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Penicillin Treatment of Early Syphilis*

A Preliminary Report

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THE number of diseases and infections which are favorably influenced by penicillin therapy continues to increase as experience in the use of the drug is gained. It is the purpose of the present report to record, in a preliminary way, certain observations which have been made in four patients with early syphilis (primary) who were treated with penicillin only.

A study of the usefulness of the drug in the management of syphilis was undertaken after limited animal experimentation indicated that penicillin

possessed some spirocheticidal activity. The plan of study embraced the concurrent carrying out of a complete delineation of the effectiveness of the drug in experimental syphilis in rabbits and the conduct of a small pilot study of the effects produced in patients with early disease. The prompt resort to the human being was sponsored by the general non-toxic character of the drug and by the knowledge that observations as to early effectiveness could be carried out without placing in jeopardy the patient's chance for ultimate recovery in event it became expedient to resort to conventional arsenic therapy.

The early results in the animal phase of the general study indicate that the time-dose relationship will prove to be as important in this therapy as in the use of other chemotherapeutic agents. Failures to sterilize experimentally infected animals with treatment schedules which utilize minimal amounts of the drug over a brief treatment period are predictable. The results from treat-

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ment schedules which utilize larger amounts of the drug and more prolonged treatment periods will require observation for approximately one year for complete evaluation.

Four male patients have been treated and observed for a period sufficiently long to permit comparison with results produced by more conventional forms of treatment. Each patient displayed a single penile ulceration. Darkfield examination revealed characteristic *Treponema pallidum* in numbers varying from 2 to 10 per microscope field. The duration of the ulcerations averaged 8 days. Not any local or systemic therapy was employed other than that recorded below. The serologic status prior to therapy is indicated in the individual charts.

The penicillin treatment consisted of an intramuscular injection of 25,000 units of the drug at 4 hour intervals, night and day, for 8 days. The total number of injections was 48, and the total amount of the drug was 1,200,000 units. The gluteal muscle was the site of injection.

Darkfield studies of secretions collected from the primary lesions were carried out at 4 hour intervals following the beginning of treatment. Not any spiral forms were observed after the 16th hour.

Some mild but definite clinical manifestations were observed during the first 8 hours of treatment. The patients complained of general malaise and mild headache. Temperature elevations not in excess of 2°F. were recorded. The penile lesions became painful and the regional lymph glands became enlarged and tender. One patient displayed a maculo-papular skin eruption resembling secondary syphilis over the trunk and thighs. The eruption was of short duration. No symptoms, either early or late, were observed which could be construed as representing toxic response to the drug. The repeated use of the gluteal

muscles as a site for injection did not give rise to irritative sequelae.

Because of the importance of the serologic reactions as an index of the response to treatment, a comprehensive routine of serodiagnostic tests was employed. As representative of the super-sensitive procedures, the Kline Exclusion method was included. Of the flocculation tests set at a diagnostic level, the Kline Diagnostic, the Kahn Standard, the Eagle, Hinton, and Mazzini were employed. The Kolmer technic was the only complement-fixation method used. In addition to the above, quantitative titrations were carried out utilizing the Kolmer, Kahn, and Mazzini methods. The results produced by the various methods are displayed in the individual charts.

The results of the blood studies indicate that the therapy was responsible for a more or less rapid and complete disappearance from the blood stream of the reacting substance which is measured by the various tests and which is usually associated with activity in early syphilis.

The further observation of the group of patients will be maintained upon a weekly basis for as long as possible for the purpose of detecting any tendency toward a recurrence of positive serologic findings and for the recording of evidence of clinical relapse. The patients will again be hospitalized for the collection of a specimen of spinal fluid and for a complete medical survey at the expiration of 6 months post-treatment observation. Subsequent hospitalization for special study will be repeated as frequently as may seem desirable. To the information supplied by this group will be added the contributions supplied by additional patients treated in an identical manner until the total material is of dimensions which warrant the drawing of final and sound conclusions.

Should the more extensive and pro-

longed experience confirm the impression which is to be gained from the pilot study, a rebuilding of the structure of syphilis therapy may become necessary. The development of an optimal therapy will require carefully controlled studies designed to determine the most effective relationship between the amount of drug and the duration of the treatment period. Also the rôle of the treatment in latent disease and visceral and central nervous

system syphilis will require careful scrutiny before the reasonably effective measures which are available at present may be replaced by a therapy based upon penicillin. Because of the long post treatment period of observation which is a requisite for the evaluation of a syphilis therapy, the progress toward the adoption of a new mode of treatment must, of necessity, be deliberate.