The Effect of Epinephrine on Immunoreactive Insulin Levels in Man *

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The mechanisms by which epinephrine elevates the blood sugar have been of considerable interest for more than 25 years. In an extensive review in 1956, Ellis suggested that the two major influences on glucose metabolism were increased glycogenolysis in the liver and peripheral tissues, and direct inhibition of glucose uptake by muscle (1). There is, however, the additional possibility that epinephrine might decrease insulin levels. The introduction of insulin immunoassay (2, 3) has allowed us to examine this third hypothesis in man. Our data show that epinephrine infusion is not associated with a rise in serum immunoreactive insulin (IRI) despite significant hyperglycemia. In addition, epinephrine was found to inhibit the expected rise in IRI after administration of exogenous glucose, glucagon, and tolbutamide.

Methods

Volunteers selected were apparently normal, ambulatory, nonhospitalized, nonobese, young adult men and women. There were 13 men of ages 21 to 29, weight range 61 to 95 kg, and height 148 to 197 cm, and 6 women, of ages 21 to 31, weight range 51 to 65 kg, and height 160 to 179 cm. None had any history of major

medical illness. None had any close relative who was known to be diabetic. All were within 15% of their ideal body weight.[1] Approximately 20% had been previously tested at random with the 100-g oral glucose tolerance test and were normal by the criteria of Mosenthal and Barry (4). All had fasting plasma glucose less than 105 mg per 100 ml. For the study, no solid food was taken after the previous evening meal at 6 to 7 p.m., and no liquids except water were taken after midnight. No smoking was allowed on the day of the test. Upon arriving at the Clinical Research Center for study the volunteer was put to bed, and a slow intravenous 0.85% NaCl drip was begun through each of two indwelling venous plastic catheters. Blood samples were taken through one catheter, and drugs or glucose was infused through the other with a constant drive syringe infusion pump. No anticoagulants were given to the patient or were present in the sampling syringe.

Blood samples were obtained every 15 minutes and sampled for measurements of glucose, IRI, free fatty acids (FFA), and glycerol. Blood for insulin assay was allowed to clot for 1 hour at room temperature, and the serum was frozen at −19° C until analyzed by the double antibody immunoprecipitation technique (5). Neither epinephrine (1 μg per ml) nor tolbutamide (50 mg per ml) had any measurable effects when added to the immunoassay system *in vitro*. The glucagon preparation assayed 5 to 7 μU of immunoreactive insulin per microgram of glucagon. This amount of insulin was considered to have no significant effect upon serum IRI with the infusion rate of glucagon used (5 μg per minute). The human insulin standard was supplied.[2] Blood samples for FFA, glucose, and glycerol were anticoagulated with heparin and kept chilled at 4° C. The plasma was separated by centrifugation in the cold and frozen at −19° C for future analysis. FFA were titrated against standard base by a modified Dole procedure (6). Plasma glucose was measured by a Technicon autoanalyzer with a ferricyanide reagent. Glycerol was measured by the enzymatic method of Wieland (7) with commercially available glycerokinase and glycerophosphate dehydrogenase.[3]

TABLE I

The effect of epinephrine and glucose infusion on serum immunoreactive insulin (IRI) and plasma glucose

Immunoreactive insulin — µU/ml
Time, in minutes, after start of experiment

Subject	15	30	45	60	75	90	105	120	135	150	165	180	195	210
Epinephrine, 6 µg/min*														
T.C.	13	15	13	14	12	12	15	15	35	33	33	26		
M.O.	7	7	8	8	8	8	10	8	26	20		17		12
H.R.	10	14	15	11	10	8	12	14	82	71		50		17
M.C.	12	10	9	12	10	11	9	7	17	23	22	22		
R.R.	13	13	13	13	8	9	10	11	40	35	30	22		
Glucose, 300 mg/min*														
R.R.	4	9	8	14	16	23	22	21						
D.M.	11	11	14	12	20	22	23	23	25	20	17	13		
A.G.	10	10	8	8	12	16	19	22	17	11		8	9	8
P.L.	6	7	4	5	6	8	7	9	9	9		8	8	6
H.T.	3	3	4	4	8	8	13	10	7	5	7	1	7	3
D.S.	3	3	4	2	6	9	10	11			5	7	7	4
D.J.	13	12	13	13	17	20	21	20	14	13			12	12
H.R.	14	15	14	12	20	24	26	26	18	14			14	11
S.P.	9	7	7	8	18	25	30	31		9		6	7	7
W.M.		4	3	2	6	8	8	9	7	4		3	2	1

Plasma glucose — mg/100 ml
Time, in minutes, after start of experiment

Subject	15	30	45	60	75	90	105	120	135	150	165	180	195	210
Epinephrine, 6 µg/min*														
T.C.	99	101	99	96	116	139	158	167	165	156	138	125		
M.O.	90	87	89	85	106	134	153	151	160	151		124		102
H.R.	95	96	94	98	150	171	195	195	185	174		138		100
M.C.	87	92	92	88	111	140	154	158	166	158	147	136		
R.R.	102	94	93	98	130	159	162	165	166	161	139	122		
Glucose, 300 mg/min*														
R.R.	102	103	100	99	123	130	138	147						
D.M.	91	93	91	89	109	121	135	139	128	115	103	91		
A.G.	101	100	98	101	120	135	148	155	140	118		102	99	98
P.L.	90	92	90	86	95	122	129	139	131	125		110	103	97
H.T.	86	85	84	83	94	104	109	112	106	93	117	85	87	87
D.S.	99	96	96	96	114	134	142	147			84	92	87	88
D.J.	84	85	85	84	101	107	108	102	83	71			79	81
H.R.	94	93	92	92	112	121	131	124	108	92			89	85
S.P.	80	80	78	79	98	112	117	118		79		74	74	75
W.M.		84	83	84	105	116	125	130	118	104		88	85	85

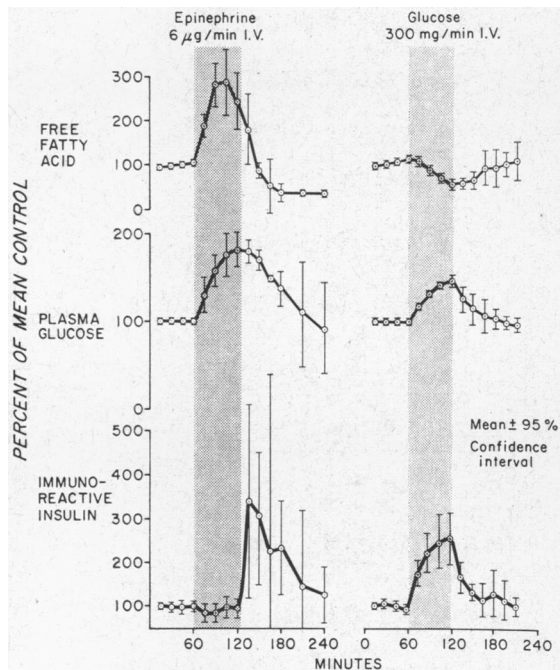* Infusion was begun at 61 minutes, terminated at 121 minutes.

FIG. 1. A COMPARISON OF THE EFFECTS OF EPINEPH-
RINE AND GLUCOSE. Five subjects were given epinephrine;
10 subjects were given glucose. Each pair of brackets
represents the 95% confidence limit of the mean value.
Brackets that do not overlap are significant at least at
the p < 0.05 level. For each study the mean of four con-
trol samples taken during the first hour is set at 100%,
and all values are compared with this mean control
value.

All drugs given to the subjects were commercially
available and included tolbutamide, 1 g per 20 ml;[4] glu-
cagon, 1 mg per ml;[5] and epinephrine, 1,000 μg per ml.[6]
When epinephrine was infused, it was protected against
oxidation by ascorbic acid (2.5 mg per ml of solution).

Results

The infusion of epinephrine, 6 μg per minute,
for 1 hour in five subjects resulted in a rise in
plasma glucose to a mean of 168 mg per 100 ml, or
180% above the basal level. Despite this rise in
glucose, serum IRI remained unchanged until af-
ter the infusion was stopped. Within 15 minutes
of stopping the epinephrine infusion, serum IRI
increased to a mean of 41 μU per ml from a mean
basal level of 12 μU per ml (Table I, Figure 1).
This rapid rise was maximal between 15 and 30

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[4] Upjohn, Kalamazoo, Mich.
[5] Crystalline glucagon, Eli Lilly Co., Indianapolis, Ind.
[6] Parke, Davis & Co., Detroit, Mich.

minutes. In a few selected patients the serum
IRI was always lower at 5 or 10 minutes than at
15 minutes after epinephrine was stopped. This
IRI response was compared to that obtained in 10
subjects with an infusion of glucose (300 mg per
minute) in an attempt to duplicate the plasma
glucose values found with epinephrine. Although
the mean plasma glucose in these 10 subjects was
lower at the end of a 1-hour glucose infusion than
at the end of the epinephrine infusion, there was a
significant (p < 0.05) rise in mean serum IRI for
all four samples taken during the glucose infusion.
This increase progressed to a maximum of 250%
above a mean control IRI of 7.8 μU per ml (Ta-
ble I). By inspection of Figure 1 it can be seen
that the mean IRI values during glucose infusion
are all significantly different from those during
epinephrine infusion. Thus, the hyperglycemia
associated with an infusion of 6 μg per minute of
epinephrine should have been sufficient to cause a
significant rise in serum IRI. Two other sub-
jects given prolonged infusions of epinephrine (6
μg per minute) for 4 and 7.5 hours showed similar
results. One of these is shown in Figure 2. De-
spite persistent hyperglycemia there was a mini-
mal, if any, rise in IRI until the infusion was
stopped, when the usual postepinephrine rebound
was found. In these studies, FFA clearly reached
an early peak and then declined during the infu-
sion to basal levels despite the stable insulin val-
ues, whereas plasma glycerol remained elevated
throughout the epinephrine infusion.

To determine the effect of epinephrine upon IRI
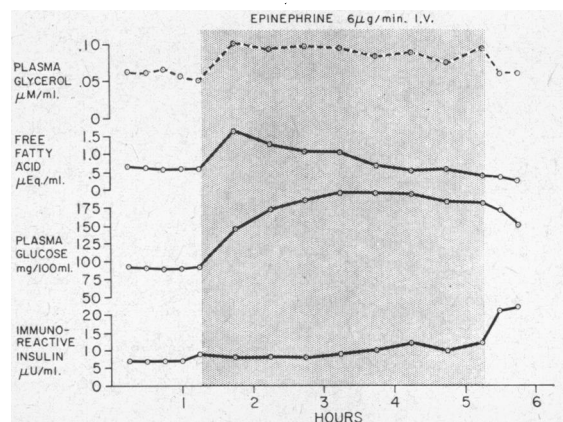when other means of elevating the plasma glucose

FIG. 2. THE EFFECT OF PROLONGED INFUSION OF EPINEPH-
RINE ON SUBJECT D.B.

or stimulating insulin secretion were used, we administered glucagon and tolbutamide. Each compound was given to each subject both with and without simultaneous epinephrine infusion.

Glucagon, 5 μg per minute, resulted in plasma glucose levels similar to those achieved with epinephrine, 6 μg per minute, but somewhat higher than those obtained with glucose, 300 mg per minute (Figure 3, Table II). In contrast to epinephrine infusion, the serum IRI was elevated during the glucagon infusion and declined after the infusion without a rebound. In contrast to glucose infusion, the serum IRI levels were much higher during the glucagon infusion, although both infusions were followed by a prompt return of IRI to basal levels. Despite the rapid decline in IRI after glucagon infusion each patient experienced a typical "hypoglycemic reaction" within 40 to 50 minutes. These reactions were characterized by subjective symptoms of nervousness and apprehension and accompanied by increased perspiration and tachycardia. They were coincident with the lowest plasma glucose and were followed by a prompt rise in plasma glucose and FFA (Figure 3, Table II). This type of reaction was not found after glucose or epinephrine infusions. When
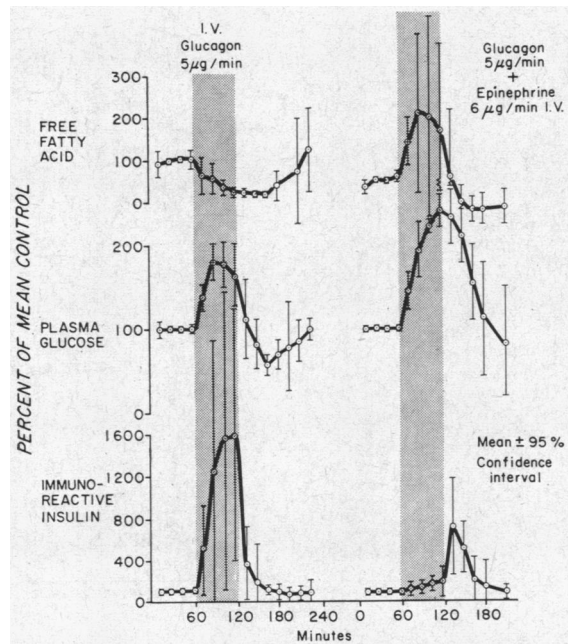

FIG. 3. A COMPARISON OF GLUCAGON INFUSION WITH GLUCAGON AND EPINEPHRINE INFUSION. The same four subjects were given both infusions. See Figure 1.

TABLE II

The effect of glucagon and glucagon plus epinephrine infusion on serum IRI and plasma glucose

Immunoreactive insulin (μU/ml) — Time, in minutes, after start of experiment

Subject	15	30	45	60	75	90	105	120	135	150	165	180	195	210
Glucagon, 5 μg/min*														
J.T.	3	2	3	3	16	32	47	55	19	8	8	5		4
D.P.	6	7	5	7	24	50	64	53	12	8	9	6	5	4
P.M.	10	10	9	9	20	32	72	103	30	15	11	11	10	9
M.W.	7	7	6	7	57	184	192	165	18	13		4	3	4
Epinephrine, 6 μg/min + glucagon, 5 μg/min*														
J.T.	5	5	6	5	10	9	10	15	60	39	35	17		7
D.P.	8	7	7	6	7	6	9	6	37	30		23		20
P.M.	8	9	8	8	10	14	13	14	42	34	19	13	6	10
M.W.	12	15	14	14	14	22	32	34	95	73	38	22		11

Plasma glucose (mg/100 ml) — Time, in minutes, after start of experiment

Subject	15	30	45	60	75	90	105	120	135	150	165	180	195	210
Glucagon, 5 μg/min*														
J.T.	90	103	103	104	127	161	184	184	152	110		73		89
D.P.	93	89	87	89	131	164	163	152	95	66	55	66	75	77
P.M.	99	94	95	92	130	179	185	166	108	76	58	50	52	63
M.W.	88	89	88	89	130	168	135	114	71	59	46	70	85	91
Epinephrine, 6 μg/min + glucagon, 5 μg/min*														
J.T.	96	102	101	102	128	171	218	255	256	222	178	146		110
D.P.	80	88	82	84	135	160	192	200	199	191		157		126
P.M.	94	92	91	90	134	216	247	256	200	187	130	94	63	55
M.W.	84	87	88	89	123	164	192	206	200	160	114	84		68

* Infusion was begun at 61 minutes, terminated at 121 minutes.

TABLE III

The effect of tolbutamide and tolbutamide plus epinephrine infusions on serum IRI and plasma glucose

Immunoreactive insulin
Time, in minutes, after start of experiment

Subject	15	30	45	60	70	75	80	85	90	95	105	120	135	150	165	180	210
1 g tolbutamide at 60 minutes (μU/ml)																	
C.H.	9	9	9	10	40		26		17		13	14		10	10		
D.K.	8	7	6	9	36		28		18		14	14					
D.B.	7	7	7	6	40		23		13		13	15					
M.W.	11	12	11	12	145		72		35		12	13			8	6	
S.S.	8	8	10	9	60		43		21		14	16			14	12	9.5
Epinephrine, 6 µg/min* + 1 g tolbutamide at 75 minutes																	
C.H.	8	7	7	7		7	14		12		12	15	28	22	17	12	10
D.K.	6	5	5	5		7	14		13		13	10	23	19		14	9
D.B.	5	6	6	10		5	13		10		11	10	28	20	13	30	6
M.W.	9	10	11	10		8	30		25		24	22	83	67	46	30	17
S.S.	7	8	8	8		8	18		22		18	17	65	59		32	21

Plasma glucose
Time, in minutes, after start of experiment

Subject	15	30	45	60	70	75	80	85	90	95	105	120	135	150	165	180	210
1 g tolbutamide at 60 minutes (mg/100 ml)																	
C.H.	96	98	96	100	94		84		74		69	69		83	82		
D.K.	78	85	85	87	76		41		31		55	69					
D.B.	95	95	96	89	89		73		64		53	65					
M.W.	96	96	95	95	82		50		35		56	66	75	75	79	77	76
S.S.	77	86	86	83	79		60		50		54	62		67			
Epinephrine, 6 µg/min* + 1 g tolbutamide at 75 minutes																	
C.H.	94	93	93	93		115			124		137	145	151	135	121	108	90
D.K.	79	79	78	75			127		136		134	126	118	86		78	57
D.B.	86	90	84	90		106	120		125		134	135	113		86	73	68
M.W.	89	92	93	91			130		153		157	173	177	152	129	86	58
S.S.	84	86	86	88			120		138		146	162	159	146	116	91	

* Infusion was begun at 61 minutes, terminated at 121 minutes.

glucagon, 5 µg per minute, and epinephrine, 6 µg per minute, were infused simultaneously into the same four subjects, the serum IRI response was significantly less during the infusion ($p < 0.05$ by paired comparisons for all four samples). When the infusion was stopped, the serum IRI levels rose in a pattern similar to that when epinephrine was given alone, and they were significantly higher than after a 1-hour glucagon infusion (Figure 3, Table III).

In an analogous fashion sodium tolbutamide, 1 g in a single iv injection, was given to five subjects on 2 different days. On 1 day epinephrine, 6 µg per minute, was infused for 15 minutes before and 45 minutes after tolbutamide, whereas on the other day tolbutamide alone was given. The insulin response was significantly diminished by the epinephrine ($p < 0.05$ for the 10- and 20-minute post-tolbutamide samples), and the usual pattern of rebound of IRI after termination of the epinephrine infusion was observed (Figure 4, Table III).
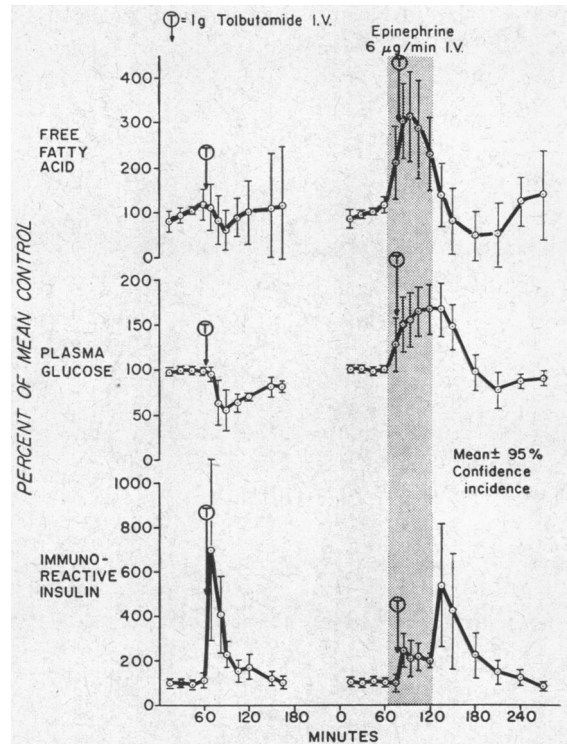
FIG. 4. A COMPARISON OF THE EFFECTS OF 1 G OF TOLBUTAMIDE GIVEN ALONE OR DURING AN EPINEPHRINE INFUSION. The same four subjects were tested twice. See Figure 1.

An attempt was then made to compare the effect of exogenous glucose upon the IRI response. This study was complicated by the much higher glucose levels when glucose, 300 mg per minute, and epinephrine, 6 μg per minute, were infused simultaneously into four different subjects. Complete inhibition of insulin rise was noted during the infusions in two subjects, but only partial inhibition was observed in the other two (Figure 5, Table IV). The partial inhibition was suggested by the observation that all subjects showed a large rebound of serum IRI after the infusions were stopped, with a peak between 15 and 30 minutes. In these latter studies, when both substances were infused, glycerol was measured to help distinguish between a fall in FFA caused by decreased lipolysis (decreasing glycerol) and that caused by increased uptake, re-esterification of FFA (stable or elevated glycerol), or both. This is based on the evidence that insulin lowers plasma glycerol, reflecting a direct inhibition of adipose tissue lipolysis (8–10). In the two individuals (D.K., M.O.) who showed no IRI rise during the combined infusions, there was a relative plateau of
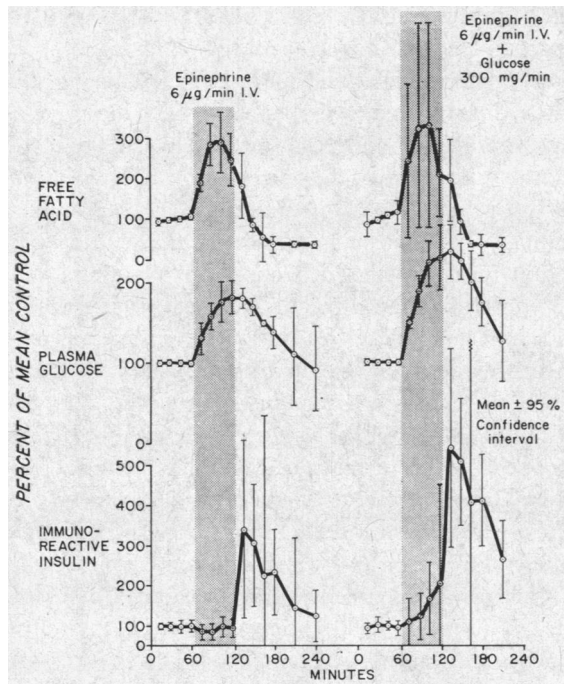

FIG. 5. A COMPARISON OF THE EFFECT OF EPINEPHRINE WITH EPINEPHRINE AND GLUCOSE INFUSION. Five subjects were given epinephrine; four different subjects were given both infusions. See Figure 1.

TABLE IV

The effect of simultaneous infusion of epinephrine and glucose on serum IRI, plasma glucose, glycerol, and FFA

Immunoreactive insulin
Time, in minutes, after start of experiment
Epinephrine, 6 μg/min + glucose, 300 mg/min*
μU/ml

Subject	15	30	45	60	75	90	105	120	135	150	165	180	195	210
D.K.	10	12	11	10	10	11		13	68	45	50	37	22	21
M.O.	7	7	8	7	8	8	9	9	34	44	32	37		21
C.H.	8	9	7	6	6	8	15	14	34	32	26	28		28
D.M.	10	11	12	13	19	21	27	36	70	66		49		

Plasma glycerol (μmoles/100 ml)
Epinephrine, 6 μg/min + glucose, 300 mg/min*

Subject	15	30	45	60	75	90	105	120	135	150	165	180	195	210
D.K.	7	7	7	6	24	28	25	13	5	5		5	4	
M.O.	5	7	7	6	17	21	18	12				6		5
C.H.	8	9	14	11	26	24	21	16	18	12	5	4		5
D.M.	10	8	5	7		17	16	9	10	8	6	5		2

Plasma glucose
Time, in minutes, after start of experiment
Epinephrine, 6 μg/min + glucose, 300 mg/min*
mg/100 ml

Subject	15	30	45	60	75	90	105	120	135	150	165	180	195	210
D.K.	87	85	81	80	120	163	202	210	222	198	162	134	105	130
M.O.	88	87	88	89	131	177	202	230	218	206	180	171		134
C.H.	91	89	89	89	136	179	210	225	220	200		166		112
D.M.	100	101	99	100	142	156	202	215	214	205		153		

Plasma FFA (μEq/ml)
Epinephrine, 6 μg/min + glucose, 300 mg/min*

Subject	15	30	45	60	75	90	105	120	135	150	165	180	195	210
D.K.	0.3	0.3	0.4	0.4	1.4	1.8	1.8	1.8	0.9	0.3	0.1	0.04	0.04	0.3
M.O.	0.6	0.8	0.8	0.7	1.4	2.0	2.0	1.7	1.6	1.4	0.4	0.8		0.3
C.H.	0.6	0.7	1.0	1.0	1.7	2.2	2.1	1.9	1.4	0.9		0.3		0.2
D.M.	0.8	0.7	0.7	0.7	1.0	1.3	1.6	1.2	0.9	0.5		0.4		

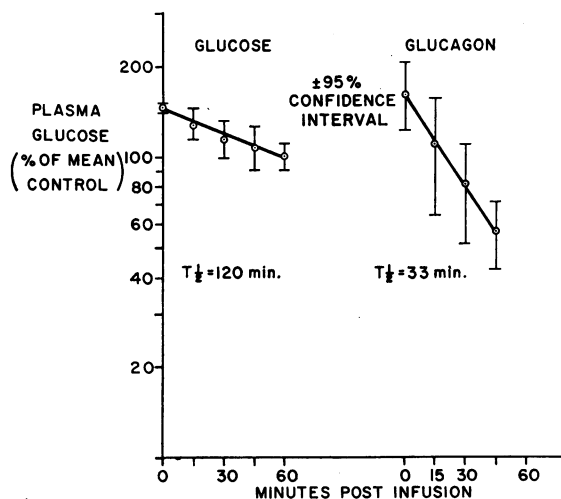* Infusion was begun at 61 minutes, terminated at 121 minutes.

FIG. 6. A COMPARISON OF THE MEAN RATE OF FALL OF THE PLASMA GLUCOSE AFTER A GLUCAGON INFUSION WITH THE RATE OF FALL AFTER A GLUCOSE INFUSION. $t_{\frac{1}{2}}$ = half-time.

plasma glycerol, whereas in the two subjects with a modest but definite rise in IRI during the combined infusions (C.H., D.M.) there was an early rise and then a decrease of about 50% in glycerol levels by the end of 1 hour, despite the continuing infusion of epinephrine (Table II).

Discussion

Epinephrine administration was associated with stable basal insulin levels despite hyperglycemia when given alone, and it inhibited the usual increases in serum IRI produced by exogenous glucose, glucagon, and tolbutamide. Those subjects with the greatest insulin responses to tolbutamide, glucose, or glucagon alone tended to be the same subjects in whom a partial response was still observed when such compounds were infused simultaneously with epinephrine. This indicates that the inhibition can be partially overcome by a sufficiently strong stimulus. Because of the variability in the magnitude of insulin responses in different subjects to any specific stimulus tested, a high degree of statistical significance was not always found in these studies. Therefore, caution must be exercised in the quantitative interpretation of results from one study. However, considered together, the pattern of responses was always the same when epinephrine was given, i.e., there was always a lesser increase in the IRI level during the

insulinogenic stimulus plus epinephrine infusion than was observed for the insulinogenic stimulus alone. Furthermore, a rapid postinfusion increase in IRI occurred in every experiment in which epinephrine was used either alone or with other compounds. This constant pattern, although not susceptible to statistical analysis, tends to reinforce the conclusion that epinephrine does indeed prevent or diminish an insulin response. The magnitude of the rebound after epinephrine was variable but appeared to be greater in those subjects with larger IRI responses to glucose, glucagon, or tolbutamide alone. The variation in individual response was not related to obesity (11) since none of the patients was obese, nor was it found to correlate well with sex, body surface area, height, or weight. No measurements of plasma epinephrine levels were made, and it is possible these might have correlated better with the degree of epinephrine inhibition. Such variations in the magnitude of a normal IRI response make it difficult to delineate a quantitatively pathologic response without a much larger experience with apparently normal population groups. However, the glucagon study was unusual in several respects. The IRI levels were higher than observed with glucose alone, all values for IRI during glucagon infusion were higher, and the 1-hour value was statistically different at the $p < 0.05$ level; more striking was the observation that each infusion was followed by clinically obvious hypoglycemia. This late hypoglycemic phase after glucagon infusion has been observed by others (12, 13) and, together with our IRI data, suggests that glucagon may raise insulin levels by some mechanism in addition to its hyperglycemic effects. Such an inference is supported by noting the rate of fall of the blood sugar after these infusions were stopped. The higher insulin values during a glucagon infusion were followed by a faster rate of glucose disappearance, whereas the lower insulin values during a glucose infusion were followed by a slower rate of glucose disappearance [half-time $(t_{\frac{1}{2}})$ = 33 minutes, glucagon; $t_{\frac{1}{2}}$ = 120 minutes, glucose; Figure 6]. These observations are consistent with the hypothesis that either more insulin is secreted or less insulin is degraded during a glucagon infusion than during a glucose infusion with comparable blood sugar levels.

The more prolonged epinephrine infusions indicate that epinephrine's suppressive effect on IRI levels can be maintained for hours. In addition we noted, as have others (14, 15), that after an initial rise FFA levels decline during continuous epinephrine infusions. This fall in FFA was attributed to the effects of insulin and glucose to re-esterify fatty acids in adipose tissue. The observation in our studies that glycerol levels remained elevated while FFA declined is consistent with low levels of insulin during epinephrine infusion, because it has been shown that raising insulin levels by exogenous insulin administration lowers glycerol levels (8, 10). If low insulin levels were present, declining FFA levels could still result from either increased re-esterification of FFA in adipose tissue by the high glucose levels alone, by increased peripheral uptake of FFA secondary to the cardiovascular effects of epinephrine, or by both.

The hypothesis that epinephrine inhibits the secretion of insulin was suggested as early as 1930 by Colwell and Bright (16) when they noted a low respiratory quotient during epinephrine infusions in cats. These early studies have been recently strengthened by studies *in vivo* in dogs, when pancreatic venous blood was biologically assayed for insulin after an epinephrine infusion (17), and by *in vitro* studies in rabbit pancreatic slices, when epinephrine was found to prevent glucose-stimulated release of IRI (18). Although this latter study suggests that the inhibition is a direct effect upon pancreatic beta cell function, several other possible mechanisms can be suggested. It is possible that circulatory changes associated with epinephrine may have been responsible for the effects upon insulin levels. In particular a decreased splanchnic or liver blood flow could result in less insulin release into the general circulation without any change in pancreatic response. Studies of hepatic blood flow in man with doses of epinephrine comparable to those used in our study have shown, however, that increased rather than decreased splanchnic blood flow would be expected (19, 20). We have estimated splanchnic blood flow with indocyanine green (21, 22) in two subjects by using a central injection site and peripheral blood sampling site (23). In both subjects clearance of indicator was unchanged by an epinephrine infusion. With the limitations of this technique, these results are compatible with either no change or an increase in splanchnic blood flow, but not a decrease. Therefore, a reduction in splanchnic flow as an explanation for the effect of epinephrine on blood insulin levels would appear unlikely. Alternative possibilities, which can be summarized briefly, include *a*) a direct or indirect effect of epinephrine on the pancreatic microcirculation; *b*) production of a metabolically active substance by epinephrine, which in turn decreases pancreatic insulin release; and *c*) acceleration of insulin removal that prevents the usual rise in insulin level. None of these other alternatives were investigated and, therefore, further studies in man will be required to evaluate them.

Summary

Epinephrine, 6 μg per minute, was infused into normal subjects. Despite marked hyperglycemia, immunoreactive insulin remained at basal levels until the infusion was stopped. This inhibition of an expected increase in immunoreactive insulin was maintained for up to 7 hours by continuous infusion of epinephrine. Immunoreactive insulin levels were lower than expected when epinephrine was infused simultaneously with glucose, glucagon, and tolbutamide. These data are considered to be consistent with an inhibitory effect of epinephrine upon pancreatic insulin release.

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