A Survey for Unknown Diabetics in a Mental Hospital

II. Men from Age Fifty

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SUMMARY

A 100 gm. two-hour oral glucose tolerance test was administered to an institutional group of 213 mentally ill men who were fifty to eighty-eight years old and without known diabetes. Thereafter, the test was selectively repeated. In thirty-two cases results were interpreted, in association with other data, as consistent with previously unknown, unsuspected diabetes — an incidence of 15 per cent. Discovery of this high incidence is attributed to universal employment of the glucose tolerance test. The influence of phenothiazine therapy on carbohydrate metabolism was partially examined with inconclusive results and requires further study. DIABETES *15*:164-72, March, 1966.

Within present knowledge, the oral glucose tolerance test is a valuable tool in the diagnosis of diabetes, even though it is a nonspecific test which may be affected by a variety of factors, including aging. In a recent study[1] a 100 gm. two-hour oral glucose tolerance test was given all eligible members of a mental hospital's population of ambulatory men under age fifty and selectively repeated. Results were interpreted as consistent with previously unknown, unsuspected diabetes in 11.7 per cent. The present, similarly designed study was done at the same hospital in an older population of 213 men.

MATERIAL AND METHOD

Because the method of investigation is very like that of the earlier report, it will not be fully described. This study was begun in March 1963 by listing all male inpatients over age forty-nine, bedridden as well as ambulatory. They totalled 305, of which seventeen (5.6 per cent) were known diabetics. Those with the following conditions were eliminated: known diabetes, thyroid, pituitary or adrenal disease, active pulmonary tuberculosis or other chronic debilitating illness, gastrectomy or gastroenterostomy. Others were lost through hospital discharge. As a result, 213 patients were left for study.

Their ages ranged from fifty to eighty-eight years. Median age was 63.6. All had chronic neuropsychiatric illnesses. Ninety-eight per cent had psychoses, the more common being schizophrenia and chronic brain syndrome due to alcoholism or cerebral arteriosclerosis (table 1, col. 1 and 2). Seventy-one per cent had been in the hospital from one year to ten years; 26 per cent, three months to a year; and only 3 per cent for less than three months. Overweight, a most important factor in precipitating diabetes in those hereditarily predisposed,[2] was less frequent than in a sample[3] of the noninstitutional population (table 2).

All subjects received a diet which averaged 2700 calories daily and contained 100 gm. of protein and 300 gm. of carbohydrate. For the three days preceding each glucose tolerance test, the subject's food intake was observed and recorded at all meals and he also drank 100 to 150 gm. of glucose in orange juice daily. Thus it was determined that every patient tested had adequate daily food intake throughout this period, including 300 gm. or more of carbohydrate daily.

Venous blood glucose was determined by the Somogyi-Nelson method.[4] Patients with a combination of blood sugar values of 160 mg. per 100 ml. or above at one hour, 140 mg. per 100 ml. or above at one and one-half hours, and 120 mg. per 100 ml. or above at two hours were classified as positive.[5] If, instead, the level at two hours was 110-119 mg. per 100 ml., the combination was considered probably positive. Those whose initial glucose tolerance test failed to meet these criteria were said to be negative. Those with initial results positive, but with second tests not confirmatory or not done, were classified as unconfirmed positive. Those patients with results positive in both initial and second tolerance tests, or positive in one and probably positive in the other, were called confirmed positive.

Urine was examined for sugar by Clinitest.* Be-

From the Veterans Administration Hospital, Brockton, Massachusetts.

*Ames Company, Inc., Elkhart, Indiana.

TABLE 1

Psychiatric diagnoses of 213 patients, number and per cent consistent with diabetes

	Number tested	Number consistent with diabetes	Per cent consistent with diabetes	
Organic psychoses:				
Chronic brain syndrome due to				
Alcoholism	49	7	14.3	
Arteriosclerosis	41	5	12.2	13.4
Other causes	22	3	13.6	
Functional psychoses:				
Schizophrenia	72	10	13.9	16.8
Others	29	7	24.0	

TABLE 2

Incidence of overweight among patients and noninstitutionalized men (Metropolitan Life Insurance Company Policyholders), Ages 50-69

	Overweight 10 per cent or more		Overweight 20 per cent or more	
Age group (years)	Patients per cent	Policyholders per cent	Patients per cent	Policyholders per cent
50-59	40	63	24	34
60-69	28	57	15	29

cause of the mental state of the group tested, urine specimens frequently were unobtainable when desired postprandially or during tolerance tests and casual samples had to suffice.

Patients were defined as helpless, sedentary, or lightly or moderately active according to their customary daily physical activity. The helpless were permanently confined to bed and chair or to bed and were not able to wash or dress. With assistance, a few partially fed themselves. The sedentary washed, dressed and fed themselves and were ambulant, but walking was essentially limited to going to dining room and toilet on or adjoining their ward. The lightly active did more walking on and off the ward and many were in light occupational therapy such as manual arts and dusting, cleaning and polishing furniture on the ward, ten to thirty hours weekly. The moderately active engaged well in walking and sports and had fifteen to thirty hours weekly of heavier occupational therapy such as painting, laundering, janitorial work or ward housekeeping.

RESULTS

Two-hundred and thirteen men received an initial glucose tolerance test. Forty-nine of them had positive and three probably positive results. After an interval varying from three weeks to nine months (mean, 2.4 months; median, 2), all but two of these fifty-two men were given a second tolerance test. Twenty-three had negative results and were classified as the unconfirmed positive group. Twenty-five had positive results and two probably positive. They constituted the confirmed positive group.

Physical activity and glucose tolerance (table 3)

The incidence of initially positive glucose tolerance tests among the helpless and sedentary was almost the same as among the lightly and moderately active. This was also true of initially positive tests unconfirmed by second examinations. Members of the confirmed positive group were found less frequently among helpless and sedentary patients than among those lightly and moderately active. The three sedentary who were confirmed positive had a family history of diabetes.

Diabetic-like reactions to glucose tolerance tests have been reported as occurring in some nondiabetic persons who have been bedridden months and years by chronic pathologic conditions.[6] Based on these observations, it has been suggested that inactivity may play an important role in the diminished carbohydrate tolerance found among institutional patients with mental disease. The results of this investigation do not support that suggestion.

Unconfirmed positive group.

Twenty-one men with positive and two with probably positive results on initial glucose tolerance test had negative results on second test, three weeks to nine months later (mean interval 2.4 months; median, 2). Only casual urine specimens were available from fourteen of these men and contained no sugar. From nine men, however, urine was obtainable one to two hours after ingestion of initial test doses of glucose, subsequent meals, or both. Three-quarters to 2 per cent glycosuria was found in five. These five men were moderately active physically, weight was stable, and they had not received hypoglycemic therapy. Their data were classified as consistent with diabetes, spontaneously

TABLE 3

Number and per cent of patients with first tolerance test positive and second test negative or positive, by daily physical activity

Patients		Number			Per cent					
		Test 1. Positive 2. Negative	1. Positive 2. Not done	1. Positive 2. Positive	1. Positive		1. Positive 2. Negative		1. Positive 2. Positive	
Helpless	16	3	1	0	25.0	21.6	18.7	13.3	0.0	5.0
Sedentary	44	5	1	3	20.0		11.3		6.8	
Light	81	5		15	24.7	24.0	6.2	9.8	18.5	15.6
Moderate	72	10		9	25.0		13.9		12.5	

improved (table 4). Cases 3 and 4 had a third test, again with positive results and glycosuria. Case 5 had negative results on a third test, but positive results and 2 per cent glycosuria on fourth and fifth tests.

As for the eighteen other men of the unconfirmed positive group, table 5 shows the mean, median and range of their blood glucose values on initial and second tests. They had not received hypoglycemic therapy. Four, of whom two had a diabetic sibling, had lost five to twelve pounds before the second test. These losses, in some, may account for their altered carbohydrate tolerance. Thirteen men were retested, four to twenty-three months after their second examination, with positive results in six (table 6, cases 1-6) and negative results in seven (cases 7-13).

TABLE 4

Positive results and glycosuria on initial glucose tolerance test, with subsequent spontaneous improvement; five cases

Case	Age (Yrs.)	Months between tests	Blood glucose (mg./100 ml.) 1 hr.	1½ hrs.	2 hrs.	Glycosuria during test (per cent)
1	51		195	152	143	1
		4				
			229	171	96	2
2	56		167	149	137	1
		4				
			154	152	152	Urine not obtainable
3	56		219	172	146	.75
		4				
			226	118	63	Urine not obtainable
		21				
			195	183	120	1
4	61		192	169	165	2
		3				
			145	109	104	Negative
		8				
			174	155	127	0.5
		12				
			137	65	98	Negative
5	55		164	143	112	2
		3				
			176	150	103	1
		8				
			154	179	135	1
		13				
			169	150	123	2
		1				
			212	183	137	2

TABLE 5

First and second glucose tolerance tests, eighteen men of unconfirmed positive group

Blood glucose (mg./100 ml.)	1 hr.	1½ hrs.	2 hrs.
Mean	179	175	163
	145	141	139
Median	175	169	150
	142	138	138
Range	160-213	140-233	117-240
	93-229	107-179	96-191

What does the unstable carbohydrate intolerance of this group of eighteen men signify? Among an elderly population, it is stated, there are those who have decreased carbohydrate tolerance somehow related to aging.[2] As a consequence, there is added difficulty in evaluating positive results of a glucose tolerance test in this population. Although the presence of glycosuria would strengthen the diagnosis of diabetes, the absence of glycosuria would not eliminate that diagnosis because sugar may not appear in the urine of an elderly diabetic despite the existence of hyperglycemia.[7]

Confirmed positive group

There were twenty-seven in this group. The mean, median and range of their blood glucose values are shown in table 7. Twenty-three of this group were given a third examination one and one-half to sixteen months after their second test. Results were positive in seventeen, probably positive in one (table 8); and eight of this number (including the one probably positive) subsequently had a fourth test with uniformly positive results (table 8).

Five men had negative results on third tolerance test (table 9). Case 1 had positive results on fourth test and negative on fifth, with 2 per cent glycosuria demon-

TABLE 6

Glucose tolerance tests in thirteen men of unconfirmed positive group

Case	Age (yrs.)	Months between tests	Blood glucose (mg. per 100 ml.) 1 hr.	1½ hrs.	2 hrs.	Wt. change (lbs.) since preceding test
1	64		160	169	156	
		1	134	131	150	0
		7	160	173	169	0
2	67		165	156	158	
		1	169	136	115	—4
		23	186	171	163	+9
3	68		184	189	184	
		9	149	140	125	—12
		4	189	140	130	—9
4	71		189	189	179	
		1	93	125	149	0
		7	179	150	150	0
		13	96	104	112	+10
5	74		184	156	140	
		1	153	164	138	+5
		8	176	148	122	+4
6	78		179	160	143	
		1	126	122	124	0
		9	162	162	127	0
7	51		204	201	180	
		3	151	151	160	0
		14	139	127	100	—17
8	54		161	140	142	
		1	130	123	118	0
		9	159	139	102	0
9	58		201	210	240	
		2	140	179	179	—12
		6	154	197	200	0
10	63		164	169	137	
		4	144	161	177	0
		20	150	189	200	—14
11	66		213	177	142	
		1	160	107	98	0
		20	96	108	139	0
12	72		160	179	182	
		1	131	144	133	0
		16	111	116	112	—20
13	80		170	201	201	
		1	136	154	150	0
		8	159	137	137	0

TABLE 7

First and second glucose tolerance tests, confirmed positive group

Blood glucose (mg./100 ml.)	1 hr.	1½ hrs.	2 hrs.
Mean	185 198	190 196	170 187
Median	183 189	195 205	164 184
Range	169-219 160-272	140-252 147-260	123-256 110-264

TABLE 8

Third and fourth glucose tolerance tests, confirmed positive group

Blood glucose (mg./100 ml.)	1 hr.	1½ hrs.	2 hrs.
Mean	204 204	204 229	183 199
Median	203 203	197 227	184 191
Range	167-249 179-230	157-249 192-263	110-236 154-245

strable during each positive test and postprandially around such periods. His data are regarded as consistent with spontaneous remissions and exacerbations of diabetes. Cases 2 and 3 resemble case 1 in having had neither hypoglycemic therapy nor weight change throughout the period of repeated testing. Results fluc-

TABLE 9

Glucose tolerance tests in five men, confirmed positive group

Case	Age (yrs.)	Months between tests	Blood glucose (mg./100 ml.) 1 hr.	1½ hrs.	2 hrs.
1	65		169	200	203
		½	207	207	195
		5	189	173	83
		4	202	173	152
		10	104	108	89
2	67		190	167	147
		1	179	160	148
		5	162	144	104
		4	160	166	154
		10	108	115	159
3	69		169	169	176
		3	234	254	264
		6	118	114	108
		10	194	235	205
		2	161	142	128
		2	142	144	158
4	53		198	165	125
		1	176	147	110
		1	233	193	107
5	52		188	172	148
		2	172	148	117
		13	156	132	98

tuated from positive to negative during the fourteen months that followed their third tolerance test. Case 4 lost only five pounds but case 5 lost sixty-two pounds before a third test. Their data are interpreted as consistent with spontaneous remissions and exacerbations of diabetes (cases 2-4) and improvement of diabetes following weight loss (case 5). It may be urged, in the absence of demonstrable glycosuria, that cases 2 and 3 are not diabetic but examples of impaired carbohydrate tolerance in the elderly. In our present state of knowledge there can be no certain answer to this. Indeed, more must be learned of the natural history of carbohydrate intolerance in the aged, and tests more specific for the diagnosis of diabetes need to be developed to assist interpretation of abnormal carbohydrate tolerance in the elderly.

Of the eighteen men with positive results on third glucose tolerance test, fasting hyperglycemia was transiently found in each of two, 116 mg. and 117 mg., respectively. In the latter case, 1 per cent glycosuria was demonstrable, and 0.5 to 2 per cent glycosuria was found sporadically or repeatedly in nine others of this particular group. Thus, eleven of these eighteen men were classified as consistent with diabetes because of fasting hyperglycemia and/or glycosuria.

As for the eleven remaining members of the twenty-seven in the confirmed positive group, their blood glucose values (table 10) resembled those of the entire group (table 7). Only casual urine specimens were available for testing from all but two of those eleven, and all were free of sugar. Diabetic family histories were present in 54 per cent of the eleven as compared with an incidence of 41 per cent for the entire group. On the basis of tolerance test results and the high incidence of diabetic family histories, these eleven were classified as consistent with diabetes.

Thus, data of all twenty-seven of the confirmed positive group and five of the unconfirmed positive group (table 4) were interpreted as consistent with diabetes. Intervals between their first and last positive tolerance tests varied from three weeks to twenty-five months, with a mean interval of thirteen months and a median of ten. Based on individual weights and surface areas of this diabetes-consistent group, the test dose of 100 gm. of glucose has been converted into grams glucose per kilogram of body weight and grams glucose per square meter of surface area. The mean, median, and range of these values are shown in table 11. Individual doses were not more than 1.72 gm. per kilogram except in six patients, and not more than 65 gm. per square meter, except in two.

Of the total population tested, 72 per cent of those in the sixth and seventh decades who had initially positive results were finally classified as consistent with diabetes, but only 37 per cent of men beyond the seventh decade were so classified. However, since spontaneous remission of diabetes may occur in the seventh decade (table 4, case 4; table 9, case 1), this factor should be weighed in the interpretation of results. The data of this and a preceding study,[1] suggest that second tolerance tests should be given to confirm initial positive results in diabetes case-finding among institutionalized mentally ill men, particularly after the fifth decade of life.

Members of the group consistent with previously

TABLE 10

Glucose tolerance tests in eleven men, confirmed positive group

Blood glucose (mg./100 ml.)	1 hr.	1½ hrs.	2 hrs.
Range	163-272	140-260	123-258
Mean	196	198	187
Median	192	199	184

Age (yrs.)	Months between tests	1 hr.	1½ hrs	2 hrs.	Family history of diabetes
77		167	147	128	Aunt
	2				
		165	174	182	
76		174	200	194	Sister
	4				
		272	252	258	
	5				
		192	205	205	
66		197	156	127	Mother
	1.5				
					2 Sisters
		184	219	258	
	6				
		174	179	174	
69		184	210	210	Grandparent
	9				
		181	206	184	
	13				
		208	218	178	
	3				
		211	243	249	
66		219	252	250	Sister
	½				
		247	260	252	
	5				
		229	249	223	
63		190	185	167	Aunt
	¾				
		181	160	164	
69		179	164	147	Negative
	1				
		198	198	184	
68		163	200	146	Negative
	1				
		220	220	234	
	8				
		212	195	185	
67		201	201	190	Negative
	1				
		212	212	190	
	22				
		205	197	178	
66		169	140	123	Negative
	4				
		169	164	148	
	5				
		180	158	147	
58		192	192	150	Negative
	2				
		192	219	198	

TABLE 11

Test dose of 100 gm. glucose converted into grams per kilogram of body weight and per square meter of surface area: diabetes-consistent group

Glucose (gm.)	Range	Mean	Median
Per kilogram	1-2.1	1.5	1.4
Per square meter	47.6-71.4	56.5	56.0

unknown diabetes were more than twice as numerous among men in the sixth and seventh decades as in the later years. Their frequency hardly changed in these two decades and tended to drop thereafter. The opposite trend in the unconfirmed positive group may be attributable to the disproportionately small sample in the ninth decade and cannot be regarded as meaningful (table 12).

The frequency of those classified as consistent with diabetes was higher among the overweight (table 13). Fifty-six per cent of those so classified were 10 per cent or more above desirable weight. There was a significant association here ($P<.01$) between diabetes and overweight. In contrast, the unconfirmed positive group and the negative group showed no significant association with overweight.

Within the total number of 213 men tested, 30.6 per cent of those with, and only 11.9 per cent of those without, diabetes in the family were said to be consistent with diabetes. A family history of the disease was present in 35.5 per cent of the diabetes-consistent group, in 20 per cent of the unconfirmed positive group and in 13 per cent of the negative group. Therefore, a positive family history was significantly associated ($P<.01$) with the diabetes-consistent group, but not with the unconfirmed positive group or the negative group. The significant association of the diabetes-consistent group with overweight and family history of diabetes resembles, in these characteristics, the prevalence of known diabetes in the general population.

One-half to 2 per cent glycosuria was demonstrable in sixteen of the thirty-two patients comprising the group consistent with previously unknown diabetes (table 14). Of the twenty-one in this group from whom multiple urine specimens were obtainable one to two hours after meals, during glucose tolerance tests or both, glycosuria was demonstrable sporadically or more often in 76 per cent. In those eleven cases where only casual urine specimens were obtainable, glycosuria was not found.

Only seven in the group were below desirable weight. Three of the five who were 2 to 7 per cent

TABLE 12

Number and per cent consistent with diabetes or unconfirmed positive, by age group

Age group (yrs.)	Number tested	Number consistent with diabetes	Number unconfirmed positive	Per cent consistent with diabetes		Per cent unconfirmed positive	
50 - 59	72	11	4	15.3	17.5	5.5	6.9
60 - 69	88	17	7	19.3		8.0	
70 - 79	49	4	5	8.2	7.5	10.0	13.2
80 - 88	4	0	2	0.0		50.0	

TABLE 13

Number and per cent consistent with diabetes or unconfirmed positive, by weight status

Weight status	Number tested	Number consistent with diabetes	Number unconfirmed positive	Per cent consistent with diabetes		Per cent unconfirmed positive	
Overweight (per cent)							
20 or more	36	9	2	25.0	25.7	5.5	10.0
10 - 19	34	9	5	26.5		14.7	
1 - 9	49	1	1	2.0		2.0	
Desirable weight	34	6	6	17.6	10.0	17.6	8.3
Underweight (per cent)							
1 - 9	36	5	3	13.8		8.3	
10 - 19	19	2	1	10.0	8.3	5.2	4.0
20 or more	5	0	0	0.0		0.0	

TABLE 14

Twenty-one diabetes-consistent patients tested for glycosuria one to two hours after meals or 100 gm. glucose, and eleven by casual urine specimens only

	Glycosuria Postprandial and/or after glucose					Casual
Age (yrs.)	0 per cent	0.5 per cent	0.75 per cent	1 per cent	2 per cent	0 per cent
50 - 59	1	1	2	2	3	2
60 - 69	4	1		1	4	7
70 - 79		1			1	2

underweight had a diabetic family history. The two other patients, 11 per cent underweight, had glycosuria associated with positive glucose tolerance tests.

Physical examination of the group consistent with diabetes disclosed no evidence of thyroid, pituitary or adrenal disorder. The frequency and degree of clinical disease of heart, arteries or kidneys among its members were not, in view of their ages, remarkable. In routine clinical practice, few of them would have prompted a search for diabetes. None had historical or physical evidence of heart disease. Two men in the sixth decade of life and six in the seventh decade had nonspecific T-wave abnormalities in their electrocardiograms. In fifteen men, fifty-three to seventy-seven years old, two or more of the dorsalis pedis and posterior tibial pulses could not be felt but only the oldest man had moderate arterial insufficiency of the legs. Cerebral thrombosis had occurred in one man in the sixth decade and two in the seventh. Retinal arteriosclerosis manifested by arteriovenous nicking was found in nine; moderate thickening of radial arteries in four; essential hypertension of mild degree in one; one-plus albuminuria in one; and chronic pyelonephritis in one.

A battery of liver function tests was administered to the group consistent with diabetes and to 132 of the patients otherwise classified. There was no statistically significant difference between these two groups in the frequency or degree of hepatic dysfunction. Liver biopsies were done in twenty-seven of those consistent with diabetes, including the seven who had chronic brain

syndrome due to alcoholism. The liver was histologically normal in twenty-one. One patient had moderate periportal fibrosis and five who were overweight had moderate or marked fatty infiltration of the liver. Biopsies were done in thirteen of the negative group and showed moderate fatty infiltration in one, marked fatty change in a second, and moderate periportal fibrosis in a third. Biopsies were also done in eleven of the unconfirmed positive group of eighteen patients. Only one was abnormal, showing moderate fatty infiltration. Thus, histological examination of the liver revealed no significant difference between the group consistent with diabetes and those otherwise classified.

Consideration of the evidence mustered in the group consistent with diabetes—repeatedly positive results on glucose tolerance test, fasting hyperglycemia, glycosuria, significant association with overweight and family history of diabetes—has led the author to regard its members as indeed diabetic.

The incidence of previously unknown diabetes was similar among those with functional psychosis and organic psychosis (table 1). The opinion has been expressed that almost all of the published work on glucose tolerance tests in the functional psychoses is weakened by the fact that malnutrition may have been responsible in an indeterminable degree for the impairment observed.[8] Only seven in this study who were considered to have previously unknown diabetes were a little underweight and only two of those had functional psychosis.

TABLE 15

Patients on phenothiazine therapy at initial glucose tolerance test

Group		On phenothiazine therapy	
		Number	Per cent
Diabetics	(32)	22	68.7
Unconfirmed positive	(20)	13	65.0
Negative	(161)	86	53.4

Phenothiazines and carbohydrate metabolism

In a previous report[1] it was concluded that, on the basis of data now in the literature, an evaluation of chlorpromazine's effect on man's glucose metabolism is difficult; that data on the effect of other phenothiazine derivatives on glucose metabolism are virtually nonexistent; and that further investigation is required.

In this study, 68.7 per cent of those with previously unknown diabetes, 65 per cent of the unconfirmed positive group and 53.4 per cent of the negative group were receiving one or two phenothiazine derivatives at the time of or within ten days preceding initial glucose tolerance test (table 15). Analysis by a 2x3 contingency table of chi square revealed no significant association of phenothiazine therapy and the positive results of this tolerance test.

TABLE 16

Phenothiazine therapy in population tested

		Thorazine	Mellaril	Compazine	Stelazine	Sparine	Trilafon
Diabetic	N	11	4	3	3	1	0
MCD*		228,323	98,338	16,922	2,228	200	—
MDD†		392±51	176±32	31±5.5	6±4.6	200	—
MLT‡		19±6.0	19±7.1	18±7.4	11±7.5	<1	—
Unconfirmed positive (15 per cent concurrently on two phenothiazines)	N	4	5	1	5	1	0
MCD		53,481	122,350	2,400	2,814	10,800	—
MDD		461±67	348±20	20	14±7.4	514	—
MLT		4±0.3	12±1.5	4	7±2.8	<1	—
Diabetic and unconfirmed positive	N	15	9	4	8	2	0
MCD		181,700	111,678	13,291	2,594	5,500	—
MDD		397±51	251±31	30±5.4	10±5.7	250	—
MLT		15±4.9	15±3.9	15±7.3	8±2.7	<1	—
Negative (7 per cent concurrently on two phenothiazines)	N	16	15	11	14	1	9
MCD		281,589	116,831	7,320	9,221	3,600	11,086
MDD		495±72	413±57	21±4.5	22±2.6	257	20±5.0
MLT		19±5.3	9±2.8	12±4.3	14±3.6	<1	18±7.6

*MCD = Mean cumulative dose (mg.)
†MDD = Mean daily dose (mg.)
‡MLT = Mean length of therapy (mos.)

Duration and total cumulative dosage of continuous therapy with phenothiazine derivatives preceding the initial test was determined for the three groups. The negative group was limited to the first hundred men taken serially by surnames alphabetically arranged. Data were analysed by Student's '*t*' test. Statistically compared, the three groups revealed only the following significant differences: the negative group received higher mean daily doses of Mellaril and Stelazine and the unconfirmed positive received a higher mean daily dose of Mellaril than did the diabetes-consistent group (table 16). The data, therefore, fail to support the proposition that phenothiazine therapy may have contributed to the positive results on initial tolerance tests.

COMMENT

Fifteen per cent of 213 men were considered to have previously unknown diabetes. Compared with an estimated national incidence of 0.81 per cent unknown diabetes,[9] this is a high figure. Even if only the sixteen patients who had positive results on tolerance test with fasting hyperglycemia and/or glycosuria were called diabetic, their 8 per cent incidence would still be relatively high. Factors believed to contribute importantly to the prevalence of previously unknown diabetes found in this study are the age of the population tested and comprehensive use of a glucose tolerance test. Whether phenothiazine therapy impairs carbohydrate tolerance in man is an open question requiring further investigation.

As a combined result of our two studies, seventy-four (12.9 per cent) of 572 men chronically hospitalized for mental illness were considered to have previously unknown, unsuspected diabetes. Its frequency rose with aging until the fifth decade, plateaued through the seventh, and then dropped (table 17). Although these men represent a special class, the surmise is strong that similar investigations among the general population, if feasible, would reveal an incidence of unknown diabetes considerably higher than 0.81 per cent.

TABLE 17

Combined results of 572 patients examined for diabetes; number and per cent classified as diabetic, by age group

Age group (yrs.)	Number tested	Diabetic Number	Diabetic Per cent	
21 - 29	25	1	4.0	6.9
30 - 39	179	13	7.3	
40 - 49	155	28	18.1	17.8
50 - 59	72	11	15.3	
60 - 69	88	17	19.3	
70 - 79	49	4	8.2	7.5
80 - 88	4	0	0.0	
Total	572	74	12.9	

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