

## THERAPY OF EARLY SYPHILIS WITH PENICILLIN ADMINISTERED BY JET INJECTION\*

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Preliminary investigative studies of the jet injection technic have established the efficacy and relative painlessness of this procedure for the administration of a number of commonly used medications such as penicillin, streptomycin, procaine, insulin, etc. Jet injection has also been used effectively in various immunization procedures and for the production of local anesthesia. The description of the apparatus (the Hypospray), the hypofils which contain the materials to be administered and the technic of giving injections have been described previously (1, 2, 3, 4, 5).

This report concerns the employment of jet injections of penicillin in the therapy of early syphilis. Gonorrhea is among the diseases which have been successfully treated by means of Hypospray administration of penicillin but there are to our knowledge no previous reports of syphilis therapy with this method (6).

The current trend in ambulatory penicillin treatment of syphilis is in the direction of increasing the amount of penicillin per injection and reduction in the number and frequency of injections (7). These regimens require the use of procaine penicillin in oil with 2% aluminum monostearate (hereafter designated as PAM), which is conceded to be the optimum available type of penicillin for ambulatory syphilis therapy. The pain associated with the administration of antisyphilitic therapy is thus already greatly minimized and of relatively minor importance. This study therefore is primarily concerned with further establishing the value of the jet injection technic in the practice of medicine. More specifically, it is concerned with determining whether syphilis can be successfully treated by means of penicillin administered by Hypospray.

### MATERIAL AND METHODS

Beginning in January of 1950, all patients with primary and secondary syphilis who presented themselves for diagnosis and treatment at the Cincinnati Rapid Treatment Center of the Cincinnati General Hospital, were hospitalized and considered as candidates for this study. Only those patients with dark-field positive lesions or unequivocal secondary syphilis who had not received previous antisyphilitic therapy were selected. Five patients who did not fulfill these qualifications were included. Three of these presented recurrent secondary syphilis following previous "adequate" penicillin administration by needle and there were two patients with early latent syphilis and pregnancy.

Hypospray injections of 300,000 units of procaine penicillin in sesame oil with

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Hypofils of penicillin furnished by Dr. Geoffrey W. Rake, The Squibb Institute for Medical Research, New York.

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2% aluminum monostearate (PAM) were administered intramuscularly, daily in alternate buttocks to a total of 9 injections except to the 3 adults with relapsing secondary syphilis and to 2 children with acquired secondary syphilis. The former received 20 daily injections or 6 million units and the latter were given semi-weekly injections of 300,000 units to a total of 2.7 million units (9 injections). The somewhat low total dosage of 2.7 million units was purposely

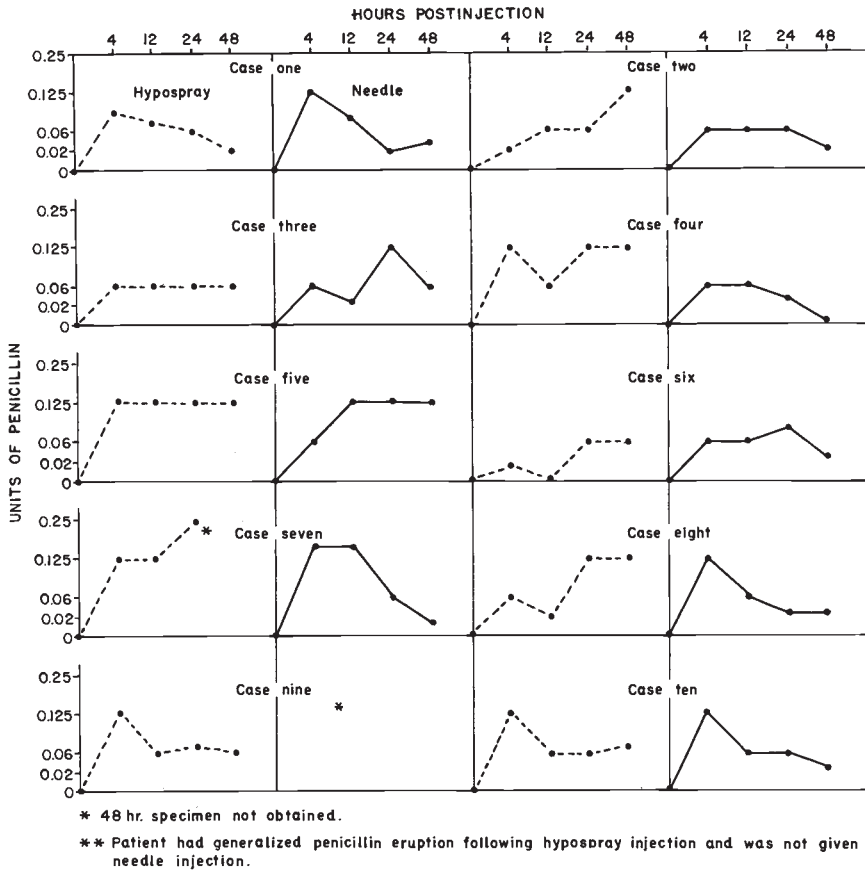


FIG. 1. Blood levels of penicillin following hypospray and needle injection of 300,000 units of PAM.

chosen since it is just above what is generally considered to be the minimum amount of aqueous penicillin necessary for successful therapy of early syphilis.

Previous determinations of blood levels of penicillin with Hypospray and needle administration have shown no essential differences in the case of aqueous penicillin preparations. However, since no similar data for PAM were available, 10 subjects (not necessarily syphilitic) were given 300,000 units of PAM by needle and by Hypospray at intervals of no less than one week and blood penicillin determinations made after 4, 12, 24 and 48 hours following each injection. These

studies were performed by Dr. Jan Schwarz of the Department of Pathology and Clinical Laboratories of the Jewish Hospital, and the method of Randolph, Price, and Welch was employed in determining blood levels of penicillin (8). This data showed that while there was some variation from patient to patient, there were no significant differences in penicillin blood levels with Hypospray versus needle injection of PAM (Figure 1). Serial dark-field examinations for *Treponema pallida* were performed at somewhat irregular intervals from the lesions of 6 patients following the initial Hypospray injection of 300,000 units of PAM. The organisms could not be demonstrated in these preparations after 18, 16, 18, 9, 12 and 24 hours, respectively in these patients.

RESULTS

A total of 67 syphilis patients have been treated by means of Hypospray penicillin administration according to the plan outlined above. Twelve of these patients were lost from observation following completion of treatment and 10

TABLE 2  
*Follow up observation data, Hypospray penicillin therapy of syphilis*

DIAGNOSIS	NO. PATIENTS	LOST (NO FOLLOW UP)	FOLLOW UP OBSERVATION LESS THAN 3 MOS.			FOLLOW UP OBSERVATION 3-5 MOS.			FOLLOW UP OBSERVATION 6-9 MOS.			FOLLOW UP OBSERVATION 10-17 MOS.		
			STS			STS			STS			STS		
			NEG.	LESS THAN 8 DILS	RELAPSE	NEG.	LESS THAN 8 DILS	RELAPSE	NEG.	LESS THAN 8 DILS	RELAPSE	NEG.	LESS THAN 8 DILS	RELAPSE
SERO-NEGATIVE PRIMARY SYPHILIS	8	2	3			2			1					
SERO-POSITIVE PRIMARY SYPHILIS	8	1		1		2			3			1		
SECONDARY SYPHILIS	49	9	1	5		5	4		13	1	2	6	2	1
EARLY LATENT SYPHILIS	2						1*			1*				
TOTAL	67	12	4	6		9	5		17	2	2	7	2	1

\* Serologic titre less than pretreatment titre but greater than 8 dils.

have been followed for less than 3 months. The other 45 patients have been followed for periods of 3-17 months and 31 of these beyond 6 months (Table 2). There was healing of the primary and secondary lesions in all patients within varying periods of time and the disappearance of surface treponemes has been referred to above. 37 of the patients have remained seronegative or have attained seronegativity and in 13 the serologic titre had been reduced below 8 dils at the time of the last observation. In the two patients with early latent syphilis and pregnancy, the last follow up serologic titre was substantially reduced but not below the level of 8 dils. There were 3 observed relapses or reinfections in this series of patients. Two of these were serologic relapses which occurred at 6 and 9 months post-therapy respectively, and one was both a clinical and serologic relapse or reinfection which occurred at the 14 month level of post therapy observation.

## POST THERAPY SPINAL FLUID EXAMINATION

Because we routinely perform spinal fluid examinations in patients with early syphilis approximately 12 months after treatment, the number of fluids examined in this series was necessarily small. Only 12 fluids have thus far been examined in this group of patients but all have been completely normal with reference to cell count, protein content, Wassermann reaction and gold curve. It thus appears that in common with other penicillin schedules in early syphilis treatment, the ultimate incidence of neurosyphilis in these patients will probably be low.

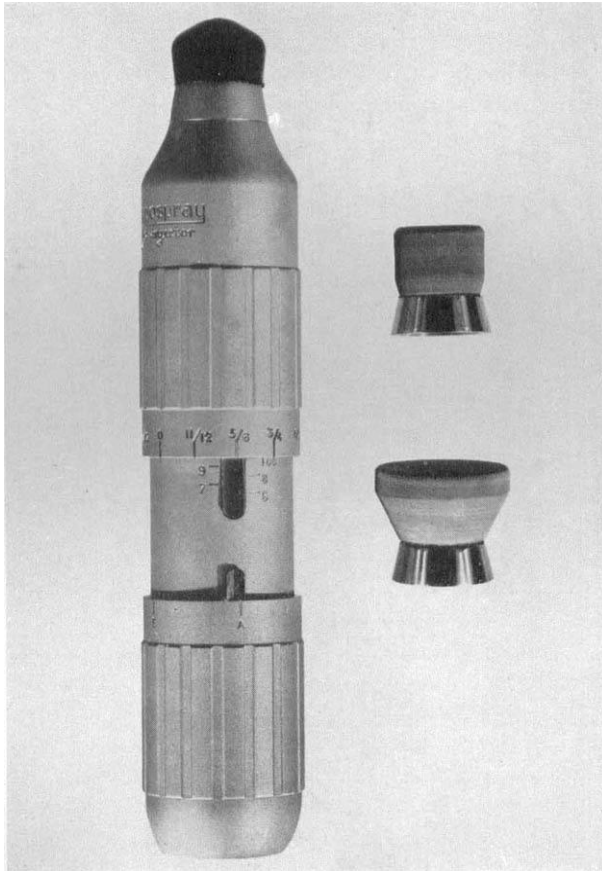


FIG. 3. The Hypospray jet injector

## REACTIONS

There was only one untoward treatment reaction in this series. This consisted of the occurrence of a generalized papulo-vesicular eruption following the 6th jet injection. In view of the character and severity of the eruption, penicillin therapy was suspended and a course of aureomycin installed. There were only 6 observed Jarisch-Herxheimer reactions in this series. These were of no particular interest except that this low incidence was somewhat surprising—especially so

since all these patients were hospitalized and carefully observed. No explanation is apparent. A few of the patients developed slightly painful subcutaneous nodules several days to one week after therapy. These nodules appeared to be the result of faulty technic of the operator in administering the injections and disappeared within a few weeks in all instances. (Previous reports as well as our own experience indicates that firm, maintained pressure with the Hypospray instrument will prevent the formation of such lesions.)

#### SYPHILIS OF PREGNANCY

Five pregnant patients were successfully treated by Hypospray penicillin injections. In two mothers with early latent syphilis the therapy was given in the third trimester. One of these patients had had antisypilitic therapy two years previously but was still seropositive. There were three patients with secondary syphilis and pregnancy. None of these had received prior treatment. Jet penicillin injections were begun in the first trimester in one patient, and in the second and third trimesters respectively in the other two. A viable, clinically normal and seronegative child was delivered in all five cases and the infants' serologic tests remained negative beyond three months of age.

#### SUMMARY

1. 67 patients with various types of early syphilis have been treated with injections of procaine penicillin in oil with 2% Aluminum Monostearate administered by jet injection. Most of these patients received only 9 daily injections of 300,000 units (total dosage of 2.7 million units).

2. 45 of the patients have been followed for 3-17 months and 31 for more than 6 months. Healing of lesions and disappearance of surface treponemes occurred in all patients and the serologic response to treatment has been comparable with penicillin therapy administered by needle. There have been three observed clinical or serologic relapses or reinfections among these patients.

3. Comparison of blood levels of penicillin with PAM administered by needle and by Hypospray failed to disclose significant differences.

4. Pain incident to penicillin syphilis therapy has already been minimized through the use of less frequent and larger doses of PAM. This report is therefore concerned with further establishing the general value of the jet injection technic in medical practice rather than in advocating Hypospray penicillin therapy for general usage to obviate the pain of needle injections. The advantages of the Hypospray method for therapy of syphilis in children and "needle shy" adult patients is however obvious. Other actual or potential advantages of the Hypospray technic, include lessening of skin contamination with penicillin (where the operator is hypersensitive) and avoidance of contamination with the virus of infectious hepatitis.

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## ADDENDUM

Since this article was submitted for publication four patients with secondary syphilis originally listed as lost or followed for less than six months have returned to follow-up observation for periods of eight to sixteen months. All of these patients are now sero negative.

In extended follow-up observation of other patients in this study a number have become sero negative and no additional clinical or serologic relapses have been noted.