

Clinical Studies with Jet Injection—Hingson and Hughes

## Current Researches in Anesthesia and Analgesia

OFFICIAL ORGAN OF THE INTERNATIONAL ANESTHESIA RESEARCH SOCIETY

Membership—Subscription Ten Dollars the Year in Advance

Volume 26

November-December, 1947

Number 6

### Clinical Studies with Jet Injection.\*

#### A New Method of Drug Administration.

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#### Introduction



THE BITE of a venomous snake, the poison arrow of primitive man, the whaling harpoon tipped with prussic acid,<sup>1 2 3 4</sup> and skin incisions for the reception of morphine paste<sup>2</sup> were the forerunners of a technique for injection therapy. In 1836 LaFargue<sup>5 6 7</sup> of France invented a needle-lancet trocar for the injection of substances under the skin. In 1839 Taylor and Washington<sup>2 8</sup> of New York began the practice of hypodermic medication by puncturing the skin with a lancet and forcing a solution of morphine under the skin with a lacrimal duct syringe. In 1853 Wood<sup>9</sup> of Edinburgh improved the Ferguson syringe and invented the hollow needle. Since this time other physicians too numerous to mention have made notable contributions and modifications of injection techniques. However ingenious these improvements have been, such as "L'Appareil Pravaz,"<sup>1 2 8</sup> Mathieu's "Seringue Decimale Hypodermique,"<sup>1 2 8</sup> the Luer Syringe,<sup>1 2 8</sup> and the Luer-Lok Syringe,<sup>1 2</sup> no fundamental change in basic principle of mechanical subcutaneous injection has been made since 1853.

#### Jet Injection Method

IT IS the purpose of this communication to present a clinical evaluation of a method of injection based upon an entirely new principle. This method, which we call jet injection, utilizes no syringe, no needles, and practically eliminates the objectionable feature of pain which is inevitably associated with all needle techniques.

The method is based upon the fact that extremely fine high pressure jets are capable of piercing the human skin without evoking the sensation of pain, or causing only slight pain. Sterile material for injection is placed within a metal ampoule which has a volume of 0.25 cubic centimeters. This so-called metapule, shaped like a blunt-nose bullet, has in its rounded tip a hole 0.003 inches in diameter. The butt end is closed with a rubber plug. The sterile metapule is encased in an aluminum container to avoid contamination before use.

Upon removal of the cap of the aluminum container, the metapule

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is locked securely in the front end of the injecting instrument, which is the size of a two-cell flashlight and contains a calibrated high tension spring, controlled by a release button on the back end. When the button is pressed, the spring is released to propel a metal plunger against the rubber plug in the butt end of the metapule. This forces the liquid contents of the metapule through the minute opening as a fine high velocity jet under pressures varying from 2300 to 3500 pounds per square inch, depending upon the instrument used. By means of a calibrated mechanism, any portion, from 0.001 cubic centimeters to 0.25 cubic centimeters, may



Fig. 1. Placing of injector in position so that blunt nose of metal metapule depresses the skin on posterior surface of arm with right thumb on the release button. Left hand has gripped medial surface of patient's arm so that skin over the lateral surface is taut.

be injected. The accompanying figures illustrate the instrument and the method of making the injections.

The instrument is being developed by a pharmaceutical firm. The basic anatomical studies were made on the cadaver and in the laboratory by Dr. Frank H. Figge<sup>10</sup> of the Department of Anatomy of the University of Maryland Medical School. In April 1947, he reported to the American Association of Anatomists that with the new device he had injected oil solutions, aqueous solutions and colloidal suspensions into cadavers and living subjects. The patients experienced practically no pain.

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### Studies with Adults

OUR JET INJECTION studies on adult patients were made by administering 0.25 cc. of 2 per cent procaine with 1:25,000 epinephrine at a pressure of 3500 pounds per square inch. In one group of patients the injections were made to anesthetize the skin preparatory to performing either caudal analgesia or spinal analgesia, and to determine pain response as compared to control injections made with a 26-gage hypodermic needle. In a group of volunteer subjects the injections were made purely to determine pain response. In one additional patient an unsuccessful attempt was made to produce intercostal and abdominal nerve block for cesarean section. Table 1 shows the results obtained in these studies on 118 subjects. The results were as follows: 60 patients (51 per cent) experienced no pain; 51 patients (43 per cent) experienced mild pain, but much less than the pain of a 26-gage hypodermic needle; 5 patients (4 per cent) experienced very slight pain associated with

TABLE 1  
Pain Response in 118 Adult Subjects Given Jet Injections of 0.25 cc. of 2% Procaine with 1:25,000 Adrenalin at 135 Pounds per Square Inch Pressure Compared to Pain of 26 Gage Hypodermic Needle Injections.

Purpose of Injection	No Pain Response	Mild Pain Response but Much Less Than Needle	Mild Pain with Skin Cuts	Failures—More Pain Than the Needle
Preparation for caudal analgesia	28	11	1	0
Preparation for spinal analgesia	12	2	0	0
Preparation for local analgesia cesarean section (intercostal n. block)	0	0	0	1
Test injections*	20	38	4	1
Totals	60	51	5	2

\*Test injections made on doctors in postgraduate anesthesia course.

superficial minor skin cuts; and 2 patients (2 per cent) felt more pain from the jet injection than that of a 26-gage hypodermic needle. The slight skin cuts in the epidermis occurred when the instrument was being used for the first time. Such cuts were eliminated in subsequent patients when the skin was allowed to dry from the alcohol cleansing before the jet injections were made. In 5 patients (4 per cent) slight ecchymosis occurred beneath the site of injection. These patients were also among the first injected. No further instances of discoloration were noted when the skin was allowed to dry before the injections were made. Figure 2 shows positions of the jet injector for anesthetizing the skin preparatory to insertion of lumbar puncture needle.

### Studies with Children

OUR JET INJECTION studies on children were made by injecting 0.25 cc. of the material used at 2300 pounds per square inch pressure. The pediatric cases were studied chiefly from the standpoint of depth of penetration and pattern of spread of the injected material. The most interesting case was that of an 11 year old diabetic girl who was kept

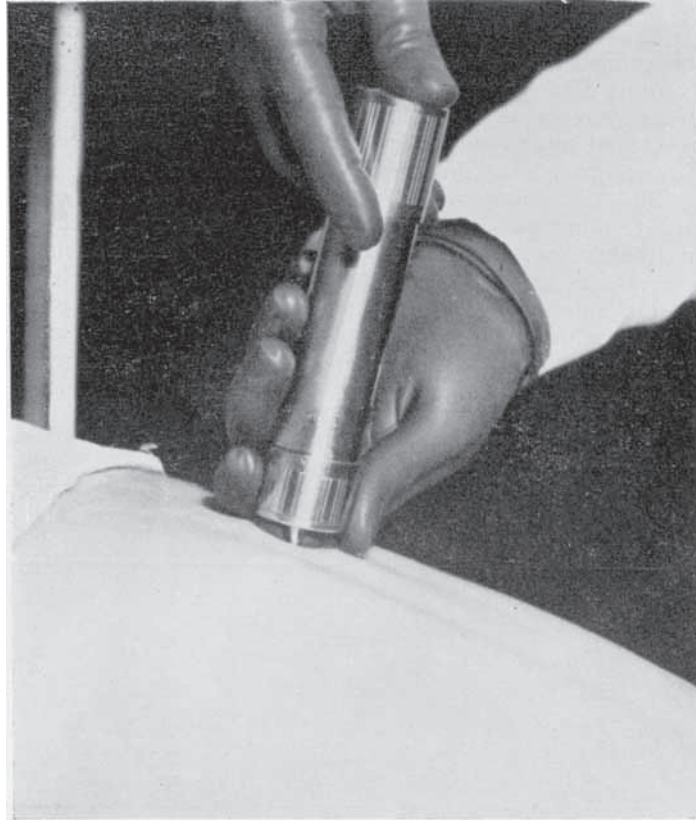


Fig. 2. Correct position of jet injector between the third and fourth lumbar spines for raising skin wheal preliminary to insertion of lumbar puncture needle.

under good control for two weeks without any pain by giving insulin by jet injection. Another pediatric patient, an infant 11 months old, appeared to have obtained a satisfactory intercostal nerve block by the jet injection method.

#### Depth of Injection and Pattern of Spread

**T**HE DEPTH to which material administered by jet injection penetrates the tissues depends upon the pressure of the jet and the resistance of the tissues, especially the skin and fascial sheets. The pressure of the jet varies from 2300 to 3500 pounds per square inch, depending upon which of the instruments is used. The resistance of the tissues varies chiefly with age, for the skin and fascial sheets become thicker as the individual grows older.

We have determined the depth of penetration and the pattern of spread of material administered by jet injection by injecting diodrast into

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living subjects and methylene blue into individuals at the moment of death. Anteroposterior and lateral roentgenograms were made immediately after the injection of 0.25 cc. of 35 per cent diodrast under a pressure of 2300 pounds per square inch. All of the patients in this series were normal, full term, newborn infants. The sites of injection were the triceps area (fig. 3), the anterior thigh area a few inches above the knee (fig. 4), and the lateral thigh area a few inches above the knee. Table 2 shows the results obtained by the diodrast-roentgenogram method. In 5 newborn infants, 0.25 cc. of methylene blue was injected at a pressure of 2300 pounds per square inch at the moment of death, before there could have been major postmortem changes in the resistance of the tissues. At postmortem examination dissections were made to determine penetration and pattern of spread. Table 3 shows the results obtained in this series.

From these studies in a limited number of cases, it appears that materials injected into newborn infants at pressures of 2300 pounds per square inch penetrate approximately 0.5 to 1 cm. in the triceps area, 1 to 2 cm. when injected in the buttocks, and only 0.2 to 0.3 cm. when

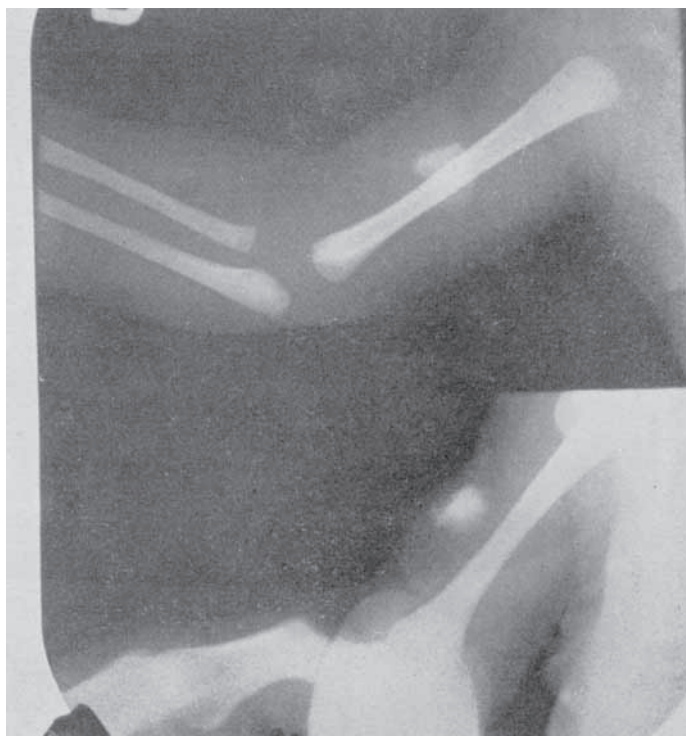


Fig. 3. Roentgenogram of dispersion shadow cast by 0.25 cc. of 35% diodrast injected under 2300 pounds per square inch pressure into triceps area of newborn infant.

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TABLE 2  
*Depth of Penetration and Lateral Spread of Diodrast Given by Jet Injections to Newborn Infants.\**

Case No.	Age	Weight	Area	Penetration	Spread
1	3 days	3200 grams	Triceps	0.5 cm.	1 x 1 cm.
2	3 days	3350 grams	Triceps	0.4 cm.	1 x 1 cm.
3	4 days	3350 grams	Triceps	1 cm.	1 x 1 cm.
4	4 days	3150 grams	Triceps	0.5 cm.	1 x 1.5 cm.
5	4 days	2500 grams	Triceps	0.5 cm.	1 x 1.5 cm.
6	4 days	3380 grams	Ant. thigh	0.3 cm.	1 x 1 cm.
7	3 days	3000 grams	Ant. thigh	0.3 cm.	1 x 1.5 cm.
8	4 days	2500 grams	Ant. thigh	0.2 cm.	1 x 1.5 cm.
9	4 days	3750 grams	Lat. thigh	0.3 cm.	1 x 1 cm.
10	4 days	3400 grams	Lat. thigh	0.3 cm.	1 x 1.5 cm.
11	4 days	3540 grams	Lat. thigh	0.3 cm.	1 x 1 cm.

\*All injections done with 0.25 cc. of 35 per cent diodrast at 2300 pounds per square inch pressure. Anterior, posterior and lateral roentgenograms made immediately after injection.

injected into the anterior or lateral thigh surfaces. The presence of the fascia lata is believed to be the reason why materials injected into anterior and lateral thigh areas fail to penetrate more deeply.

In the triceps, and in the anterior and lateral thigh areas, the material appears to spread over a diameter of 1 to 2 cm., while in the buttocks it is dispersed more widely. One full term stillborn infant was injected in the buttock immediately after birth with 0.25 cc. of 35 per cent dio-

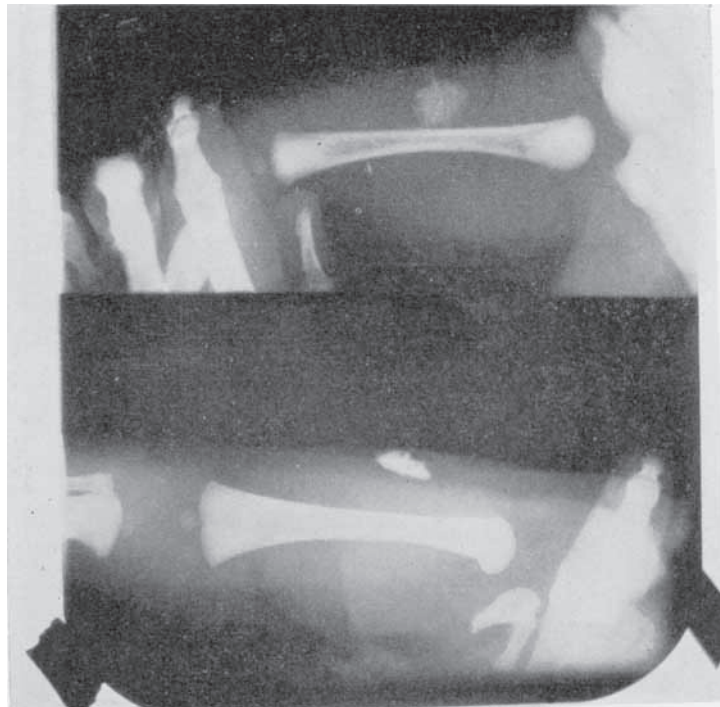


Fig. 4. Roentgenogram of dispersion shadow cast by 0.25 cc. of 35% diodrast injected under 2300 pounds per square inch pressure into lateral thigh of newborn infant.

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TABLE 3  
*Depth of Penetration and Lateral Spread of Methylene Blue Given by Jet Injection to Infants at Moment of Death.\**

Case No.	Age	Weight	Area	Penetration	Spread
1	1 day	810 grams	Buttock	2.5 cm.	2.5 x 2.5 cm.
2	6 weeks	3110 grams	Triceps	1 cm.	1.5 x 1.5 cm.
3	2 weeks	4250 grams	Buttock	1 cm.	2 x 2 cm.
4	1 week	3170 grams	Buttock	2.5 cm.	6 x 6 cm.
5	5 hours	3600 grams	Buttock	1 cm.	2 x 2 cm.

\*All injections done with 0.25 cc. methylene blue at 2300 pounds per square inch pressure immediately after death.

drast at 3500 pounds per square inch pressure. The roentgenograms showed that the material penetrated for a depth of 3.5 cm. to encircle the head of the femur. This indicates that such a pressure is much in excess of what is required for ordinary jet injections in the newborn.

### Control of Diabetic Patient

ONE of the most interesting possibilities in the use of jet injection is in the field of diabetes. The fact that insulin may be injected with practically no pain by means of this method is a prospect which has great



Fig. 5. Jet injection of protamine insulin in diabetic girl. The patient was controlled in this manner without pain for a trial period of two weeks.

potentialities and deserves a more extensive and detailed investigation. We have kept an 11 year old diabetic girl under control by the use of protamine insulin with the method of jet injection (fig. 5). The metapules used contained either 10 units or 20 units of protamine insulin. The injections were made chiefly in the anterior surfaces of the thighs, with the sites of injection being altered daily.

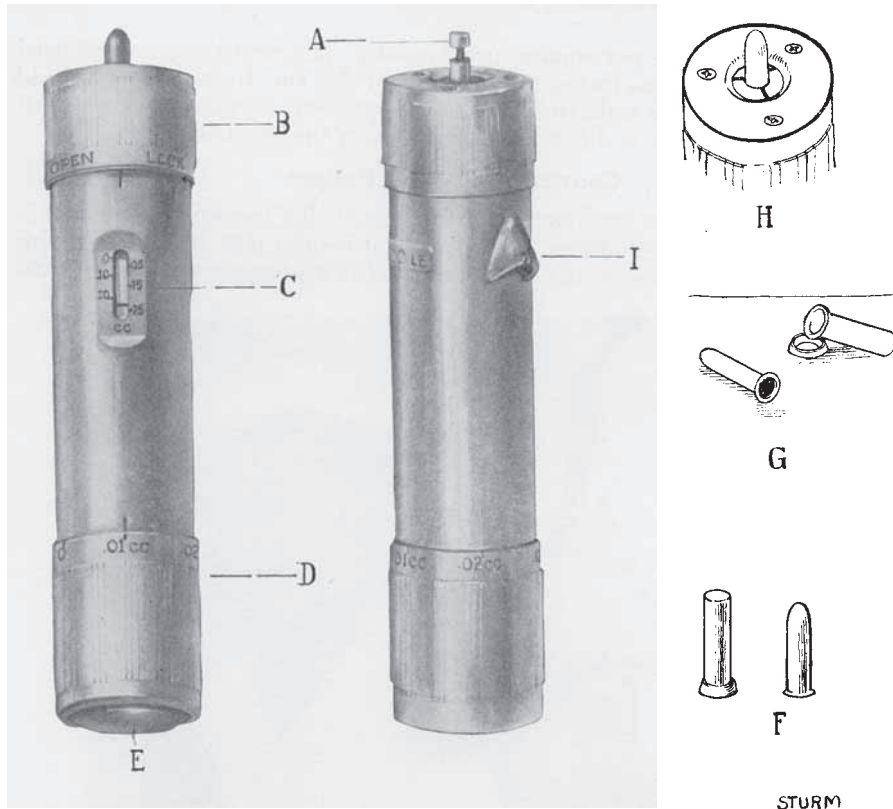


Fig. 6

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| <p>A. Metallic metapule ejector and plunger.<br/>         B. Metapule ratchet lock.<br/>         C. Gross micrometer gage graduated for dispensing solution from 0.05 cc. to 0.25 cc.<br/>         D. Fine micrometer gage for dispensing medication from 0.01 cc. to 0.05 cc.</p> | <p>E. Release button.<br/>         F. Capped aluminum container and metapule.<br/>         G. Container and metapule with rubber disk in back end.<br/>         H. Metapule in ratchet lock.<br/>         I. Cap remover of aluminum container G.</p> |
|--|---|

This patient was one of our first who was given jet injections, and for the first three days unfamiliarity with the new method led to certain technical errors. First, it was found that when the metapule was not tightly locked in the front end of the injector, some of the material remained on the skin, not having penetrated it. When the metapule was locked tightly in place, no grossly detectable amount of the drug remained



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on the surface of the skin. Secondly, when the injection was made while the skin was still moist with alcohol, there was a tendency for the blunt nose of the metapule to slip slightly, which led to the jet being directed at the skin from a slight angle. The result of this tilting of the instrument was the production of a superficial cut in the skin one-half centimeter long. After the arm had been allowed to dry from the alcohol application a firmer contact was achieved between the blunt nose of the metapule and the dry skin, and no further cuts were obtained. The third error observed was that when the instrument was lifted from the skin immediately after the release button had been pressed, some of the material was squirted over the surface of the skin, or raised an intradermal wheal. To prevent these errors in technique, the metapule must be locked tightly in the front end of the injector, the skin must be allowed to dry thoroughly, and the instrument must be held firmly against the skin for a period of two to three seconds after the release button has been pressed. When these precautions were observed, it was possible to control this diabetic patient without any pain from the jet injections during two weeks. Since, at present, 20 units of protamine is the maximum amount contained in the metapules at our disposal, it was necessary to give this particular patient two injections each morning in order to give her the 40 units of protamine insulin required to keep the diabetes under control. In addition, some regular insulin, the amount of which was kept constant, was given each morning, and the patient was on the usual dietary regulation which was not changed during the period of jet injections.

#### Intercostal Nerve Block in Infant

**W**HILE AN ATTEMPT to produce intercostal and abdominal nerve block by jet injections in an obstetric patient being prepared for cesarean section was not successful, it appears that the method was successful in an infant who received intercostal block for relief of apparent severe pain caused by pleurisy. Difficulty in interpreting the result stems from the fact the patient was only 11 months old. He was admitted with high fever, grunting, labored respirations, and distended abdomen, which was somewhat rigid. No friction rub was heard, but a chest roentogram showed evidence of thickened pleura. Subsequently, he developed clearcut physical and x-ray signs of pleural fluid, bearing out the admission diagnosis. Shortly after entering the hospital, when the symptoms mentioned above were present, jet injections of 0.25 cc. of 6 per cent procaine at a pressure of 2300 pounds per square inch were made inferior to the eighth through the twelfth ribs. In five minutes the baby began breathing much more easily, the grunting respirations ceased, and the abdominal rigidity decreased greatly. The baby went to sleep promptly.

#### Discussion

**T**HE HYPODERMIC SYRINGE has been so accurate, simple, dependable, and flexible for introducing a variety of substances under the skin, and is so universally employed, that any device intended to supplant it must demonstrate unquestioned merit.

In spite of the attractive possibilities of the new method of jet in-

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jection, especially its relative freedom from pain, there are certain possible disadvantages: (1) the cost of the instrument and the metapules; (2) the present limited maximum dose of 0.25 cc.; (3) the necessity for developing different inert metallic containers for different active drugs; (4) the possible injury to tissue from high pressure jet injections; (5) the relatively wider dispersion of injected material as compared with the needle-syringe method (This might prove to be a real disadvantage in the injection of toxoid, where slow absorption is desired. Fast absorption, on the other hand, might be a distinct advantage in the use of certain stimulant and analeptic drugs.); (6) the necessity of using less viscous solutions for certain medications, so that the solution will pass readily through the minute opening in the metapule; (7) the mechanical difficulties associated with maintaining this more technically complicated apparatus in operation.

The advantages are the following: (1) the complete absence of pain in half the subjects so injected, and the diminution in pain in the great majority of the other individuals injected; (2) the mechanical protection and preparation of the metapules, so that sterilization of the instrument before use is unnecessary; (3) the tested fact that children about to be injected do not fear the instrument so much as 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 time of multiple sterilizations of equipment; (5) for the administration of drugs by daily injection over long periods, such as insulin and penicillin, this seems to be the instrument of choice; (6) the use of the instrument in anesthesia appears to be limited to the preparation of skin wheal and deeper infiltration prior to insertion of needles for block anesthesia.

From our experience we believe the use of this instrument offers real promise to a medical profession dedicated to the alleviation of pain. Jet injection presents the first basic change in injection technique in almost one hundred years.

We wish to express our appreciation to the Resident Staff in the Department of Pediatrics who made most of the injections in children.

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