

# Experience with a Steroid-Tolbutamide Test for the Detection of Impaired Pancreatic Reserve

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## SUMMARY

A procedure utilizing a combination of pretreatment with oral steroids followed by intravenous tolbutamide has been described and performed safely in 152 subjects with normal glucose tolerance tests. Criteria for an abnormal response include two of the following three findings: 1. a fasting blood glucose level over 113 mg. per 100 ml.; 2. thirty minutes after the tolbutamide, a fall in glucose of less than 16 per cent; 3. failure of the ninety-minute glucose to rise 4 mg. per 100 ml. above the lowest recorded glucose. Using these criteria an increase in abnormal responses has been found in: 1. young individuals with a positive family history of diabetes, 2. individuals over the age of sixty, and 3. patients with peripheral vascular disease or significant obesity. Seven of the abnormal responders have developed overt diabetes in a five-year period. None of the negative responders has become diabetic. Eighteen thyrotoxic subjects were studied and revealed some unusual findings.

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Early detection of the individual with clinical diabetes or of the prediabetic individual who will at a later date develop clinical diabetes is desirable. The latter group of patients who, by present routine tests of carbohydrate metabolism are normal, is of special interest metabolically as well as from the viewpoint of ultimate prevention of development of diabetes.

Fajans and Conn in 1954,<sup>1</sup> and subsequently others,<sup>2-5</sup> have described steroid provocative oral glucose tolerance tests for detecting individuals with subclinical impairment in pancreatic function or insulin reserve. Because of certain variables encountered in any oral test, an intravenous procedure seemed appropriate for this problem.

Unger and Madison<sup>6</sup> first reported the use of intravenous sodium tolbutamide for the diagnosis of diabetes. The response in the diabetic was characterized by a limited fall in the fasting blood glucose level observed twenty minutes after tolbutamide. In addition, in diabetics the blood glucose continued to decline over

a sixty to ninety-minute period, while in normal subjects a secondary rise in blood glucose occurred.

Baretto and Recant<sup>7</sup> showed that a normal tolbutamide tolerance test could be converted to a "diabetic" curve by administration of steroids to certain individuals. Since these individuals might well have had diminished pancreatic function, this procedure was studied in a larger group of subjects with efforts made to correlate the effect of age, general health and family history of diabetes with the response.

The present communication is a report of our experience with the steroid-tolbutamide test and emphasizes the variety of factors which may influence the interpretation and usefulness of the procedure.

## METHODS AND MATERIALS

All individuals tested had either a normal two-hour postprandial blood glucose or a normal glucose tolerance curve following a 100 gm. oral load of glucose (except for thyrotoxic subjects), and all were eating a normal diet. Normal values for glucose tolerance included fasting levels under 100, levels thirty to sixty minutes after glucose of 160 or less and a two-hour blood glucose level of less than 120 mg. per 100 ml. The subjects were fasted overnight and were given Dexamethasone 3.0 mg. once eight and one-half hours before and once two hours before the test. Blood glucose was determined by Somogyi-Nelson technic<sup>8</sup> on samples obtained in the fasting state and at thirty, forty-five, sixty and ninety minutes following the rapid intravenous infusion of 1.0 gm. of sodium tolbutamide in 20 ml. of sterile water. Of the 170 test subjects, 111 were ambulatory and fifty-nine were hospitalized. Some test patients were obtained from the wards and the outpatient services of the Barnes Hospital, and a considerable number of subjects were medical students, laboratory personnel, and secretarial personnel at the Washington University School of Medicine. The influences of family history of diabetes, existence of various disease states, and aging per se on the results of the tests were investigated. A positive family history was here defined as diabetes known to exist in parents, siblings, parental-siblings, or grandparents.

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## RESULTS

A. *Criteria for analysis of the steroid-tolbutamide tests.* The designation of a test as negative, or normal, as contrasted with positive, or abnormal, presented no difficulty in many subjects since curves were obtained characteristic of either the normal response or the diabetic response to tolbutamide alone. However, the establishment of criteria for the intermediate group of responses was considerably more difficult.

In an effort to define such criteria, tests were per-

formed in forty-two healthy, young adults with a negative diabetic family history (table 1). Their curves were compared with those of six individuals who had normal glucose tolerance at the time of testing but who developed overt diabetes (ranging from abnormal glucose tolerance tests to symptomatic diabetes) at a later date—hence were latent diabetics at the time of the original steroid-tolbutamide test (table 2). The means and standard deviations were determined for each blood glucose level in the two groups and are plotted in figure

TABLE 1  
Steroid-tolbutamide test in normal subjects with negative family history of diabetes

Name	Age	Fasting	Blood glucose mg. per 100 ml.				Per cent fall 30 min.	Mg. per 100 ml. rise 90 min.	Sex
			30 min.	45 min.	60 min.	90 min.			
R.A.	25	98	69	64	74	79	30	15	M
M.A.	18	91	56	54	65	69	38	15	F
E.A.	22	120	64	58	73	83	47	25	F
C.B.	20	94	62	54	57	71	34	17	F
J.B.	22	95	65	65	77	79	32	14	F
B.B.	20	102	79	64	49	76	23	27	M
R.B.	27	100	75	66	70	73	25	7	M
B.B.	21	82	44	46	56	50	46	6	F
J.C.	25	101	81	80	69	76	20	7	M
N.C.	22	118	103	95	91	90	13	-1	M*
M.C.	20	112	104	86	85	77	7	-8	F*
P.C.	20	112	76	63	68	81	32	18	F
C.C.	18	112	70	61	69	79	38	18	F
C.G.	21	88	51	41	41	66	42	25	F
M.G.	21	94	73	70	62	79	22	17	F
D.H.	23	98	47	40	53	66	52	26	F
D.H.	20	106	87	80	71	72	18	1	F
S.H.	20	91	50	60	69	76	45	26	F
S.K.	22	102	67	58	63	76	34	18	M
J.K.	22	105	77	71	68	82	27	14	F
C.K.	34	127	110	107	97	97	13	0	M*
S.L.	20	83	40	40	57	70	52	30	F
N.L.	21	100	70	63	56	63	30	7	F
M.L.	24	87	64	62	68	77	26	15	F
S.L.	20	105	77	77	65	76	27	11	F
M.M.	28	98	69	53	59	72	30	19	F
L.M.	22	100	77	77	70	77	23	7	M
C.M.	22	103	86	78	58	83	17	25	M
L.M.	24	116	92	83	77	81	21	4	M
J.M.	29	111	77	67	67	88	31	21	M
I.N.	22	101	88	81	81	88	13	7	M
M.P.	20	102	71	68	68	75	30	7	F
B.P.	20	105	78	77	66	63	26	-3	F
S.R.	28	103	88	75	70	74	15	4	F
L.R.	35	110	60	54	59	75	45	21	F
A.R.	20	91	75	68	61	70	18	9	F
P.S.	22	94	78	74	71	83	17	12	F
B.S.	22	110	79	61	68	81	28	20	M
K.S.	21	106	77	42	47	68	27	26	F
M.T.	20	118	111	100	91	89	6	-2	F*
A.V.	20	97	75	61	63	73	23	12	F
P.Z.	20	108	78	63	72	79	28	16	F
Mean	22.5	102.2	74.3	66.8	67.2	76.2	27.9	+13.2	
S.D.		10.0	16.1	15.2	11.4	8.4	11.4	9.4	
Total number	42								
M Males	13								
F Females	29								

\*Abnormal response.

TABLE 2  
Steroid-tolbutamide tests in proven latent diabetic subjects

Name	Age (years)	Fasting	Blood glucose mg. per 100 ml.				Per cent		Sex
			30 min.	45 min.	60 min.	90 min.	fall 30 min.	Mg. per 100 ml. rise 90 min.	
R.D.	28	99	92	88	84	77	8	-7	M
A.H.	59	114	93	89	87	79	17	-8	F
M.K.	45	128	110	103	99	77	15	-22	F
R.M.	32	126	112	106	100	96	11	-4	M
H.V.	31	129	133	100	102	100	-3	-2	M
W.A.	24	116	107	103	95	96	7	1	M
Mean	36.5	118.7	107.8	98.2	94.5	87.5	9.2	-7	
±S.D.		12.1	15.0	7.7	7.4	10.9	7.4	8	
Total number	6								
M Males	4								
F Females	2								

I. Review of the individual curves of the six subjects reveals that each patient had at least two, while most had three points on the curve greater than one standard deviation away from the mean of the normal group. The most consistent changes were seen in the fasting level, the thirty-minute level, and the ninety-minute level. In view of these findings, the fact that Unger and others use the per cent fall of blood glucose in the interpretation of the tolbutamide test, and since the authors have been impressed by the diagnostic value of the shape of the curve (failure of blood glucose to rise at ninety minutes in diabetics), it seemed reasonable to evaluate responses in the following terms: (1) the level of the fasting blood glucose; (2) the per cent fall in blood glucose at thirty minutes; and (3) the mg. per 100 ml. rise in glucose at ninety minutes above the lowest recorded level prior to that time. If two of the three points are greater than one standard deviation from the normal mean in the direction of the abnormal mean, such curves can be interpreted as abnormal with a confidence level approaching 95 per cent.\* The normal criteria are fasting

blood glucose of less than 113 mg. per 100 ml.; a thirty-minute fall of 16 per cent or greater; and a ninety-minute rise of 4 mg. per 100 ml. or greater. If two of these three criteria are abnormal, the test is considered abnormal. It should be noted that these criteria are arbitrary in that the normal subjects have not been systematically restudied after a long enough interval.

B. *Influence of a positive family history.* Of 170 individuals tested, fifty-six (32.9 per cent) showed abnormal tests, and only twenty-four (half of this group) had a positive family history of diabetes (table 3). At first glance, this would suggest that the family history had little influence on the response to the steroid-tolbutamide test. When the results are broken down into various age categories, however, 36 per cent of those subjects in the younger age group (fifteen to forty) with a positive family history of diabetes showed abnormal responses, while only 14 per cent of those with a negative family history showed abnormal responses. Apparently after the age of forty, the effect of a positive family history becomes less important in determining the response to the test.

In an attempt to define more clearly the role of family history per se, only those subjects in the fifteen to forty age group who were healthy and ambulatory

\*The discriminant function was the statistical method used. See Palmer O. Johnson in "Statistical Methods in Research," New York, Prentice-Hall Inc. 1949.

TABLE 3  
Influence of age and family history of diabetes by response to steroid-tolbutamide test\*

Age (years)	Negative F.H.			Positive F.H.			Total		
	No. tests	No. +	Per cent +	No. tests	No. +	Per cent +	No. tests	No. +	Per cent +
15 - 40	58	8	14	47	17	36	105	25	23.8
41 - 59	19	7	37	14	6	43	33	13	39.4
60+	28	17	61	4	1	25	32	18	56.3
Total	105	32	30.5	65	24	37	170	56	32.9

\*These subjects include both normal healthy individuals and some subjects with obesity or peripheral vascular disease.

were examined. Forty-one young adults (mean age 25.4 yrs.), with a positive family history of diabetes — siblings, parents and their siblings, grandparents — (table 4) were compared with the previously described forty-two control subjects (mean age 22.5 yrs.) having a negative family history of diabetes (table 1). Figure 2 plots the mean blood glucose responses for each group. It should be noted that the curve of the positive family history group resembles the negative family his-

tory group but the blood glucose levels are higher. Fifteen abnormal responses (36.5 per cent) were obtained in the positive family history group while only four abnormal curves (9.5 per cent) were observed among the control group. It is of interest that three subjects having diabetes in both parents showed normal responses to the steroid-tolbutamide test.

C. *Influence of age.* One hundred and five subjects in the age group of forty years or under were tested.

TABLE 4  
Steroid-tolbutamide test in subjects with positive family history of diabetes

Name	Age (years)	Fasting	Blood glucose mg. per 100 ml.				Per cent fall 30 min.	Mg. per 100 ml. rise 90 min.	Sex
			30 min.	45 min.	60 min.	90 min.			
R.A.	20	103	82	74	72	72	20	0	M
H.B.	30	107	85	77	72	80	21	8	M
B.B.	22	119	100	92	89	89	16	0	M*
R.B.	20	100	85	80	73	75	15	2	F*
J.C.	22	110	93	77	76	93	15	17	M
N.C.	22	101	71	69	77	81	30	12	M
M.C.	25	100	67	63	61	67	33	6	F
D.D.	22	104	93	84	79	80	9	1	M*
R.D.	28	99	92	88	84	77	7	—7	M*
R.D.	22	143	109	87	73	72	24	—1	M*
D.E.	23	102	69	62	70	84	32	22	M
J.F.	26	97	70	61	60	68	28	8	M
D.F.	35	108	82	100	105	105	24	18	M
P.G.	31	110	86	77	71	73	22	2	M
H.G.	24	108	89	75	73	77	18	4	M
B.G.	22	96	81	71	67	67	16	0	M
J.G.	18	95	76	68	69	75	20	7	F
J.H.	24	91	82	81	84	97	10	16	M
J.H.	22	106	87	78	74	71	18	—3	F
R.H.	23	107	106	100	95	95	9	0	M*
D.K.	24	104	66	65	64	76	38	12	M
M.K.	21	106	74	64	63	69	30	6	F
S.L.	25	99	82	75	72	80	17	8	M
M.M.	24	109	49	46	49	65	55	19	M
C.M.	24	113	71	70	76	91	37	21	F
I.M.	39	111	81	65	66	87	27	22	F
R.M.	32	126	112	96	100	96	13	—4	M*
K.Ms.	26	103	92	85	81	79	11	—2	M*
L.M.	21	108	91	76	74	70	16	—4	M
W.M.	35	101	70	66	66	79	31	13	M
L.N.	27	109	80	65	65	83	27	18	M
O.	26	115	90	80	83	93	22	13	M
R.P.	38	115	81	88	88	92	30	11	M
L.S.	21	102	91	83	82	72	11	—10	M*
J.S.	24	97	73	57	52	56	25	4	M
S.S.	21	115	89	88	87	87	23	0	M*
F.T.	18	126	85	80	74	74	33	0	F*
H.V.	31	129	133	100	102	100	—3	0	M*
W.W.	30	116	103	96	91	89	11	—2	M*
W.	24	116	107	103	95	96	8	1	M*
W.W.†	30	122	115	107	105	98	6	—7	M*
Mean	25.4	108.5	86.3	78.8	77.0	81.2	20.9	+ 5.6	
S.D.†		10.4	15.7	14.3	13.5	11.3	10.9	8.6	
Total number	41								
Males	33								
Females	8								

\*Abnormal response.

†Since testing has become overtly diabetic.

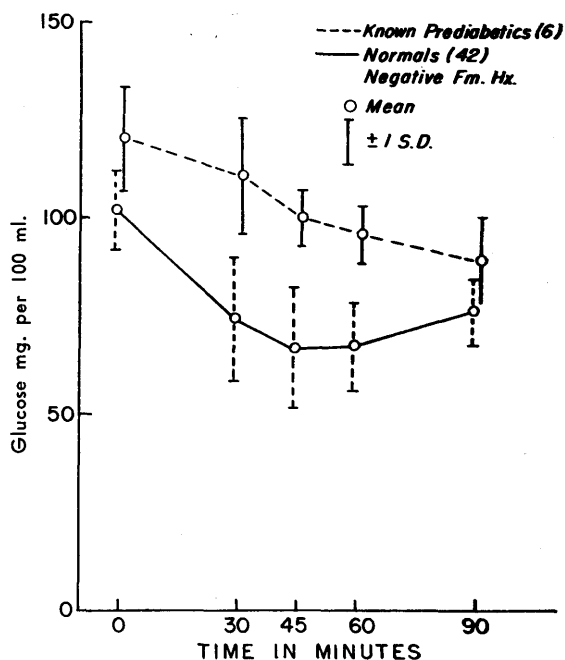


FIG. 1. Steroid-tolbutamide tests in normal subjects and in proven latent diabetic subjects. The mean blood glucose and standard deviations are plotted against time.

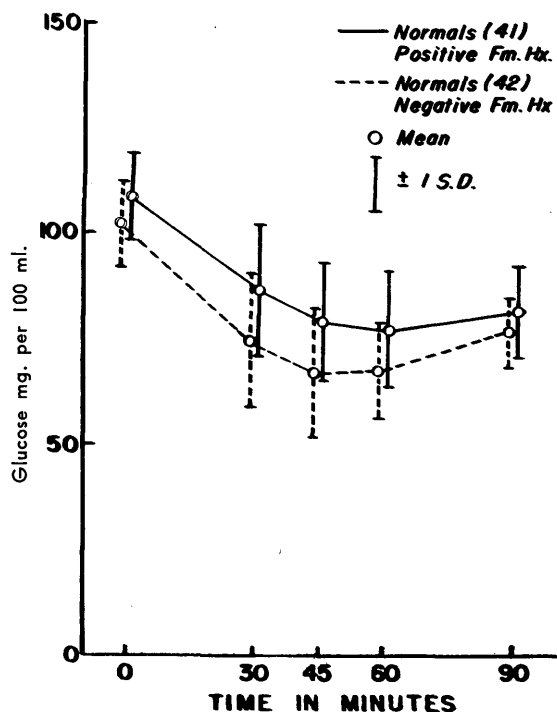


FIG. 2. Comparison of steroid-tolbutamide tests in healthy young adults with a negative or positive family history of diabetes. Means and standard deviations are plotted.

Twenty-five of these responses (23.8 per cent) were positive. Thirty-three individuals, ranging in age from forty-one to fifty-nine years, showed thirteen (39.4 per cent) positive responses. Of thirty-two individuals sixty years of age or older, eighteen (56.3 per cent) were positive responders. These data suggest that in individuals with normal glucose tolerance tests, aging per se results in progressive impairment of pancreatic responsiveness as measured by the steroid-tolbutamide test (table 3).

D. *Influence of disease states.* Table 5 compares the effects of certain disease states on the results of the test in the three age groups previously noted. The disease entities chosen for study were those known to predispose to abnormal carbohydrate metabolism: obesity, premature or advanced peripheral vascular disease, and thyrotoxicosis. Those patients with disease, when compared to disease-free individuals of comparable age, showed significant increase in positive tests. Once again, in the age group over sixty, no further influence upon the test response was seen.

TABLE 5

Influence of disease on steroid-tolbutamide test

Age	No disease			Disease*		
	Number of tests	Number+	Per cent+	Number of tests	Number+	Per cent+
15-40	87	18	21	18	7	39
41-59	11	2	18	22	11	50
60+	19	11	58	13	7	54
	117	31	26	53	25	47

\*Hospitalized and ambulatory subjects with significant obesity, peripheral vascular disease, or thyrotoxicosis.

The effect of thyrotoxicosis on the steroid-tolbutamide test was examined in greater detail since the possibility presented itself to restudy certain patients after control of thyrotoxicosis. Eighteen patients with untreated thyrotoxicosis were included (table 6). Glucose tolerance tests were abnormal in twelve of the eighteen subjects. The intravenous tolbutamide test was performed in eleven subjects and the results were normal. Despite normal intravenous tolbutamide response, nine of these eleven subjects had abnormal glucose tolerance tests. All eighteen patients had steroid-tolbutamide tests and seven (39 per cent) showed an abnormal response. A rather striking elevation of fasting blood glucose level following the two doses of Decadron was noted in the entire group of thyrotoxic patients (mean 121 mg. per 100 ml.), a level higher than the mean of 118 per 100 ml. in known prediabetic subjects and considerably higher than the mean of 102

TABLE 6

Various tests of carbohydrate metabolism in untreated thyrotoxic subjects

Patient	Age	Sex	F.H. Diabetes	Tolbutamide test	Glucose tolerance test	Steroid-tolbutamide test FBG mg. per 100 ml.*	Response
E.C.	49	F	—	N	Abn.†	136	Abn.
M.D.	13	M	—	N	N	133	N
E.D.	43	F	+	N	Abn.†	140	N
B.M.	57	F	—	N	Abn.†	159	Abn.
R.I.	73	F	+	N	Abn.†	150	Abn.
G.C.	57	M	—	N	Abn.†	130	Abn.
A.T.	42	F	—	N	N	136	N
C.S.	23	F	—	—	N	105	N
G.W.	20	F	—	—	Abn.	93	N
C.C.	54	M	—	N	Abn.	112	N
T.B.	59	F	—	—	N	106	N
M.B.	39	F	—	N	Abn.†	123	N
M.A.	30	F	+	—	Abn.	108	N
H.B.	65	M	—	—	N	102	N
L.C.	69	F	—	—	Abn.†	101	Abn.
C.C.	73	F	—	N	Abn.	101	Abn.
C.L.	51	F	—	—	N	104	N
M.D.	63	F	—	N	Abn.†	137	Abn.

\*Mean value of fasting blood glucose 121 mg. per 100 ml.

†Two-hour blood glucose greater than 120 mg. per 100 ml. Those abnormal tests not marked showed abnormal one-hour glucose with normal two-hour levels.

mg. per 100 ml. in the normal subjects.

After a six-month interval following therapy and with the development of clinical and chemical euthyroidism, seven of the original eighteen subjects were restudied (table 7). While thyrotoxic, these seven subjects had shown a mean fasting blood glucose level of 141 per 100 ml. after steroids, compared to a mean of 112 per 100 ml. when euthyroid. Four of the seven had positive steroid-tolbutamide tests when thyrotoxic, and three persisted positive when euthyroid. One patient developed a positive test, and another reverted to normal. It is of further interest that glucose tolerance remained abnormal in three subjects and reverted to normal in two.

## DISCUSSION

The intravenous tolbutamide test, modified by pre-treatment with steroids, was evaluated in 170 subjects. The influences of age, family history of diabetes, and existence of various disease states on the response were studied. The test was used for the purpose of detecting impairment of pancreatic responsiveness prior to development of overt diabetes (defined here as ranging from abnormal glucose tolerance to symptomatic diabetes) in the hope that it might be of predictive value and that ultimately measures might be developed which could delay or prevent onset of diabetes.

This test is similar in principle to the cortisone-

TABLE 7

Tests of carbohydrate metabolism before and after therapy for thyrotoxicosis

Patients	Glucose tolerance test	Thyrotoxic		Rx	Glucose tolerance test	Euthyroid	
		Steroid-tolbutamide FBG mg. per 100 ml.	Response			Steroid-tolbutamide FBG mg. per 100 ml.	Response
E.C.	Abn.*	136	Abn.	Surg.	N	88	N
H.D.	N	133	N	Drugs	N	103	N
E.D.	Abn.*	140	N	RAI†	Abn.*	130	Abn.
B.M.	Abn.*	159	Abn.	RAI	N	126	Abn.
R.I.	Abn.*	150	Abn.	RAI	Abn.*	126	Abn.
G.C.	Abn.*	130	Abn.	RAI	Abn.*	120	Abn.
A.T.	N	136	N	RAI	—	89	N
Mean		141				112	

\*Elevated two-hour blood glucose.

†Therapeutic Radioactive Iodine-131.

glucose tolerance test although significantly different responses to glucose (as opposed to tolbutamide alone), particularly in patients with thyrotoxicosis, have been observed. In essence, both of these procedures provide a stimulus to the pancreas following the stress of steroids. In the Fajans test, the stimulus is a glucose load<sup>9-12</sup> while in the presently described work, it is tolbutamide. The latter has been shown to result in direct pancreatic stimulation with subsequent insulin release.<sup>10,11,13</sup>

The initial adjustment to the steroid stress is assessed by the fasting blood glucose level prior to the intravenous injection of tolbutamide. The response to the second stimulus is measured by the rate and degree of fall of the blood glucose as well as the shape of the blood glucose curve. In this way, impairment of pancreatic function which may be unapparent with the single stimulus of a glucose load or tolbutamide alone may become manifest. An abnormal response might be interpreted as already existing diabetes mellitus, detected by a more refined procedure than the glucose tolerance test, or as subclinical diabetes, latent diabetes or even "prediabetes."

The correct term to describe such responses is dependent upon long term follow-up. During the five-year period of observation, seven individuals with previously normal oral glucose tolerance tests and abnormal steroid-tolbutamide tests have developed chemically overt diabetes. None of the individuals with normal steroid-tolbutamide tests has yet developed overt diabetes although only the medical-student group has been periodically examined. It is obvious that the predictive value of this procedure is quite limited without longer and more complete follow-up. It seems clear that the test does not detect genetic prediabetes in that three individuals with an immediate bilateral positive family history of diabetes showed normal responses to the steroid-tolbutamide test. Similar results have been obtained using steroid-glucose tests.<sup>14,15</sup> Such observations imply that these tests measure already impaired pancreatic reserve and not genetic potential for diabetes.

Despite the above, the family history of diabetes appears to manifest a significant influence on the test response. In the younger age group (under forty) healthy ambulatory individuals with a positive family history showed a four-fold increase in abnormal responses compared with an equivalent group of subjects having a negative family history. In the older age groups, family history showed less influence on the response to the test. With advancing age, a progressive decrease in tolbutamide response was found: under the age of forty, 23.8 per cent positive responses; age forty-one to fifty-nine, 39.4 per cent positives, and over age sixty, 56.3 per cent positive.

Other reports have called attention to the effect of aging on glucose tolerance. Whatever the mechanism of this impairment, it may represent an additive factor in the delayed development of overt diabetes in genetically susceptible individuals.

In all age categories tested, the presence of extreme obesity or peripheral vascular disease significantly increased the frequency of abnormal responses. In the age group under sixty the coexistence of such disease was associated with a two- to three-fold increase in abnormal responses. Impairment of pancreatic reserve in such individuals implies either that these diseases in some fashion produce the impairment or that these disease states are in themselves manifestations of the diabetic syndrome of which impaired carbohydrate tolerance is only one facet.<sup>16</sup> The factors that determine the sequence of appearance of vascular disease as opposed to hyperglycemia are provocative unknowns.

Since the original description of metathyroid diabetes by Houssay,<sup>17</sup> thyrotoxicosis is a disease entity which has been implicated in the production or exaggeration of carbohydrate intolerance. As a result, it seemed pertinent to examine the effects of this disease on the response to the steroid-tolbutamide test. Of the eighteen untreated thyrotoxic subjects studied, over 60 per cent showed abnormal oral glucose tolerance tests (manifested in most by abnormal two-hour glucose levels). However, none of the tested patients showed an abnormal tolbutamide test. This discrepancy confirms similar observations reported by Kaplan.<sup>18</sup>

In consideration of those toxic subjects under age sixty, only three of thirteen showed positive responses to the steroid-tolbutamide test. The incidence of 23 per cent positive is no different from the expected incidence in a healthy population of similar age. Apparently unimpaired pancreatic response as measured by tolbutamide testing procedures is in marked contrast to the impaired oral glucose tolerance seen in these patients. This can be explained only in part by increased rates of gastrointestinal absorption of glucose.

Despite the unimpaired response to tolbutamide, a marked hyperglycemic response to the steroids was noted. This hyperglycemic response was restored towards normal with development of the euthyroid state. (Fasting glucose after steroids 141 mg. per 100 ml. compared with 112 mg. per 100 ml. following control of thyrotoxicosis.)

These finds, though somewhat difficult to interpret, do suggest that the major impairment in thyrotoxicosis may not be a deficiency of insulin per se but rather a marked increase in gluconeogenesis, sensitivity to

steroids, and possibly increased hepatic glucose output. Another possible explanation may be found in a differential response of the pancreas to glucose as compared to tolbutamide. This problem is currently under study.

In conclusion, the results of our experience with the steroid-tolbutamide test indicate that the test may be of research interest. However, it appears at the moment to have only a limited area of usefulness in clinical practice. Prolonged and thorough follow-up studies may increase the value of the procedure; but in view of the major effects of aging and disease, it may be useful only in the diagnosis of decreased pancreatic reserve in healthy, young, ambulatory subjects.

#### SUMMARIO IN INTERLINGUA

##### *Experientia in le Uso de un Test Steroideo-Tolbutamidic pro le Detection de Defective Reservas Pancreatic*

Es describe un technica combinante pretractamento a steroides oral con subsequente administrationes intravenose de tolbutamida, le qual esseva salvemente executate in 152 subjectos con normal tests de tolerantia pro glucosa. Le criterio pro anormalitate del responsa esseva presentia de duo del sequente tres constatationes: (1) Un nivello de sucro sanguinee in stato jejun de plus que 113 mg per 100 ml. (2) Trenta minutas post le administration de tolbutamida, un declino in le sucro de minus que 16 mg per 100 ml. (3) Le facto que a novanta minutas le sucro non monta a 4 mg per 100 ml in supra del plus basse registrate nivello. A base de iste criterio, anormalitate del responsa esseva trovate in (1) juvene subjectos con antecedentes familial de diabete, (2) subjectos de plus que sexanta annos de etate, e (3) patientes con morbo periphero-vascular o formas significative de obesitate. Septe del anormal responsos ha disveloppate patente diabete in un periodo de cinque annos. Nulle del negative (i.e. normal) responsos ha devenite diabetic. Dece-octo subjectos thyrotoxic esseva studiate e monstrava certe inusual constatationes.

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