SYNNEMATIN B IN THE TREATMENT OF SYPHILIS AND GONORRHOEA*

A PRELIMINARY REPORT

BY

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Failure of penicillin in the treatment of acute gonorrhoea has recently been reported (Epstein, 1959), and this development poses a serious problem. The increasing sensitization of individuals to penicillin and the development of penicillin resistant strains of *Neisseria gonorrhoeae* show that there is great need for another antibiotic which is effective in both gonorrhoea and syphilis.

Synnematin B,† an antibiotic described by Gottshall, Roberts, Portwood, and Jennings (1951), was shown to be treponemicidal *in vitro* and in rabbits by Wheeler, James, Lea, and Curtis (1957), who also reported the successful treatment of a case of primary syphilis. Olson (personal communication) states that Synnematin B is also effective *in vitro* against species of *Neisseria*.

Synnematin B, produced by the mould *Cephalosporium salmosynnematum* strain 3590 A, is known to be related to penicillin chemically and in some of its pharmacological properties (Abraham, Newton, Olson, Schuurmans, Schenck, Hargie, Fisher, and Fusari, 1955). It is inactivated by penicillinase. Its toxicity is extremely low and doses as high as 5 g./kg. body weight have been given without adverse effects. No evidence of a sensitizing property has been discovered in individuals treated with Synnematin B, and attempts to sensitize laboratory animals to Synnematin B have been uniformly unsuccessful.

Synnematin B, unlike penicillin, has been shown to be active against many Gram-negative bacteria. Bacteria known to be susceptible *in vitro* to low concentrations of Synnematin B include *Brucella*, *clostridia*, *corynebacteria*, *Leptospira*, *Neisseria*, *Pasteurella*, *Proteus* (*mirabilis* species only), *Sal-*

monella, *Treponema*, and *Vibrio*. Gram-positive bacteria susceptible to Synnematin B include diplococci and streptococci (haemolyticus). *Staphylococcus aureus* is not consistently susceptible to Synnematin B.

Besides being effective against syphilis (Wheeler and others, 1957; Kahn, Henderson, and Olson, unpublished data), clinical experience has shown Synnematin B to be effective against typhoid fever (Benavides, Olson, Varela, and Holt, 1955; Henderson, Garlock, and Olson, 1959), and against salmonellosis due to *S. reading* (Henderson and Olson personal communication). Investigations in the laboratory have shown that it is also effective against experimental meningitis in rabbits caused by *Diplococcus pneumoniae* (Henderson and Olson, personal communication).

Because of the known treponemicidal action of Synnematin B in man and animals and the marked susceptibility to it of species of the genus *Neisseria*, a clinical trial of this drug was organized to test its efficacy against syphilis and gonorrhoea. The present preliminary report describes the treatment of five cases of gonorrhoea and one case of darkfield positive, secondary syphilis. It is to be emphasized that these six patients were selected because the laboratory diagnosis was available before beginning therapy, and each was known to be sensitive to penicillin.

The total dose of Synnematin B selected for syphilis was 3,600,000 units, given by intramuscular injection of 300,000 units every 6 hours for 3 days. This dosage schedule was based on the recommendations of Curtis (personal communication), which were later modified as a result of the experience of Kahn, Henderson, and Olson (unpublished data) in the treatment of a case of late secondary syphilis. The injectable preparation is the only one currently available for clinical use.

* Received for publication May 12, 1959.

† Synnematin B used in this study was supplied by the Division of Laboratories, Michigan Department of Health.

Case Reports

Syphilis.—A 21-year-old coloured male homosexual was seen in the clinic on January 5, 1959, with the complaint of a penile sore of one month's duration, and a rash of 3 week's duration with pain in the joints. He had a generalized, dull red, moderately indurated, macular and papular eruption. The lesions were uniform in size and slightly indurated, and measured 3×6 mm. A generalized, firm, non-tender adenopathy was present. There was erythema of the pharynx. A ragged, indurated, moderately shallow ulcer, 1 cm. in diameter was seen on the prepuce. The Kahn test was positive 1:16, and the darkfield examination of serum from the penile lesion was positive.

The patient was admitted to hospital on January 12, 1959, and received Synnematin B, 300,000 units every 6 hours for 3 days (total 3,600,000 units). The first darkfield examination after admission, 16 hours after the first injection, was negative. The lesions on the skin were more prominent at that time, and the patient stated that they flared up about 12 hrs after the first injection. There was no fever or other evidence of a Herxheimer reaction. The arthralgia disappeared in one day, and the lesions were flatter and completely macular in 3 days. The patient complained of pain after each injection.

On January 22, 1959, the Reiter protein complement-fixation test was positive 4+, the Kolmer test positive 4+, and the Kahn test positive 4+. The penile lesion had completely healed. The generalized adenopathy remained. The skin lesions showed further fading.

Gonorrhoea.—Five male patients with acute gonorrhoea, confirmed by positive smear, culture, and fermentation reaction, were each treated with one injection of 300,000 units Synnematin B.

- (1) The smear was negative in 24 hrs, and the patient stated that the urethral discharge stopped 5 hours

after the injection. A culture was not done. The patient complained of stinging and burning at the site of injection 2 hrs after the injection.

- (2) and (3) The smear and culture were negative in 24 hrs and there was no discharge.
- (4) This patient was treated on a Friday. The smear and culture were negative on the following Monday, and there was no urethral discharge. The patient did not remember how long it took for the urethral discharge to stop. He was seen again in the clinic 26 days later with a purulent urethral discharge and a positive smear, but this was presumably due to a re-infection.
- (5) The patient did not return for his 24-hr smear and culture, but a week after treatment he had no urethral discharge and a negative culture.

Summary

The use of Synnematin B in the treatment of one case of syphilis and five cases of gonorrhoea is reported. Each patient was known to be sensitive to penicillin, to which Synnematin B has certain structural and pharmacological similarities. There were no allergic manifestations, early or delayed. There was a satisfactory clinical response in all the cases of gonorrhoea and the syphilis patient has shown no evidence of relapse or progression of his disease.

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