Jet Injection of Insulin During Self-Monitoring of Blood Glucose

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Insulin-dependent diabetes mellitus has been treated with four jet injections of insulin (regular insulin before each meal and intermediate insulin at bedtime) during self-monitoring of blood glucose levels. The blood glucose levels generally remain within 60 and 150 mg/dl. DIABETES CARE 1: 27–33, JANUARY–FEBRUARY, 1978.

It has been both proposed and denied that precise control of blood glucose in diabetes mellitus will prevent or defer the onset and progression of microangiopathy, with its possibily devastating effects on vision and kidney function.[1–16] However, with currently available treatment modalities, a commitment to control undue hyperglycemia and avoid hypoglycemia in insulin-dependent diabetes may not be attainable even with meticulous attention.

This preliminary report suggests that self-monitoring of blood glucose levels and four daily injections of insulin i.e. at bedtime and before each meal, are not unduly burdensome and usually improve the control of glycemia in juvenile- or young-adult-onset type of diabetes. The insulin was administered by jet injection rather than with syringe and needle.

MATERIALS AND METHODS

Patients in the program herein reported now measure glucose levels in capillary blood and take insulin by jet injection four times daily. Our first two patients are in the fifth and in the third year of the regimen, but they were started before the current protocol was developed and detailed data are not available. This report describes the next five patients who have just completed their first year on the program (table 1).

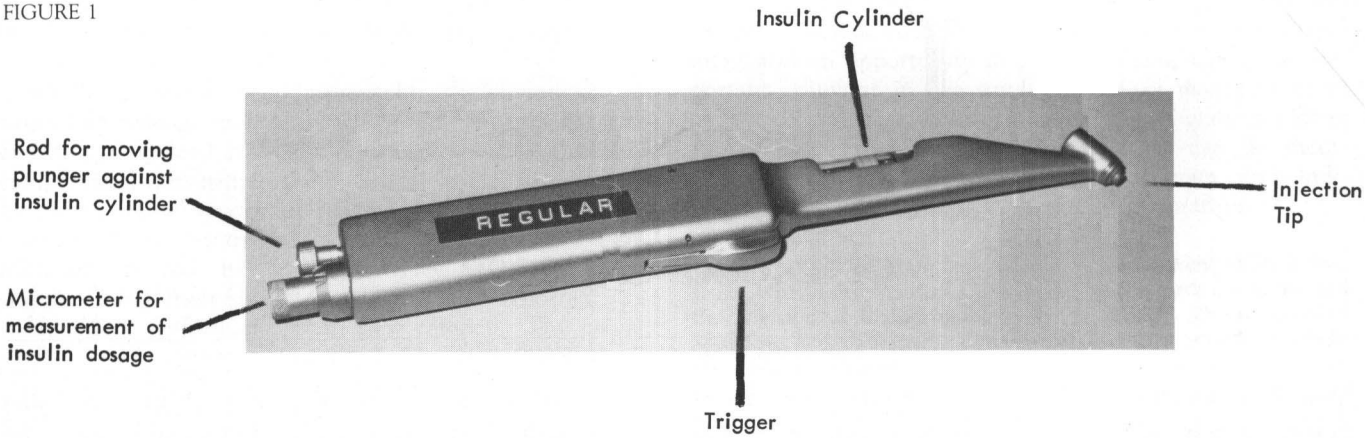
The patients were instructed in the use of Dextrostix and the Eyetone reflectance meter[17] to measure glucose levels in fingertip blood. When simultaneous measurements by the patients, nurses, a company representative, and by our laboratory indicated that they had become adept, they began to measure their before-breakfast blood glucose levels. They did so for approximately one month while taking their usual amounts of insulin injected by needle by syringe. During this month also, glucose was measured in venous blood[18] by the nurses and laboratory personnel in the course of two days before and after each meal and at 9 p.m., 12 midnight, and 3 a.m.

They were next taught to inject insulin with the Syrijet jet injection device (figure 1). The insulin schedule was then altered to include a bedtime dose of intermediate insulin and three before-meal injections of regular insulin. Blood glucose was measured each morning before breakfast and at one other time, i.e. after breakfast one day, before lunch another day, after lunch, before supper, after supper, and at bedtime. The cycle was then repeated. Also, at intervals, the patients monitored their blood glucose before and after each of the three meals of one day. They continued to test the urine for sugar and acetone one or more times each day.

The starting dose of bedtime NPH or other intermediate insulin was small, 2 to 6 U., with increases at intervals of one week until the fasting glucose level had decreased to approximately 120 mg./dl. The dose of regular insulin taken before each meal approximated one-third of the total daily amount administered previously by needle and syringe. The patients were then guided in increasing or decreasing the bedtime and before-meal dosages of insulin in accord with their self-monitored glucose levels. After several weeks they began to make these adjustments on their own.

Perforated filter paper was used to test for possible loss of insulin during jet injection. The aperture of the jet injector out of which the stream of insulin emerges at 2,900 psi was fitted into a hole in the center of a filter paper disc. A slight weal and a tiny pink dot at the site of injection and absence of a wet spot on the filter paper indicated that

FIGURE 1



the injection was complete. If the instrument was inadvertently lifted from the skin during the moment of injection, the loss was absorbed by the filter paper. The magnitude of the loss, if any, was estimated by weighing the filter paper before and after the injection. Losses of insulin become rare once the patient had perfected the injection technic; and, when present, limited to 2 per cent or less of the dose.

The patients kept a careful record of blood glucose, urine tests, and insulin administration and noted in writing such events as dietary excess or deficiency, increased or decreased physical activity, emotional stresses, respiratory infections, menses, symptoms of or actual hypoglycemia, etc. The patients were checked at weekly or more frequent intervals.

RESULTS

Blood glucose values prior to and after starting four daily jet injections of insulin in the five patients treated during the past year are shown in figures 3 through 7. For detailed explanation of the symbols, see figure 2.

Patient JBe, 24-year-old Male Hospital Worker (Figure 3)

On 68 units of insulin injected by needle, the blood glucose before and after meals, and at 9 p.m., 12 midnight, and 3 a.m. (jagged lines—"Needle Injection") ranged from 46 to 410 mg./dl.

While the patient was measuring his own glucose levels and injecting insulin by jet four times daily, the fasting glucose levels decreased to 100 mg./dl. or less (large dot: mean of seven daily fasting glucose values). The night calls of his hospital job were unusually frequent and interrupted his sleep during the 13th week, when the mean fasting glucose level rose to 215 mg./dl.

The before- and after-meal and the 9 p.m., 12 midnight, and 3 a.m. blood glucose levels (middle set of jagged lines) were between 60 and 210 mg./dl. during the eighth week and between 50 and 140 mg./dl. (third set of jagged lines) during the 20th week. Each letter "x" identifies the weekly mean of either before-meal, after-meal, or bedtime glucose levels (exclusive of the fasting sample) measured in sequence on successive days.

Urine examined one to three times daily contained zero to trace glucose once the hyperglycemia was controlled and was invariably acetone-free. Urine glucose excretion was 10 gm./day during the 22nd week.

The total insulin dosage during the 54th week of therapy was approximately 80 units. Four daytime and two nighttime hypoglycemic episodes occurred during this year of therapy, all explicable by delayed meals or night-call activity.

Patient KKa, 11-year-old Female (Figure 4)

On two injections of insulin per day by needle, the blood glucose ranged between 230 and 500 mg./dl. in 13 samples, with one other value of 112 mg./dl. (first set of jagged lines).

On four jet injections of insulin, the mean fasting glucose levels (solid dots) ultimately ranged between 85 and 130 mg./dl. The fasting glucose levels increased during a respiratory infection (URI) during weeks 15 and 16.

The daytime and evening levels were decreased between 100 and 140 mg./dl., when measured throughout one day (jagged lines at 25th week). Also, the weekly mean of before- or after-meal or bedtime blood glucose levels (one measurement each day in addition to the fasting level) indicated by the letter "x" decreased.

The 24-hour excretion of glucose decreased from 105 to 0.4 gm./day, and fractional urine specimens became glucose- and acetone-free.

Total insulin dosage had tripled. Hypoglycemic symptoms occurred once, at a time when the patient was unable to measure blood glucose levels.

Patient RSo, 14-year-old Male (Figure 5)

Fasting blood glucose levels (each solid dot indicates the mean of one week) decreased progressively to 100 mg./dl. by the 30th week as the jet doses of insulin increased to 92 units, almost twice the 50 units taken by needle.

The consecutive before- and after-meal and evening glucose levels ranged between 80 and 130 mg/dl (jagged lines—week 31) in contrast to 100 and 460 mg./dl. during needle injections of insulin. Also, the weekly mean of one of the daily before- and after-meal or before-bed blood glucose levels (each "x" indicates the mean of seven consecutive days) decreased progressively.

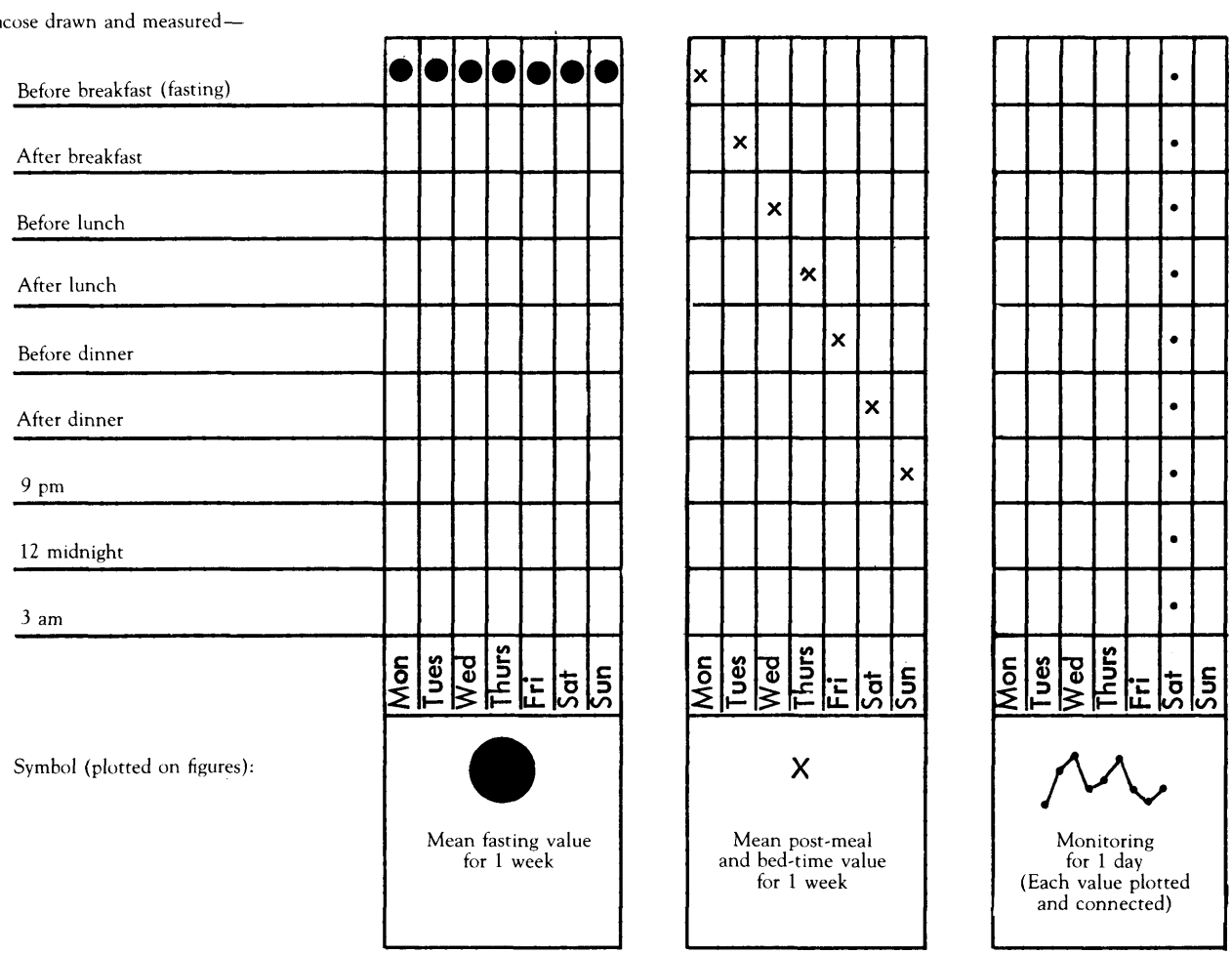
Urine glucose decreased to 33 gm. from a previous high of 282 gm./day. Acetonuria occurred twice early in the program.

Hypoglycemic symptoms occurred three times before breakfast after 2-½, 4, and 4-½ hours of strenuous basketball prior to bedtime.

Patient TRo, 14-year-old Male (Figure 6)

The blood glucose was as high as 450 mg./dl. during injections of NPH insulin by needle (initial set of jagged lines). The weekly fasting mean glucose levels (solid dots) decreased below 100 mg./dl. on approximately 90 units per day administered by jet injection, from a mean of 152 ± 13 during the first 27 weeks to 90 ± 9 during the next 23 weeks ($p < 0.001$). The consecutive daytime glucose levels ranged between 70 and 120 mg./dl. during the 51st week (fifth set of jagged lines). The weekly mean of before- or after-meal or bedtime glucose levels (indicated by x) decreased to normal, i.e. from 186 ± 73 mg./dl. during the initial 27 weeks to 124 ± 30 during the subsequent 23 weeks ($p < 0.01$). Urine glucose had decreased to 8 gm./day from initial value of 50 gm./day, and there was no acetonuria. Hypoglycemia occurred once at 3 a.m. following strenuous evening activity.

FIGURE 2



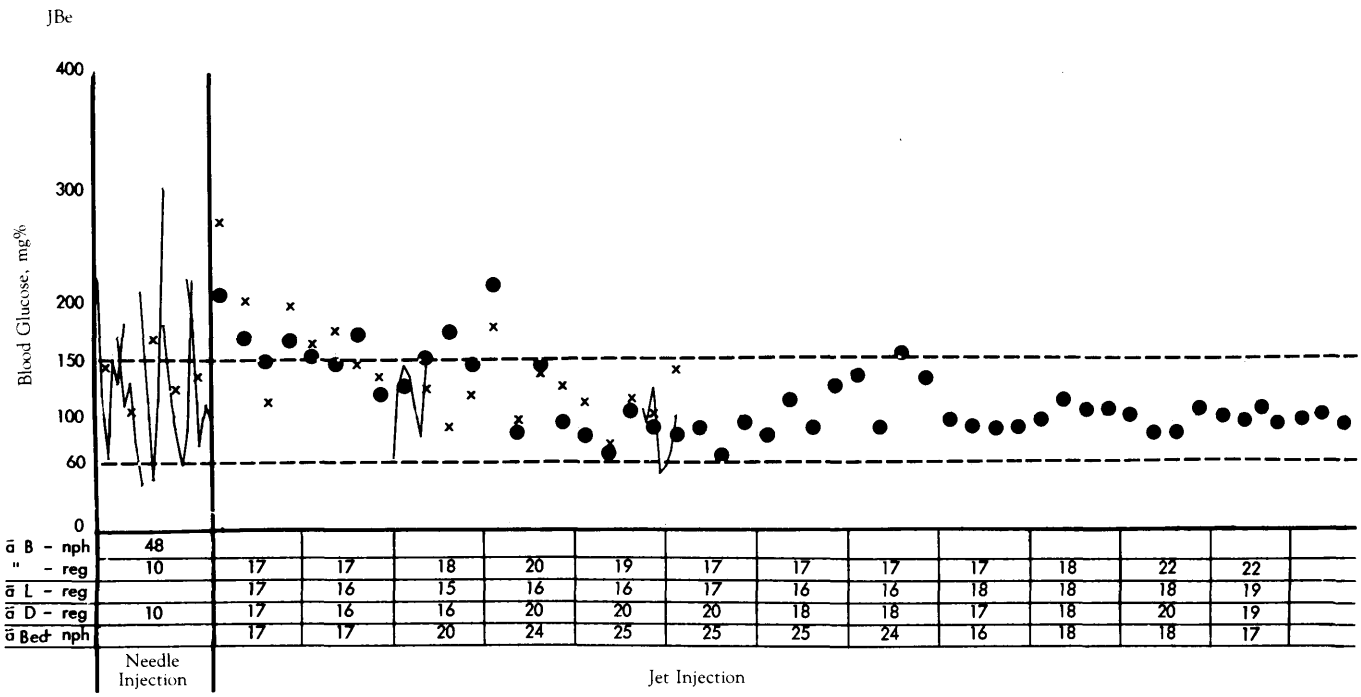


FIG. 3. JBe. During the first 13 weeks on the jet-injection program, the mean of the daily fasting glucose levels (each solid dot represents the mean of one week) was 155 ± 30 mg./dl. During the next 20 weeks it decreased to 101 ± 25 mg./dl. ($p < 0.001$). The fasting glucose levels remained in this range, viz. 104 ± 55 mg./dl., during the subsequent 13 weeks. A similar decrease occurred in the mean levels of blood glucose measured before and after meals on the schedule shown in figure 2.

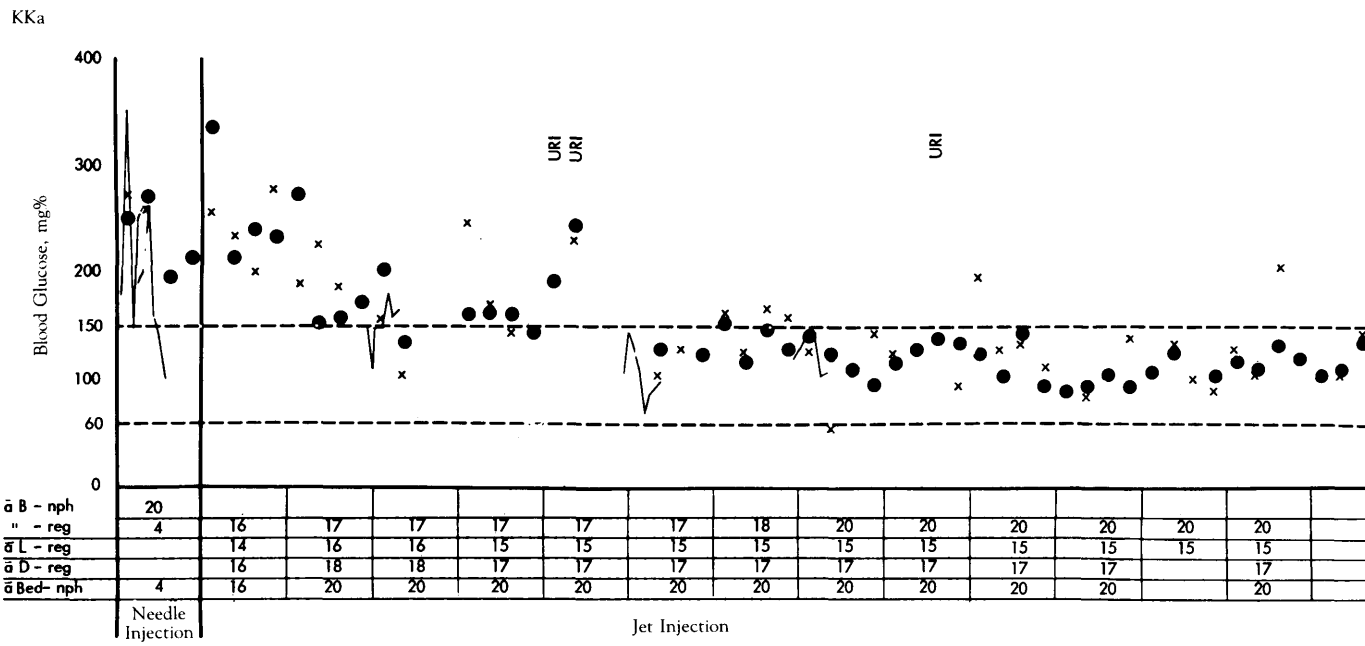


FIG. 4. KKa. In this 11-year-old female, the fasting glucose values (dots) decreased from a mean of 194 ± 52 mg./dl. recorded during the first 16 weeks to 119 ± 17 mg./dl. ($p < 0.001$). During these intervals, the daytime glucose levels (X) also decreased from 200 ± 48 to 124 ± 31 mg./dl. ($p < 0.001$).

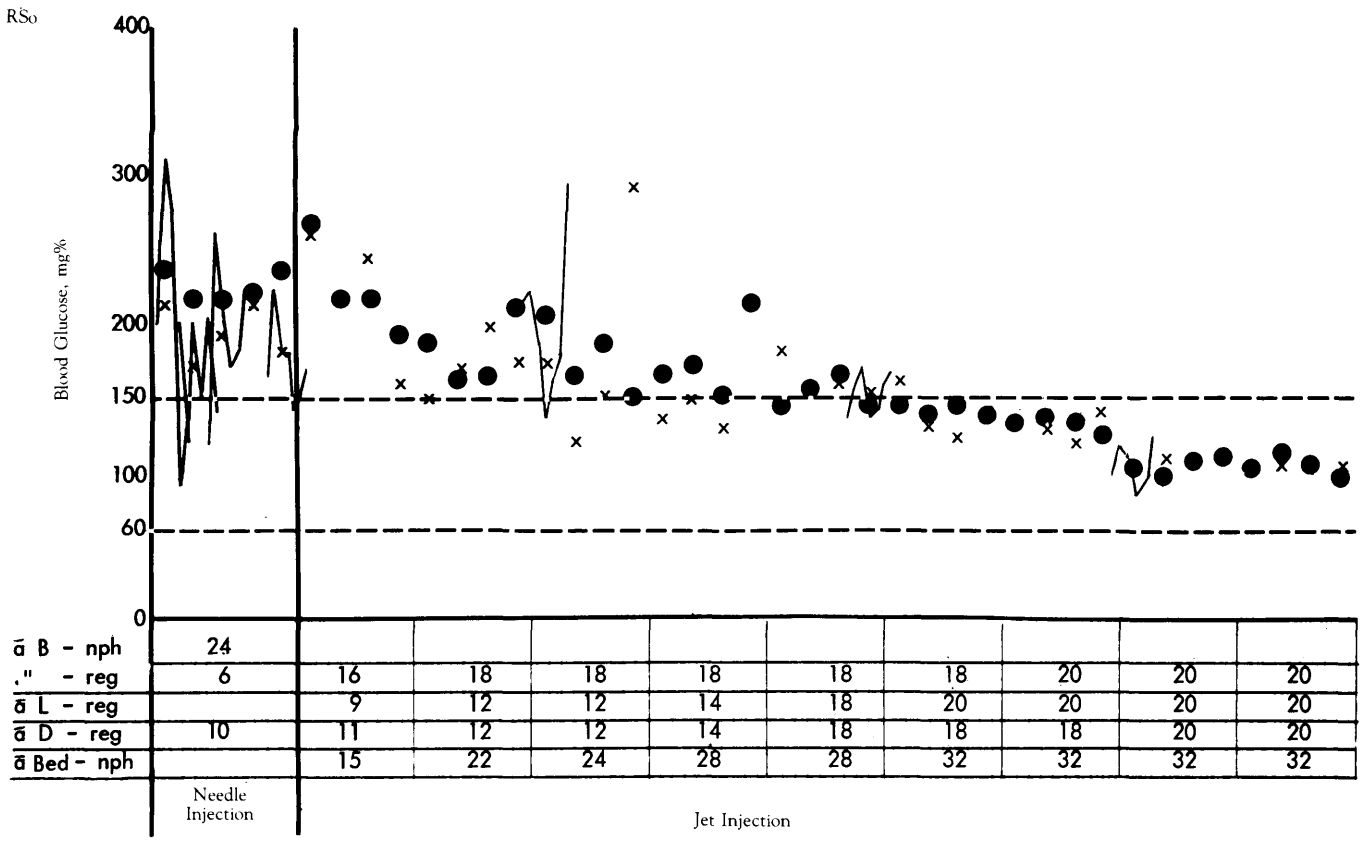


FIG. 5. RSo. During the first 20 weeks, the fasting glucose levels (dots) averaged 180 ± 31 mg./dl. They decreased in the succeeding weeks to a mean of 104 ± 5 mg./dl. during the last two months ($p < 0.001$). The daytime glucose levels (X) followed a similar course.

Patient VRo, 23-year-old female (Figure 7)

Mean weekly fasting glucose levels of about 110 mg./dl. appeared within eight weeks of starting four doses of jet-administered insulin. Daytime blood glucose levels at that time ranged between 70 and 160 mg./dl. (jagged lines—week 8) and urine glucose had decreased from a high of 74 gm. to 1 gm./day; there was no acetonuria.

She became pregnant during the third month of this program. Mean fasting glucose levels were high during week 14 when traveling interfered with diet and testing and during weeks 18 and 28 when she had a flu-type illness; but they also fluctuated inexplicably at other times. Delivery of a normal baby with birth weight of 6 lbs, 6 oz. was induced during the 35th week of gestation.

DISCUSSION

A program of self-monitoring of blood glucose while intermediate-acting insulin is injected at bedtime and regular insulin is taken before each meal offers promise of closer regulation of hyperglycemia but without hypoglycemia in insulin-dependent diabetes. Dextrostix and a reflectance meter (Eyetone) provide the patient with a ready means of estimating glucose levels in capillary blood. The administration of insulin by jet injection (Syrijet) lightens the burden of multiple doses of insulin by needle. To date acceptance of and compliance with the regimen has been high in most patients, and that this persists for a long time in at least some is evident from the continued enthusiastic use of these two instruments by two patients for three and for five years. In addition, the jet injector permits the use of previously inaccessible insulin administration sites. The cost of the instruments is offset in part by the decrease in trips to the laboratory to measure glucose and the reduced need for needles and syringes.

In our experience to date, the program, though ultimately relatively simple, requires detailed indoctrination. Thus, in measuring glucose levels, fingertip capillary blood is obtained each time with a new lancet, a stopwatch is used to assure exactly one minute of glucose oxidase

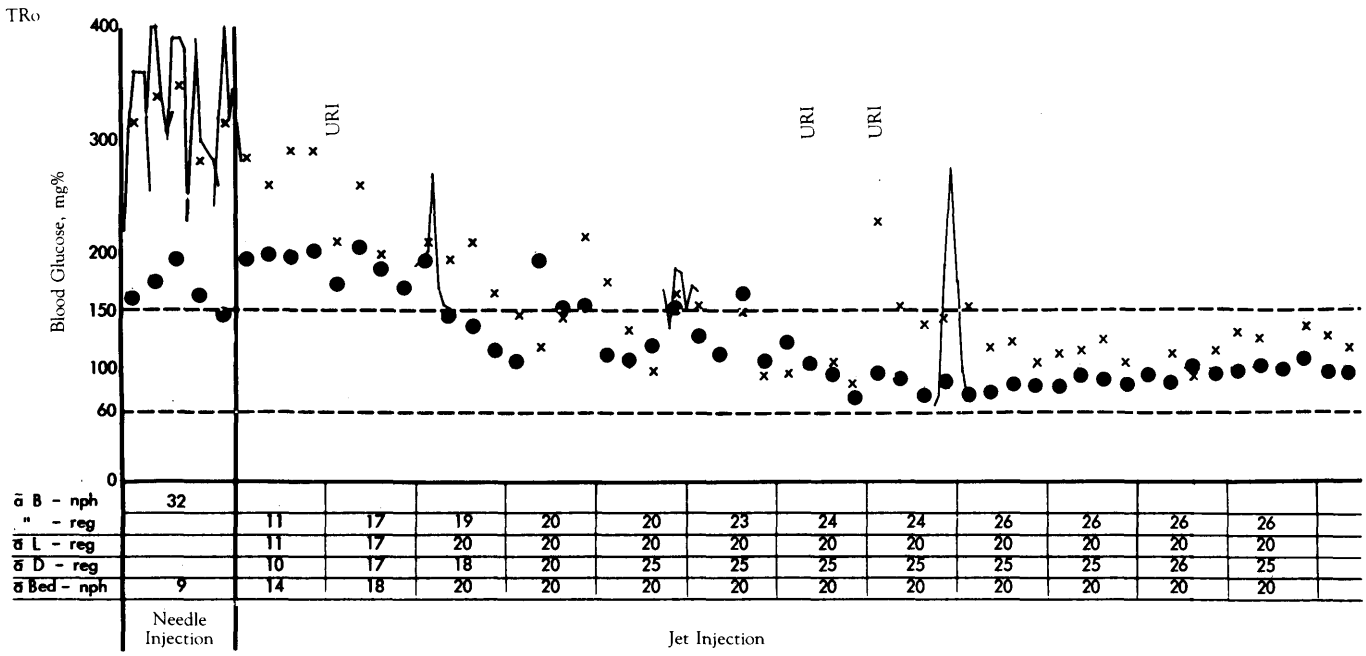


FIG. 6. TRo. In this 14-year-old male, the fasting glucose levels (dots) between the 28th and 51st weeks, inclusive, averaged 90 ± 9 mg./dl. while he was taking a total of 90 U. of insulin per day. The mean of daytime glucose levels (X) during this interval was 124 ± 30 mg./dl.

reaction time, and the Dextrostix is washed in a standard manner to achieve close agreement between the Dextrostix/Eyetone technique and other glucose-oxidase laboratory methods.[18]

The use, storage, and transport of the jet injector are simple provided care is taken to follow the instructions. The performance of the instrument in our patients has been in keeping with its excellent record of use in administering local anesthetics in medical and dental practice.[19,20] It does require the usual aseptic technique in preparing it for use, inserting the vial of insulin, and wiping off the tip of the injector. In administering the insulin, the tip of the jet injector rests against the skin firmly enough to indent the tissues approximately ¼ inch. To limit the injection to one tiny entry point and to avoid or minimize loss of insulin during administration, the trigger is pressed while care is taken not to allow any vertical, lateral, or other movement of the tip of the jet. Slashing motions are to be avoided.

Not all patients with insulin-dependent diabetes require multiple injections of insulin, a fact that can be established in candidates for the program during the initial weeks of self-monitoring of blood glucose levels while the patient continues with their usual one or two daily injections of insulin by needle. Also, not all patients on the program can be guaranteed better control of glucose at all times, because the intensity of diabetes can and does vary for known and unknown reasons. Moreover, it is obvious that as euglycemia is achieved, the possibility of inadvertent hypoglycemia is increased and must be guarded against. However, the experience with these patients suggests that the combined use of the glucose oxidase/reflectance meter technique to measure glucose levels and bedtime and before-meal jet injections of insulin usually moves the degree of control closer to the optimum.

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Aided by grants and/or instruments and supplies from John and Rosalind Redfern, The Pennsylvania Lions Sight Conservation and Eye Research Foundation, Mr. and Mrs. Nat J. Weiss, and, in memory of their husbands, Mrs. William Felger and Mrs. C. Bernard Shea: Mizzy, Inc., Ames Company, The Addison H. Gibson Foundation, and The Medical Research Foundation of Pennsylvania, Inc.

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ACKNOWLEDGMENTS: The authors cite with gratitude the cooperation of the patients and the dedicated services of Jean Denne, Donna Lees, and Rosemary O'Connor.

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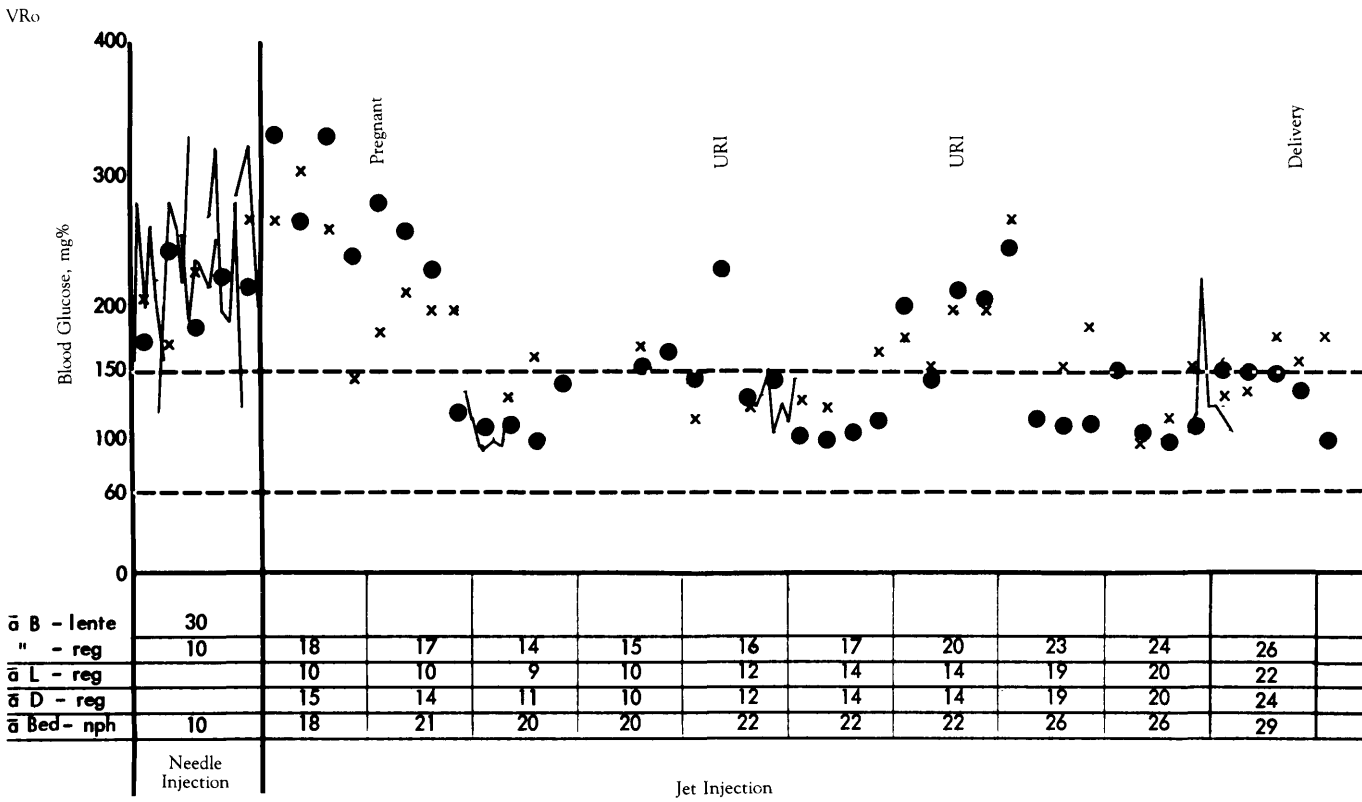

FIG. 7. VRo. This 24-year-old female became pregnant during the first seven weeks of the jet injections, when her fasting glucose values (dots) averaged 276 ± 42 mg./dl. During the next five weeks, they averaged 123 ± 13 ($p < 0.01$). Intermittent increases were then recorded during weeks 6 to 10, 24 to 29, and 38 to 43, but differences between the respective mean fasting glucose levels and that recorded during the first seven weeks remained statistically significant. The average daytime glucose values (X) followed a similar pattern.

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