service*

*U. S. Marine Hospital, Carville, Louisiana*

and

R. C. POGGE

*Assistant Surgeon (R), U. S. Public Health Service*

*U. S. Marine Hospital, Carville, Louisiana*

Since there is no specific remedy in the treatment of leprosy all new drugs which offer any hope of chemotherapeutic action should be put to experimental trial. It was for this reason that penicillin was used at the National Leprosarium. Even though Smith and Emmart (1) had demonstrated that penicillin had no bacteriostatic action against the tubercle bacillus *in vitro* and no therapeutic effect on experimental tuberculosis in guinea pigs, it was felt nevertheless that the drug should be tried in leprosy before it could be concluded to be likewise powerless against *Mycobacterium leprae*.

PRESENT STUDY

Seven patients with the lepromatous (nodular) type of leprosy were selected for treatment since this is the type of disease which shows the least tendency toward spontaneous remission. The first and second patients were chosen to note if penicillin had any effect on recently developed nodules. From past experience at the National Leprosarium, new nodules seemed most amenable to treatment. Hence it was rational to expect favorable changes in new lesions if penicillin exhibited any specific action in leprosy. This expectation did not materialize.

The third patient was selected because the disease was of an early minimal type of lepromatous leprosy. It was felt that such a case offered penicillin an excellent opportunity to produce a favorable reaction if it had any merit in the treatment of leprosy. It did not do so.

The other four patients treated had more or less advanced lepromatous leprosy which had not responded to any previous treatment. In these cases it was thought interesting particularly to observe whether penicillin had any influence upon certain complications of the disease which were present. These complications included leprosy ulcerations, erythema nodosum, iridocyclitis, leprosy keratitis, leprosy rhinitis and leprosy laryngitis. Some of these complications were being activated by secondary infections. No beneficial effects

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were demonstrated in any of these patients, except for the healing of secondarily infected ulcers in one case.

#### CASE REPORTS

Only the first 3 cases are included here in brief reports, since they are the ones considered to have been most favorable for treatment.

**CASE 1:** A colored male, 30 years of age, had moderately advanced lepromatous leprosy of 6 years' duration. For the last 5 years he had been under treatment at the National Leprosarium which included chaulmoogra oil, diphtheria toxoid, and Internal Antiseptic 307, a sulfone. The course of the disease had continued progressively worse except for a short period of improvement under the influence of the sulfone drug. This temporary improvement had been followed by the development of new nodular lesions on the face and upper extremities. At the time penicillin was started, besides the new lesions, there were multiple old nodular lesions of the face, torso, and limbs. Some nodules had coalesced into small plaques. Several superficial ulcers were present on the forearms and legs.

It was primarily to test the therapeutic effect of penicillin on the newly developed nodules that this case was selected for study.

**Penicillin therapy:** For approximately 3 weeks 50,000 units of penicillin were administered daily. In the morning 25,000 units were given by slow intravenous drip lasting 3 hours, and at night 25,000 units were injected intramuscularly. In this manner 1,000,000 units of penicillin were administered in 23 days.

**Results:** The ulcers of the extremities healed. Some of the old nodules became dry and scaly. Ten days after treatment had been discontinued, multiple ulcers, measuring up to 4 cm. in diameter and 0.5 cm. in depth, developed on the upper and lower extremities.

Treatment was then resumed on a smaller scale, 12,500 to 16,000 units a day, and was continued for more than 4 months, totaling an additional 417,000 units.

**Final results:** The new ulcers promptly healed. The nodular lesions have for the most part remained stationary. Bacteriologic skin and nasal smears continued as strongly positive as before treatment. Although the patient considered himself improved and said that his general health was much better, his improvement was only subjective and there were no objective changes to substantiate it. This case was classed as a therapeutic failure as far as any specific action of penicillin on leprosy was concerned.

**CASE 2:** A white female, 19 years of age, had moderately advanced leprosy of 5 years' duration. Institutional treatment for four years had consisted of courses of chaulmoogra oil, diphtheria toxoid, and Internal Antiseptic 307, a sulfone. During the diphtheria toxoid therapy, multiple small nodules erupted on the face. Some of these new nodular lesions decreased in size in response to the sulfone drug and a plantar ulcer of the right foot healed.

At the onset of penicillin therapy the condition of the patient was as follows: There were numerous old and new nodules on the face, nodular lesions peppered the upper and lower extremities, large lepromatous plaques covered the knees and there were a few bone cysts in the fingers.

**Penicillin therapy:** Penicillin was administered in 25,000-unit doses by slow intravenous drip in the morning and 25,000-unit doses by intramuscular injection at night. This was continued daily for a period of approximately 3 weeks, during which time 1,000,000 units were given. Thereafter the daily intramuscular injections were re-

duced to from 12,500 to 16,000 units, making an additional 450,000 units during 150 days.

*Results:* There was questionable improvement in the nodules early in the course of treatment. Soon the skin of the extremities became dry and superficial ulcers appeared on the hands and feet. There was a recurrence of the penetrating plantar ulcer of the right foot. A bone cyst of the index finger of the right hand grew progressively larger while the patient was under treatment. The unfavorable progress in the bone cyst was recorded in serial x-ray films. Material aspirated from the cyst showed numerous *M. leprae* proving that it was caused by formation of leproma in the bone marrow. Skin and nasal smears remained strongly positive for *M. leprae*.

The clinical impression was that penicillin therapy was not beneficial in this patient. The lepromatous lesions of the skin were not affected and an increase in size of a lepromatous bone cyst of the index finger was not prevented.

CASE 3: A white female, 17 years of age, was recently admitted to the National Leprosarium with an early minimal type of lepromatous leprosy. She had had no previous treatment. The disease consisted of a few discrete nodular lesions on the face and a fairly early mucosal leprosy of the nasal septum. Skin and nasal smears from these lesions were lush with *M. leprae*.

This case was considered an ideal one for experimental treatment with large doses of penicillin, since the early lesions presented an excellent opportunity to test the drug's merit in leprosy, if it had any.

*Penicillin therapy:* One hundred thousand units of penicillin were administered daily in equally divided doses at 8 hours' intervals. Because of local irritation and pain, the subcutaneous injections of the drug were later replaced by intramuscular injections. This intensive treatment was continued for approximately 1 month and totalled 3,000,000 units of penicillin.

*Results:* The skin and nasal lesions were practically unchanged by this treatment. Skin and nasal smears remained strongly positive for *M. leprae*. During the last week of treatment the patient experienced her first acute lepra reaction with outcropping of erythema nodosum on the extremities.

#### CONCLUSIONS

Penicillin in doses up to 50,000 to 100,000 units daily continued for a period of several weeks is ineffective in the treatment of leprosy.

#### ADDENDUM

Six months have elapsed since beginning the treatment of the 7 cases included in the body of the paper and no beneficial effects attributable to treatment have been observed in any case during that time.

Since submission of our penicillin paper for publication 4 other patients have been treated at the National Leprosarium with much larger doses of penicillin without any appreciable changes in leprosy lesions. Two of these patients had the moderately advanced lepromatous type of leprosy and the two others the far advanced mixed type. The doses given in 3 cases including both lepromatous cases, were 40,000 units of penicillin intramuscularly every 3 hours totalling 320,000 units in 24 hours. The other patient, a woman who weighed less than 90 pounds, was given 33,000 units of penicillin intramuscularly every 3 hours for a total of 264,000 units in 24 hours.

One of the patients with lepromatous type of leprosy was treated during a subacute lepra reaction to note if penicillin had any favorable effect on this condition. By the second day of the treatment the reaction became much worse with outcropping of new erythema nodosum lesions, chills and high fever, muscular aches, nausea, and great debility. In spite of this, penicillin therapy was continued in undiminished doses for 2 more days. It then had to be discontinued because of the severity of the reaction and the extreme debility of the patient. Altogether this patient received 1,280,000 units of penicillin. There were no changes in lepromatous lesions during or for a period of more than one month following treatment.

The two mixed cases received 10 days of treatment each, totaling 3,200,000 and 2,640,000 units of penicillin respectively. There were no observable effects on any of the leprosy manifestations during treatment or for a period of over one month thereafter in either patient.

The final patient, who had numerous discrete lepromatous nodules, received 3,640,000 units of penicillin over a period of 10 days. No observable changes occurred in the leprosy nodules either during treatment or for over two weeks thereafter.

Therefore penicillin in doses even larger than those usually found adequate in the treatment of syphilis are ineffective in the treatment of leprosy.

#### REFERENCES

- SMITH, M. I. and EMMART, E. D. The action of penicillium extracts in experimental tuberculosis. *Pub. Health Rep.* **59** (1944) 417.