# PRELIMINARY STUDY OF THE HYPOSPRAY FOR PARENTERAL THERAPY IN ITS RELATION TO THE MANAGEMENT OF LEPROSY\*

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In 1947 Figge (1), an anatomist, and Hingson and Hughes (2) began a study with a new instrument for parenteral injection. This instrument was developed by the R. P. Scherer Corporation of Detroit upon a basic patent of Lockhart, a diesel engineer. This instrument has been called the "hypospray."

In its present form (Fig. 1) the hypospray is of the size of a two-cell flashlight, activated by 125 pounds of spring pressure which is projected against a small rubber disc plunger 0.5 cm. in diameter, which in turn is propelled into the butt end of a bullet-sized medicinal container called a "metapule." This container, which is made of nickel, holds .25 cc. of solution. The sterile metapule of medicament is kept free from contamination by an outer encasing jacket of aluminum (Fig. 2). Other forms of the instrument have been devised which inject 1 cc. of medication or any fraction thereof in units of 1/100.

According to Pascal's law, when the 125 pounds of spring pressure is released against the small (0.5 cm.) rubber target there is momentarily built up within the metapule a pressure of 3,900 pounds per square inch. This tremendous pressure propels the solution of medicament through an orifice in the nose of the "bullet" .003 inch in diameter—1/137 the size of a 26-gauge hypodermic needle, and approximately that of the proboscis of a mosquito. The solution leaves the orifice at a velocity calculated to be 600 miles per hour (Fig. 3). However, because of

\*Presented at the Fifth International Leprosy Congress, April 6, 1948. Published by authority of the Surgeon General, United States Public Health Service. the microscopic size of the orifice the pressure exerted on the skin surface which is brought into apposition with the metapule (Fig. 4) is only 11 gm. This is about twice the amount of pressure needed for so fine a jet to pierce the skin and subcutaneous fat (Figs. 5 and 6).

This new instrument creates the basis for a potential revolution of present-day methods of parenteral therapy. Its advantages are the following: (1) the complete absence of pain in one-half of the subjects so injected, and the diminution in pain in the great majority of the others; (2) the mechanical preparation and protection of the metapules, which make sterilization of the instrument before use unnecessary; (3) the tested fact that children do not fear the instrument as much as they do the syringe and needle, when they are approached for a first injection; their actual experience with one injection convinces them that subsequent injections will be painless or nearly so; (4) in the field of pediatrics and in military immunizations, the use of this instrument would save the time of multiple sterilizations of equipment; (5) for the administration, by daily injection over long periods, of drugs such as insulin, penicillin, streptomycin, liver extract and possibly promin, this instrument seems to be the one of choice.

The use of the hypospray in anesthesia has already been established at the Carville Marine Hospital in the instantaneous relief of excruciating nerve pains of leprosy. It can be used also in the preparation of a skin wheal and deeper infiltration prior to insertion of needles for block anesthesia. Already a controlled clinical study has been completed by physicians in the Venereal Disease Division of the United States Public Health Service, which proved that 97.5 per cent of 158 patients with established gonorrhea were cured with 200,000 units of penicillin administered by the hypospray, as compared to 97.9 per cent of 48 patients with gonorrhea cured by needle injection. Thus the therapeutic efficacy of the two technics are essentially identical.

#### USE IN THE INJECTION OF PROMIN

At the suggestion of Assistant Surgeon General R. C. Williams, the staff of the U. S. Marine Hospital at Carville, Louisiana, began the use of this instrument as an adjunct for therapy in leprosy.\* Because of the increased diffusion area of the medicament propelled through the hypospray (see Figs. 5

<sup>\*</sup> We were assisted in this project by Parke, Davis and Company and the R. P. Scherer Corporation.

and 6), we are begining the use of solutions containing 40, 20, and 10 per cent promin in vehicles of a 1 per cent procaine solution in the treatment of isolated and resistant lesions of leprosy. After it was determined, from injections made on the medical staff, that little or no tissue irritation resulted from even 40 per cent solutions of promin so injected, we have begun unilateral injections of promin into the ear lobe and under early and resistant lepromatous lesions. The other side of the patient is used as a control and receives no therapy except that derived from systemic absorption from the sites injected on the opposite side.

### USE IN THE NEURITIS OF LEPROSY

Of the complications associated with leprosy peripheral neuritis is usually the most distressing one since the pain is so intractable and does not respond readily to the widely employed medications. Because of a wider diffusion-spread of hypospray medicament, the 10 patients complaining the most bitterly of this complication were selected for an evaluation of this form of treatment. Most of them had bilateral, painful, palpable enlargement of the ulnar nerve; two had radial and medial nerve involvement. All had great difficulty in obtaining rest or sleep during the prolonged attacks, even when given usual sedative drugs. These pains, so commonly seen in leprosy, are described by the patients as constant, sharp and radiating, sometimes associated with a burning sensation along the entire distribution of the nerve.

The bullet nose of the metapule was depressed with about 10 pounds of pressure (Fig. 5) in the anatomical position of the nerve. At the point of maximum discomfort the trigger was depressed and 6 per cent procaine was sprayed through the skin into the region of the nerve. Within fifteen seconds all of the patients so treated admitted some relief, and within three to five minutes all pain had disappeared. Immediately upon relief of pain the cold, clammy hands or feet would become pink, warm and dry, with the vasomotor flush so often seen in conduction-nerve blocks of the sympathetic nervous system.

One of the male adult patients, who was actually crying with pain after several practically sleepless nights, was so relieved that he appeared to have been unshackled. He described his pain and the relief produced by the hypospray injection of procaine in the following way:

"On the morning of March 31st I came to the hospital suffering so much with both of my arms with the worst attack of nerve pain I ever had. Both of my arms were so sensitive that I could not let anyone touch them. My hands were burning like fire, yet they were cold. About three minutes after the 'shot' I was completely relieved of the pains and both of my hands were warm. The shot was given at 11:00 a.m., and there was complete relief until 10:00 p.m.; at that time the pain came back in one arm, not enough to bother me to say. Thanks to the shot, I am sure it is the best treatment I ever had. Three days later there is no pain."

The relief of pain achieved in these patients has lasted from one or two to several days. The pain which returned was declared, in most cases, to be less severe than the original one. These pains have been relieved a second or third time by further 6 per cent hypospray procaine injections. We are prepared to use, later, alcohol with the hypospray if necessary. It should be pointed out that, following these injections, the enlarged nerve trunks can be vigorously manipulated without discomfort even several days after injection, whereas before injection intolerable discomfort was elicited by light pressure from either the palpating finger of the doctor or wearing apparel.

# USE WITH ANTIBIOTICS

Among the most painful injections performed with a needle are those containing the antibiotics, penicillin and streptomycin. Since these drugs are usually injected every two to three hours for periods of days or weeks, many patients complain bitterly. At Carville the patients were enthusiastic in their descriptions of the comparative relief afforded them by the hypospray method. This fact has already been reported by the Venereal Disease Division of the United States Public Health Service (3) in the use of penicillin in the treatment of 216 patients with gonorrhea.

### USE IN SUPPORTIVE THERAPY IN LEPROSY

Since the incidence of infectious and metabolic diseases is perhaps more prevalent in patients weakened with chronic leprosy, the problems of injection therapy are greater for both patients and doctors treating them than in the usual population group. Some of our patients, because of the multiple promin injections they receive, have an abnormal dread of a needle; consequently, it has been an emotional relief to many of them who receive insulin, liver extract, and vitamins by hypospray.

### USE IN DENTISTRY

In a selected group of patients 6 per cent procaine in .25 cc. metapules was injected through the skin over the mental foramina, and through the gum into the region of the anterior palatine foramina. In none of the patients was there sufficient anesthesia to permit dental extractions. However, it is believed that with the use of the 1 cc. instrument the use of such blocks will be a practical dental procedure.

# MECHANICAL PROBLEMS

Following the injection study of Figge upon fresh cadaver material, we have tested 125-, 100-, and 75-pound spring pressures on patients with leprosy, varying in age from 8 to 78 years. X-ray photographs show that the 125-pound spring pressure projects the medicament for approximately one inch through the skin and subcutaneous fate to the fascia plane of the muscle. The material from a .25 cc. metapule spreads over an area of 4 sq. cm. This wide diffusion indicates the attractive possibilities in treating local circumscribed lesions of leprosy. The 100pound spring pressure is less than 75 per cent effective in the healthy adult, and penetrates to less than one-half the depth. However, in aged individuals with atrophic skin, and in certain ear lobe injections, this is the instrument of choice. The 75pound spring pressure is relatively ineffective in the adult, but should be used on babies and small children.

Since the orifice of skin penetration is so much smaller than that produced by hypodermic needles, there is much less trauma to the skin. Histological tissue sections have revealed no consequent trauma to underlying tissues. Intramuscular injections can be made with the 125-pound spring pressure hypospray if it is used on the volar skin surfaces, which are about one-half as resistant as the thicker dorsal surfaces. Indurated leprous skin macules are so resistant that it is more wise to inject the medicament at an angle toward the center from the polar side peripheries of the lesions.

# PRODUCTION PROBLEMS

Obviously the demand for such an instrument by the American medical profession is tremendous, and very soon it will be demanded by the profession throughout the world. The manufacturer has not yet released the instrument commercially because there are many envisioned improvements which would make the present one antiquated within six months. It is believed that the instrument will be available commercially for the American market within one year, and for the foreign market within 18 months. The packaging of medicaments in inert metallic containers will, for the present, be done exclusively by the Scherer Corporation, which is carefully assaying the pH values of a large number of drugs commonly administered by injection.

It is our belief that the hypospray instrument can be manufactured at a reasonable cost. A single instrument will outlast the life of several syringes and many needles. The metapules can be packaged at a cost of one to two cents each, exclusive of the cost of the drugs. Many drugs will remain stable and sterile under such packaging for months. Certain other drugs, however, such as penicillin, must be packaged once a week to maintain therapeutic potency. Both watery and oily medications can be used through the hypospray. However, suspensions with particle sizes larger than 25 microns can not be used in the present instrument.

We will draw no further conclusion in this preliminary report, except to say that the hypospray opens a new horizon to the medical profession generally, and to leprologists particularly, who are dedicated to the alleviation of human suffering.

#### REFERENCES

- (1) FIGGE, FRANK. Anatomical studies with hypospray. To be published.
- (2) HINGSON, ROBERT A., AND HUGHES, JAMES G. Jet injection in parenteral therapy. Anesthesia and analgesia, November-December 1947.
- (3) HINGSON, et al. The use of the hypospray in the evaluation of penicillin in the treatment of gonorrhea. Venereal Disease Information, March 6, 1948.

#### DESCRIPTION OF PLATES

Photographs by Dr. Frank H. Figge, Professor of Experimental Anatomy, University of Maryland School of Medicine, made in the laboratories of that university.

#### PLATE 7.

FIG. 1. Two lateral views of the hypospray, an instrument about the size of a two-cell flashlight which propels a microscopic jet of medication at a velocity of 600 miles per hour through the skin and subcutaneous fat. Between them are shown nickel metapules, small black rubber plungers, and a 75-micron wire projecting through the orifice of the metapule. A mosquito with a proboscis of about the same size, and 25,-26- and 22- gauge hypodermic needles at least 37 to 57 times as large as the micro-jet, are included for comparison.



PLATE 7

#### PLATE 8.

FIG. 2. Removal of the aluminum jacket from the sterile nickle metapule containing the medicament to be injected. This metapule is securely locked in the head of the hypospray.

FIG. 3. The micro-jet being projected from the orifice of the metapule, fixed in the head of the hypospray, photographed by indirect lighting.

FIG. 4. The technique of holding the skin taut before hypospray injection of 40 per cent promin through and under a leprosy lesion.

FIG. 5. X-ray photograph of diodrast injected by hypospray, spreading along the fascia plane of the triceps brachiae.

FIG. 6. Pattern of spread and depth of penetration of three .25 cc. doses of diodrast, injected with graded spring pressures (75 to 125 pounds) into the arm of a young adult with leprosy.



PLATE 8