INTERPRETATION OF THE RAPID INTRAVENOUS GLUCOSE TOLERANCE TEST IN NORMAL INDIVIDUALS AND IN MILD DIABETES MELLITUS [1]

By DONALD S. AMATUZIO,[2] FRANCIS L. STUTZMAN, MURIEL J. VANDERBILT, AND SAMUEL NESBITT

(From the Veterans Administration Hospital and the Department of Medicine, University of Minnesota Medical School, Minneapolis, Minn.)

(Submitted for publication November 7, 1952; accepted January 21, 1953)

The glucose tolerance test is an important diagnostic procedure in metabolic diseases. As the test is currently employed, glucose is administered either orally or intravenously and there is *no uniform* interpretation of the results.

A study of the rapid glucose tolerance test is found in a review by Tunbridge and Allibone (1). The present study was undertaken to test the validity of the concept that the rapid intravenous glucose tolerance test might properly and readily be interpreted by following the rate of disappearance of glucose from the blood. It was our hope also to evolve a simple test for routine use. The uniformity of the single injection method was studied as a means of separating the normal from the known mild diabetic patient.

MATERIAL AND METHODS

Twenty-five grams of glucose as a 30 per cent solution in distilled water were administered intravenously within four minutes. A fasting blood specimen was obtained, and then at four minutes following the glucose administration and subsequently every eight minutes for 72 minutes. Blood was obtained from an ear lobe that was kept moist with a heparin sponge. Determination of blood glucose was done by the Horvath and Knehr modification (2) of the Folin-Malmros micromethod (3).

The control group consisted of 70 healthy men ranging in age from 25 to 50 years with no family history of diabetes mellitus. The test was repeated with 25 grams of glucose at intervals of from one to three months in 20 subjects, and with 35 grams of glucose in 13 who had been on an adequate carbohydrate intake. The abnormal group consisted of 26 patients with known mild diabetes mellitus controlled by diet alone (the majority had normal fasting blood sugars) and 13 patients with severe diabetes mellitus. Diabetes mellitus had been diagnosed in these patients by clinical evaluation and the 100 grams standard oral glucose tolerance test.

RESULTS

The blood glucose values of the 25 grams rapid glucose tolerance test, expressed as mgm. per cent glucose excess,[3] in 70 normal men with no family history of diabetes mellitus are given in Table I. Similar blood (mgm. per cent) glucose excess values were found in 20 normal men who had a repeat 25 grams test one to three months later

[1] Published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

[2] Present address: Lt. D. S. Amatuzio, MC, USNR (Staff), U. S. Naval Hospital, Oakland 14, California.

[3] Milligram per cent glucose excess is defined as that amount of glucose in excess of the fasting blood glucose in mgm. per cent.

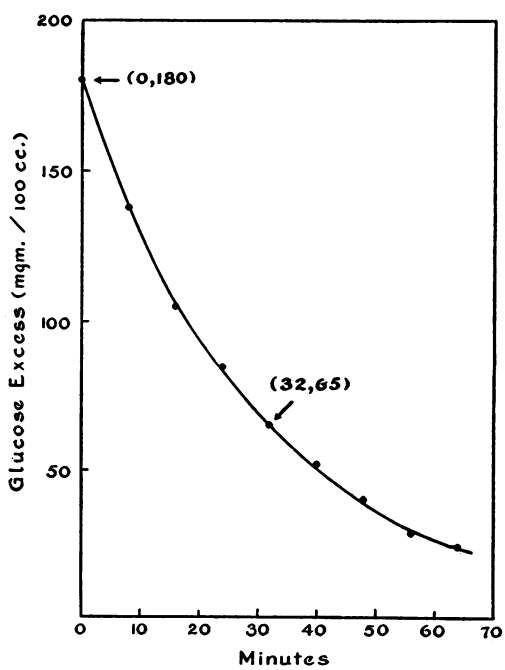

FIG. 1. GLUCOSE DISAPPEARANCE PLOTTED ON COORDINATE GRAPH PAPER—PATIENT W. B.

and who had been on an adequate carbohydrate intake (Table II). A comparison of the 25 grams to the 35 grams test showed different mgm. per cent glucose excess values at determined times in 13 normal men who had been on an adequate carbohydrate intake (Table IV). In 39 patients with diabetes mellitus (26 were mild and 13 were severe diabetics) the 25 grams glucose tolerance test gave higher mgm. per cent glucose excess values (Table V).

The rate of disappearance of glucose was found to be apparently proportional to the concentration if the glucose excess in mgm. per 100 cc. is plotted against time using the four minute glucose value after injection as that value at time zero (Figure 1). This is best represented by an equation of a monomolecular reaction:

$$C(t) = C(o)\, e^{-kt} \qquad (1)$$

where

C(t) = the glucose excess in mgm. per 100 cc. at any time, t,

C(o) = the glucose excess in mgm. per 100 cc. at time zero,

and

k = the disappearance rate of glucose from the blood.

TABLE I

The rapid intravenous glucose tolerance (25 grams) and its rate of removal in normal men

Patient	Fasting glucose	Glucose excess (mgm.%) 0	8	16	24 (time in minutes)	32	40	48	56	Rate of removal (%/min.)
C. B.	78	182	140	100	80	57	47	35	17	3.44
P. D.	88	207	142	109	77	65	38	27	12	4.30
R. P.	104	140	91	66	44	31	20	1	1	4.81
S. B.	105	151	95	80	60	47	33	10	1	3.75
G. S.	115	145	108	73	45	34	25	−6	−6	4.60
P. W.	93	215	155	107	82	39	40	30	−10	3.98
R. G.	93	205	150	108	71	50	28	15	−6	4.53
J. D.	93	169	122	94	65	50	41	34	15	3.51
L. I.	95	160	121	83	58	40	40	23	6	4.21
P. K.	90	225	173	133	110	85	77	55	30	3.05
W. B.	122	153	106	76	56	41	28	5	1	4.14
A. K.	115	195	141	100	73		30	10	−13	4.53
M. C.	88	199	141	104	70	52	34	12	−8	4.37
D. C.	91	211	157	119	105	103	72	57	41	3.00
W. B.	123	173	120	85	65	45	35	23	7	4.06
C. C.	88	195	134	100	72	52	28	23	16	4.06
W. K. N.	84	241	184	142	104	89	76	50	42	3.12
V. C.	83	183	124	95	67	51	42	29	19	3.90
W. B.	85	177	138	105	85	65	52	40	29	3.20
R. C.	97	183	141	109	82	65	53	41	26	3.20
M. W.	85	157	112	82	67	56	48	36	18	3.30
W. W.	98	192	139	107	87	64	50	25	9	3.44
G. T.	93	179	140	101	81	59	50	35	19	3.51
J. J.	95	182	152	98	81	70	50	38	17	3.08
K. H.	128	190	132	124	89	57	46	34	25	4.06
E. M.	100	140	116	86	69	50	38	30	8	3.43
H. O.	90	175	126	100	78	56	48	36	20	3.35
E. R.	80	191	165	118	95	75	58	48	36	3.32
L. E.	92	188	143	105	85	69	52	36	29	3.20
C. L.	78	197	132	114	73	55	43	28	22	3.90
A. S.	105	160	113	81	67	51	36	32	22	3.49
F. Mc.	92	183	125	91	62	41	26	18	8	4.84
C. A.	83	204	141	94	75	59	34	28	10	4.16
B. H.	81	167	115	85	55	29	29	21	−3	4.45
E. S.	95	178	140	107	87	68	43	42	23	3.04
S. R.	88	150	111	92	72	59	46	13	25	3.12
H. H.	95	165	118	95	70	51	37	29	11	3.67
K. N.	97	158	131	106	86	73	49	36	28	3.04
J. S.	87	164	135	110	82	61	42	35	23	3.82
B. D.	97	167	116	88	71	52	28	28	1	3.95

TABLE I—*Continued*

Patient	Fasting glucose	Glucose excess (mgm.%) 0	8	16	24	32 (time in minutes)	40	48	56	Rate of removal (%/min.)
R. F.	87	206	143	101	85	54	40	28	10	4.30
T. R.	82	188	133	96	68	44	35	20	14	4.10
R. C. H.	87	185	134	95	74	48	35	17	5	4.53
F. R.	91	230	150	124	114	84	67	57	36	3.35
E. E.	110	173	113	80	50	35	25	−3	−5	4.84
D. R. U.	102	161		100	78	56	38	28	13	3.98
V. K.	102	165	123	103	76	62	45	33	24	3.36
S. L.	93	137	113	98	72	55	42	37	25	3.36
H.	98	177	120	92	76	53	41	27	15	3.84
R. A. J.	82	156	114	88	74	51	40	30	13	3.46
G. F. E.	95	138	99	77	57	43	38	27	21	3.38
E. G.	85	187	143	97	63	43	30	−1	−12	4.62
M. K.	95	153	119	100	82	71	57	38	31	3.01
A. Z.	78	196	142	117	90	77	53	46	27	3.30
I. P.	84	180	144	112	82	55	28	7	−3	3.74
W. G.	88	169	123	97	72	53	50	30	17	3.56
W. M.	98	174	133	118	102	74	57	46	34	3.08
W. J.	87	168	130	101	76	58	35	28	13	3.64
E. G.	86	175	133	107	94	76	55	45	34	3.01
S. D.	97	128	107	76	65	53	39	30	26	3.20
N. H.	102	159	118	96	84	72	64	46	34	3.00
G. D.	98	182	138	113	85	62	40	37	12	3.36
W. L.	102	151	108	86	54	56	51	31	24	3.34
A. B.	97	138	109	83	63	52	39	30	21	3.44
F. L. T.	92	156	114	76	46	37	0	8	−18	4.62
H. H.	102	159	118	96	84	72	64	46	34	3.00
B. K.	75	170	129	100	79	58	43	19	16	3.55
L. A. S.	92	173	126	86	58	40	0	1	−10	4.62
M. P.	98	149	110	87	70	52	41	23	20	3.30
A. S.	122	116	80	69	53	42	30	14	11	3.22

A simple expression for finding the disappearance rate of glucose is to let $C(t) = \frac{1}{2} C(o)$, then on substituting in eq. (*1*)

$$\tfrac{1}{2} C(o) = C(o)\, e^{-kt}$$

or

$$k = \frac{\log_e 2}{t} = \frac{0.693}{t} \qquad (2)$$

ANALYTIC AND GRAPHIC ANALYSIS

As it is well appreciated in the application of mathematics to practical problems, one deals with inaccurate data. All measurements entering into the calculation involve errors of some magnitude and many of the numerical values used are rounded off. If one plots the observed mgm. per cent of glucose during the rapid glucose tolerance test against time, a parabola is formed. However, assuming that the fasting blood glucose is a constant baseline during the rapid glucose tolerance test, then by plotting $\log_e$ (mgm. per cent glucose excess) against time one will get a linear rela-

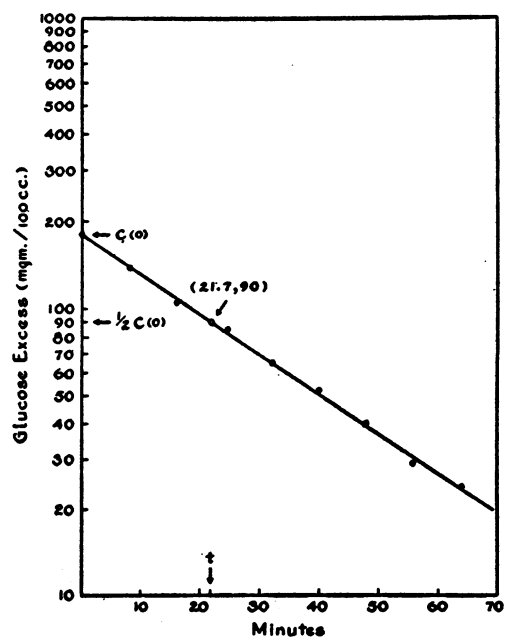

FIG. 2. GLUCOSE DISAPPEARANCE OF FIG. 1 PLOTTED ON SEMILOGARITHMIC PAPER—PATIENT W. B.

tionship (eq. [1]). By fermentation we found that the non-glucose reducing substances during the rapid glucose tolerance test remained relatively constant (the greatest difference being 5 mgm. per cent) in seven normal individuals and six patients with diabetes mellitus. It should be emphasized that any errors inherent in the method, technical or personal, may, at times, be magnified so as not to give a good fit on plotting $\log_e$ (mgm. per cent glucose excess) against time. From this graph one can readily find k (the disappearance rate of glucose from the blood) by eq. (2). This is graphically illustrated by plotting glucose excess on the ordinate of semilogarithmic paper against time on the abscissa (Figure 2), where k is the number of multiples of 2.30 minutes corresponding to each power of 10 through which the glucose excess changes. An analytical and graphical sample is given in Table III.

a. Analytical method

The graph of the relation between the blood mgm. per cent glucose excess and time is shown in Figure 1. Substituting into eq. (1), one readily

TABLE II

The rapid intravenous glucose tolerance (25 grams) and a repeated (25 grams) test with its rate of removal in normal men

Patient		Fasting glucose	Glucose excess (mgm.%) 0	8	16	24	32 (time in minutes)	40	48	56	Rate of removal (%/min.)
R. C.	a.*	83	183	124	95	67	51	42	35	19	3.90
	b.	91	177	130	82	57	44	35	21	14	4.06
W. B.	a.	85	177	138	105	85	65	52	40	29	3.20
	b.	80	165	123	103	84	67	50	38	23	3.20
R. C.	a.	97	183	141	109	82	65	53	41	26	3.20
	b.	105	184	147	104	79	68	48	38	15	3.28
M. W.	a.	85	157	112	82	67	56	48	36	18	3.20
	b.	117	118	80	70	55	43	38	23	17	3.36
G. T.	a.	93	179	140	101	81	59	50	35	19	3.59
	b.	80	230	160	128	93	72	54	33	29	3.60
Dr. J.	a.	95	182	152	98	81	70	50	38	17	3.08
	b.	80	176	148	107	80	70	55	47	23	2.97
K. H.	a.	128	190	132	124	89	57	46	34	25	3.98
	b.	128	172	120	87	59	46	16	8	8	4.06
E. R.	a.	80	191	165	118	95	75	58	48	36	3.24
	b.	100	187	143	102	86	62	48	29	21	3.35
L. E.	a.	92	188	143	105	85	69	52	36	29	3.20
	b.	90	216	160	135	105	83	66	53	38	3.20
F. Mc.	a.	92	183	125	91	62	41	26	18	8	4.84
	b.	87	203	147	103	61	55	30	15	6	4.92
C. A.	a.	83	204	141	94	75	59	34	28	10	4.16
	b.	83	207	147	108	72	65	36	19	7	4.21
H. H.	a.	95	165	118	95	70	51	37	29	11	3.67
	b.	89	180	137	107	76	55	47	38	11	3.67
H. N.	a.	97	158	131	106	86	73	49	36	28	3.04
	b.	96	200	150	109	95	82	71	64	55	3.00
B. D.	a.	97	167	116	88	71	52	28	28	1	3.95
	b.	102	140	93	74	48	29	27	19	4	3.98
F. R.	a.	91	230	150	124	114	84	67	57	36	3.35
	b.	85	160	139	103	81	58	45	36	28	3.43
G. F. E.	a.	95	138	99	77	57	43	38	27	21	3.38
	b.	83	147	105	83	57	45	43	26	20	3.41
A. Z.	a.	78	196	142	117	90	77	53	46	27	3.30
	b.	83	164	125	95	75	59	48	42	28	3.31
E. G.	a.	85	187	143	97	63	33	9	−1	−12	4.62
	b.	93	167	119	80	46	36	−5	−18	−20	4.62
R. C. H.	a.	87	185	134	95	74	48	35	17	5	4.53
	b.	92	138	102	67	45	33	14	3	−11	4.62
W. W.	a.	98	192	139	107	87	64	50	25	9	3.36
	b.	90	186	135	115	95	74	53	40	23	3.36

* a. 25 grams of Glucose.
b. 25 grams of Glucose.

TABLE III

Observed blood glucose values of W. B., with the four minute value set at time zero

Time (minutes)	Fasting	4	12	20	28	36	44	52	60	68
Observed glucose (mgm.%)	85	265	223	190	170	150	137	125	114	109
Time (4 minutes at time 0)		0	8	16	24	32	40	48	56	64
Glucose excess (mgm.%)		180	138	105	85	65	52	40	29	24

finds the k, the disappearance rate of glucose from the blood for two points.

$$k = \frac{2.3 \log_{10} 180/65}{32-0} = 0.0319$$

or

$$k = 3.19 \text{ per cent per minute.}$$

b. Graphic method

The semilogarithmic graph of the relation between the blood glucose excess and time is illustrated in Figure 2.

By using the relationship shown in eq. (2) where C(t) equals $\frac{1}{2}$ C(o), to find t from Figure 2 we see that $\frac{1}{2}$ C(o) equals 90 mgm. per 100 cc. with a corresponding t equal to 21.7 minutes. Substituting into eq. (2), one finds the average disappearance rate of glucose.

$$k = \frac{0.693}{21.7} = 0.0319$$

or

$$k = 3.19 \text{ per cent per minute.}$$

The skill required for drawing an accurate freehand curve is not required with the graphic method and the average k for all points is more readily and easily obtained.

It appears that the disappearance rate of glucose from the blood is apparently the resultant of a number of simultaneous processes that best fit a simple unimolecular equation. The disappearance rate of glucose in 70 normal men with no family history of diabetes mellitus who received 25 grams of glucose intravenously was found to range from

TABLE IV

The removal rate on comparing the 25 grams and 35 grams rapid intravenous glucose tolerance in normal men

Patient		Fasting glucose	Glucose excess (mgm.%) (time in minutes) 0	8	16	24	32	40	48	56	64	72	Rate of removal (%/min.)
R. C.	a.*	105	184	149	103	79	68	48	38	15	15	10	3.28
	b.	96	249	200	143	112	87	74	35	15	−6	−1	3.28
G. T.	a.	93	179	140	101	81	59	50	35	19	8	0	3.59
	b.	84	311	228	191	140	109	89	69	49	35	14	3.51
Dr. J.	a.	80	176	148	107	80	70	55	47	23	6	0	2.97
	b.	92	256	192	171	143	118	95	75	75	46	34	2.97
L. E.	a.	92	188	143	105	85	69	52	36	29	16	4	3.20
	b.	96	302	209	161	126	94	79	49	32	16	−5	3.20
F. Mc.	a.	87	203	147	103	61	55	30	15	6	6	−2	4.92
	b.	96	214	166	114	69	46	47	24	16	10	2	4.71
E. S.	a.	95	178	140	107	87	68	43	42	23	17	0	3.04
	b.	90	238	188	172	140	120	98	84	73	55	34	3.12
R. S.	a.	88	150	111	92	72	59	46	13	25	17	7	3.12
	b.	88	204	165	130	120	92	72	55	37	32	12	3.05
H. H.	a.	89	180	137	107	76	55	47	38	11	3	−4	3.67
	b.	77	227	184	144	109	85	56	45	30	19	8	3.67
K. N.	a.	96	200	150	109	95	82	71	64	55	41	32	3.00
	b.	87	198	170	138	124	105	83	61	49	38	38	3.00
J. S.	a.	87	164	135	110	82	61	42	35	23	8	3	3.82
	b.	98	197	148	115	91	59	46	29	18	17	9	3.90
B. D.	a.	102	140	93	74	48	29	14	19	4	−4	−12	3.98
	b.	105	245	177	149	120	100	74	48	35	20	11	3.98
R. F.	a.	87	206	143	101	85	54	40	28	10	4	−10	4.30
	b.	100	230	150	107	73	46	22	22	−10	−27	−22	4.60
R. C. H.	a.	87	185	134	95	74	48	35	17	5	−4	−5	4.21
	b.	91	230	147	109	87	71	54	25	13	0	0	4.21

* a. 25 grams of Glucose.
b. 35 grams of Glucose.

TABLE V

The rapid intravenous glucose (25 grams) tolerance test in diabetes mellitus

Patient	Fasting	Glucose excess (mgm.%) 0	8	16	24	32	40	48	56	64	72 (time in minutes)	Rate of removal (%/min.)
						Very mild diabetes mellitus						
O. D.	105	187	168	142	123	105	90	71	63	38	38	2.03
W.	94	149	134	109	100	88	81	66	48	42	19	1.64
E. J.	95	170	138	119	108	90	83	73	53	48	37	1.79
R. S.	147	106	99	89	78	71	61	60	57	43	48	1.21
L. L.	146	174	136	110	102	78	68	48	44	38	30	2.46
A. R.	160	236	172	156	130	116	100	94	72	64	70	1.83
M.	115	153	138	105	98	85	79	79	46	28	35	2.10
O. T.	98	202	157	139	121	112	102	65	58	45	47	2.27
D. H.	105	130	105	90	75	67	60	52	45	38	37	1.83
W. G.	97	213	155	128	114	98	93	89	54	40	34	2.42
M. B.	94	179	134	117	100	88	73	66	52	42	31	2.22
O.	80	210	153	138	118	105	95	77	56	35	31	2.18
B.	94	153	124	111	100	92	78	71	56	43	31	1.79
A. P.	102	134	113	93	83	78	65	58	45	28	23	1.87
W. S.	135	135	110	93	68	65	59	51	40	20	30	2.07
C. F.	95	175	132	121	113	85	71	63	45	33	16	2.42
W. W.	115	125	116	102	87	75	68	64	62	56	56	1.26
A. K.	158	122	100	75	64	52	43	31	28	20	19	2.19
E. C.	145	154	125	99	85	72	60	49	40	35	27	2.32
W. W.	143	119	106	101	90	79	81	72	71	65	56	0.93
J. E.	111	143	131	119	107	99	90	83	81	72	66	1.09
J. L.	113	142	130	112	97	82	76	65	55	45	36	1.77
R. S.	104	148	124	103	84	76	60	47	44	36	29	2.35
B. O.	134	131	120	114	99	99	88	83	76	69	62	0.99
E. F.	104	149	143	126	126	109	110	99	91	74	78	0.93
F. S.	89	125	109	99	83	78	73	67	61	55	53	1.23
						Severe diabetes mellitus						
J. U.	206	210	160	124	116	110	106	84	70	62	50	1.64
G. E.	322	152	116	114	102	104	78	76	74	66	60	1.13
M. C.	136	200	154	124	124	104	104	104	82	82	82	1.09
E. J.	224	196	136	108	96	84	80	76	50	48	46	1.87
B. P.	155	161	152	146	132	122	108	109	102	102	87	0.85
A. N.	155	133	99	97	90	75	77	66	59	54	57	1.12
E. W.	198	65	73	70	67	64	62	65	65	62	64	0.23
F. D.	228	90	72	64	64	56	52	47	43	39	39	0.97
A. D.	192	112	100	92	81	76	69	63	61	58	56	1.06
W. H.	168	222	176	158	146	132	136	102	92	82	80	1.48
O. N.	192	64	62	58	57	61	63	61	57	57	55	0.15
A. B.	262	76	70	62	58	49	45	46	43	36	30	1.23
A. D.	168	110	110	100	92	85	79	75	74	66	52	0.85

3.00 to 4.84 per cent per minute (Table I). The test was repeated with 25 grams of glucose one to three months later on 20 normal subjects who had a dietary intake of at least 150 grams of carbohydrate daily. The disappearance rate of glucose (k) was constant for each subject (Table II), *i.e.*, the disappearance rate was reproducible.

In order to study the effect of a larger dose the test was repeated with 35 grams of glucose in 13 normal individuals who had been previously studied with the 25 grams dose and who had a dietary intake of at least 150 grams of carbohydrate daily (Table IV). It was found that the disappearance rate was unaltered by the larger dosage, *i.e.*, it was constant for the individual tested. Figure 3 illustrates the observed data of the two dosage tests in subject W. B. plotted on semilogarithmic graph paper. It is obvious that the slopes of the curves, and therefore the removal rates, are the same and are unaltered by this change in dosage. It should also be noted that an apparent oscillation of the curve is exaggerated with the 35 grams dose but

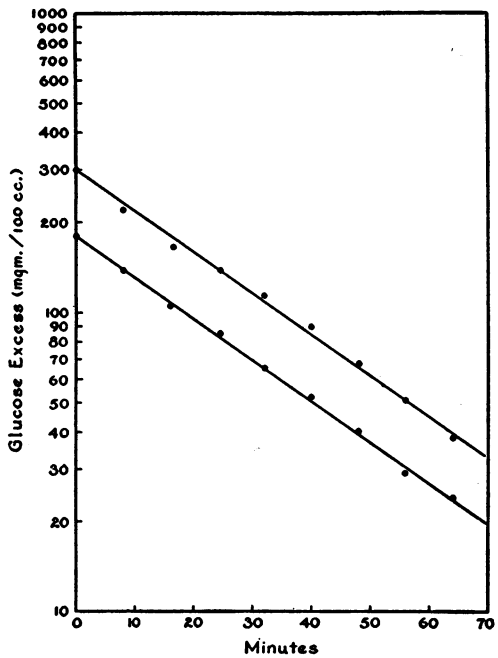

FIG. 3. COMPARISON OF THE GLUCOSE DISAPPEARANCE AFTER 25 AND 35 GRAM TEST OF GLUCOSE—PATIENT W. B.

that the values of the disappearance rate of glucose following dosages of 25 and 35 grams are the same. The apparent oscillations may be related to numerous simultaneous processes in the body.

A group of 26 patients with known mild diabetes controlled by diet (the majority had normal fasting blood sugar values) was similarly studied with the 25 grams test. The disappearance rate of glucose was found to range from 0.93 to 2.46 per cent per minute (Table V). This difference is obviously highly significant on comparison with the normal series. A distinct, sharp separation of the mild diabetic patients from the normal subjects is readily apparent. Also studied were 13 patients with severe diabetes who were found to have a lower range (0.23 to 1.64 per cent per minute) for the rate of removal of glucose (Table V).

The mean quantity of glucose lost in the urine during the test varied from 0.2 to 1.0 gram in 22 normal men, and from 0.7 to 2.9 grams in 19 mild and severe diabetics.

DISCUSSION

The first attempt to analyze the rapid glucose tolerance curve was by Jörgenson (4) (1926) and Ross (5) (1938) who measured the area under the observed curve to interpret their data. Fishberg (6) (1930) found that the rate of disappearance of foreign sugars injected into the blood stream obeyed a monomolecular reaction velocity equation. An excellent detailed treatment for determining the intravenous glucose tolerance equation was shown by Greville (7).

The fate of the intravenously administered glucose has not been definitely determined. Loss of glucose in the urine is not an important factor since only a small amount was found in the patients tested (0.2 to 2 grams). The disappearance of glucose from the blood merely by diffusion into the tissues is unlikely because: (*1*) the disappearance rate of glucose from the blood in mild diabetics and in normal individuals with a similar fasting blood sugar level showed a distinct difference, and (*2*) the disappearance rate did not vary with the dose of glucose. It may be suggested that changes in blood volume resulting from the injected glucose may produce an apparent loss from the blood stream. However, Pijoan and Gibson (8) using the Evans blue dye method found that there was no significant change in blood volume after the injection of 25 grams of glucose in 55 cc. of water.

The ferricyanide reaction as a method of determining blood glucose was introduced by Hagedorn and Jensen (9, 10). For routine purposes the disadvantage of this procedure was that it measured all *reducing* substances in the blood in addition to glucose. Measurement of the mgm. per cent *glucose excess* in blood, determined by the difference in reducing power before and after the injection of glucose, avoids consideration of the non-glucose-reducing substances and thus, for this purpose, the ferricyanide procedure becomes the method of choice.

The variation in the disappearance rate of glucose in normal individuals could not be correlated with the height, weight (*i.e.*, non-obese patients), age or dose administered. It was apparent that the disappearance rate was reproducible for the individual regardless of dose. An apparent oscillation of the plotted curves was noted with the 35 grams injection. By the rapid glucose tolerance test, one can obtain an index of the disappearance rate of glucose from the blood. With values of glucose excess below 30 mgm. per 100 cc. the plotted curve tends to become distorted.

The above interpretation has some advantages in that (*1*) the disappearance rate of glucose in normals is constant, reproducible, and independent of dosage for each individual, (*2*) there is a marked separation of the normal from known borderline diabetes mellitus, (*3*) a precise manner of interpreting glucose tolerance curves is possible, (*4*) a rapid glucose tolerance test may be completed within 60 minutes, and (*5*) the disappearance rate of glucose from the blood appears to fit best a simple expression (eq. [*1*]).

SUMMARY

A study has been made of the rapid intravenous glucose tolerance test by following the disappearance rate of glucose. It was found that the rate of removal in the normal individual maintained on an adequate carbohydrate diet remained constant on repeated tests and was independent of the dose administered for each subject.

By determining the removal rate, a sharp separation was found between the patients with known mild diabetes (*26*), severe diabetes (*13*), and the group of normal controls (*70*). A decreased rate of removal has been observed in other conditions, including obesity unrelated to a family history of diabetes, inflammatory disease, uremia, weight loss due to diet, and decompensated portal cirrhosis.

REFERENCES

1. Tunbridge, R. E., and Allibone, E. C., The intravenous dextrose tolerance test. Quart. J. Med., 1940, **9**, 11.
2. Horvath, S. M., and Knehr, C. A., Adaptation of the Folin-Malmros micro blood sugar method to photoelectric colorimeter. J. Biol. Chem., 1941, **140**, 869.
3. Folin, O., and Malmros, H., An improved form of Folin's micro method for blood sugar determinations. J. Biol. Chem., 1929, **83**, 115.
4. Jörgensen, S., Comparison between the intravenous and oral application of glucose for loading of the carbohydrate-metabolism. Acta med. Scandinav., 1926–27, **65**, 116.
5. Ross, C. W., with the technical assistance of Tonks, E. L., The determination of glucose tolerance. Arch. Dis. Childhood, 1938, **13**, 289.
6. Fishberg, E. H., The rate of disappearance of foreign sugar from the blood stream. J. Biol. Chem., 1930, **86**, 665.
7. Greville, G. D., The intravenous glucose tolerance equation. Biochem. J., 1943, **37**, 17.
8. Pijoan, M., and Gibson, J. G., II, The rate of disappearance of intravenously administered dextrose in the human subject. Am. J. Physiol., 1938, **121**, 534.
9. Hagedorn, H. C., and Jensen, B. N., Zur Mikrobestimmung des Blutzuckers mittels Ferricyanid. Biochem. Z., 1923, **135**, 46.
10. Hagedorn, H. D., and Jensen, B. N., Die Ferricyanidmethode zur Blutzuckerbestimmung II. Biochem. Z., 1923, **137**, 92.