

PENICILLIN IN TREATMENT OF LEPROSY

TRIAL IN EIGHT CASES

by

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The remarkable results obtained with penicillin in the treatment of diseases produced by gram-positive micro-organisms, its proven efficiency in certain infections due to gram-negative micro-organisms (gonococcus and meningococcus), and the encouraging reports of its action in syphilis appeared to provide sufficient evidence to justify a trial of this antibiotic in the treatment of leprosy. The results of treatment of tuberculosis with penicillin, however, had been negative and considering the bacteriological and histological similarity between tuberculosis and leprosy, there was little cause for optimism. Nevertheless its trial was considered worthwhile, especially in cases of lepra reaction and patients with extensive ulcerations where secondary infections, chiefly with streptococcus and staphylococcus, are an important factor impeding cicatrization even where there is favorable response to general treatment.

METHODS

Eight patients were selected, 5 males and 3 females between 28 and 57 years of age. Seven of the cases were of the lepromatous type, of 5 to 15 years duration, bacteriologically positive and with early and late reaction to lepromin repeatedly negative (Table 1). One was a neural-tuberculoid case in reaction, of one years duration, bacteriologically positive in skin and nasal mucosa and with a positive reaction to lepromin. Four of the patients (2 males and 2 females) gave a history of syphilis, incompletely treated, with strongly positive serology (Wassermann, Kahn Standard, Eagle, and Briceño Rossi or Hecht) although without cutaneous, nervous or cardiovascular symptoms at the time the experiment was started.

The patients were divided into 3 groups and treated with sodium penicillin (Lilly and Squibb) as follows:

Group I: 2 patients, given 50,000 units daily in 1000 cc. of normal saline by intravenous drip during 8 to 10 hours.

Group II: 2 patients, given 60,000 units daily by intramuscular injections, one every 3 hours with 8 doses daily.

Group III: 4 patients, given 25,000 units daily in a single intramuscular injection in 1 cc. of peanut oil-beeswax suspension, according to the method of Romansky-Rottman (1) and Freund and Thompson (2).

Treatment continued for from 21 to 53 days with a follow-up of 3 months (Table 1). Previous to, during, and subsequent to treatment, the following examinations were done: red and white blood cell count, hemoglobin determination, differential blood count, sedimentation rates (method of Westergren), bacteriological examination of skin, nasal mucosa, and of the flora from the ulcers (Gram and Ziehl-Neelsen stain), and lepromin tests using antigens prepared according to the technic of Dharmendra (3) and Fernandez-Olmos Castro (4).

The effect of the penicillin therapy on the general condition, lepra reaction, ulceration, blood picture, sedimentation rate, bacteriology, and lepromin reactions was compared with that in patients treated with promin (47 patients), diasone (24 patients), ethyl esters of chaulmoogra oil and of chaulmoogra oil itself in doses of from 15 to 30 cc. per week over similar periods of time. When ulcers were present, comparisons were also made with results obtained after topical treatment with promin jelly, tyrothricin, 5 per cent sulfathiazole ointment, penicillin ointment (Lederhillin, 1000 units per Gram), Muir method (5), and with gentian violet, tannic acid, and silver nitrate. These comparisons will be reported on separately.

CLINICAL OBSERVATIONS

All data relative to the cases have been summarized in table 1.

Table 1. Summary of clinical observations

Case No.	Clinical picture and age	Days of treatment	Daily dosage units	Method of administration	Total dosage units	Results
1	Lepromatous, 28 yrs. male, in reaction, repeated reactions since Jan. 1945.	50	50,000	I. V.	2,550,000	Negative; sedimentation rate increased; lepra reaction unaffected.

2*	Lepromatous, 32 years, male, extensive painful ulcers, frequent reactions.	43	50,000	I. V.	2,050,000	Marked improvement in general condition, ulcers, and sedimentation rate; increase of 2 million R.B.C. and 2 Gm. of Hb; decrease of neutrophils from 76 to 62%**
3	Neural tuberculoid, 53 years, male.	43	25,000	I.M.O.	1,050,000	Improvement in skin lesions; bact. negative; decrease in sedimentation rate.***
4*	Lepromatous progressive, 33 years, male, poor condition, extensive ulcers, repeated erysipela.	53	25,000	I.M.O.	1,300,000	Improvement; gain in weight; healing of ulcers; sedimentation rate stationary.
5*	Lepromatous progressive, 45 years, female, small multiple ulcers.	53	25,000	I.M.O.	1,300,000	Negative; increase in sedimentation rate.
6*	Lepromatous progressive, 45 years, female, ulcers, iridocyclitis in both sides and leucoma in right side.	53	25,000	I.M.O.	1,300,000	Slight decrease in sedimentation rate; no healing of ulcers****
7	Lepromatous progressive, 29 years, female, extensive ulcers.	21	60,000	I.M.	1,260,000	Cicatrization of ulcers; decrease in sedimentation rate; fall in neutrophil count from 78 to 65%; increase in R.B.C. from 3.7 to 4.1 million.

8	Lepromatous progressive, 48 years, male, multiple ulcers, W.B.C. of 12,000, sedimentation rate of 100 mm. the first hour.	21	60,000	I.M.	1,260,000	Cicatrization of ulcers; decrease in sedimentation rate to 70 mm., of W.B.C. to 8,000, and of neutrophils from 69 to 60%; increase of R.B.C. from 3.8 to 4.25 million and of 1 gm. in hemoglobin.
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I.M.—intramuscular injection of penicillin in water solution every 3 hours; I.M.O.—single injection daily of oil suspension: I.V.—intravenous drip, 8 to 10 hours daily, in normal saline solution.

* Patients with history of syphilis and with strongly positive serology.

** No effect on lepra reaction, reoccurrence within one month after end of treatment.

*** It must be remembered that the tuberculoid form in reaction tends to become bacteriologically negative spontaneously, after several weeks or months, with general improvement even to disappearance of cutaneous lesions. Consequently, these results are not necessarily attributable to the penicillin therapy, although the possibility of an indirect accelerating action cannot be denied.

**** Ulcers healed subsequently after 2 weeks treatment with tyrothricin, 0.33 mg. per cent daily.

SUMMARY

Penicillin has been used for the treatment of seven lepromatous and one neural (Nt. in reaction) cases of leprosy in daily doses of 25,000 to 60,000 units over periods of 21 to 53 days for a total of 1,050,000 to 2,550,000 units. Three technics have been used: the first, intramuscular injections every 3 hours (8 injections per day and 168 in total); the second, intravenous drip, 8 to 10 hours a day; the third, one intramuscular injection a day, in oily suspension (mixture of peanut oil and beeswax).

Observation was carried on for three months after treatments were completed. Except for general improvement and/or healing of ulcers in 4 patients, decrease of blood sedimentation rate in 5 patients (with increase in 2) and increase of red corpuscles and hemoglobin in 3 patients, no clinical, bacteriological, or immunological sign was recorded revealing any specific action of penicillin on *Mycobacterium leprae* or on the normal course of the disease either during the time of treatment or in the three months thereafter.

In two cases with lepra reaction, penicillin appeared to have no effect. Four of the patients subjected to this treatment had strongly positive serological tests for syphilis (Wassermann, Hecht,

Kahn Standard, Eagle, and Briceño Rossi reactions) with past history of syphilis. Treatment with penicillin did not modify the serological results.

At the time this trial was ending, a similar article by Faget and Pogge (6) confirmed the major part of the observations herein described.

CONCLUSION

Penicillin appears to have no influence either on the *Mycobacterium leprae* or on the course of the human disease. It does have considerable value in treatment of patients with secondary infections (streptococcus or staphylococcus). In such cases the single daily intramuscular injection in oil suspension is sufficient to give good results.

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