Analysis of Tests for Diabetes in 250,000 Persons Screened for Diabetes Using Finger Blood after a Carbohydrate Load

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SUMMARY

The results of a detection program for diabetes over a four-year period, using a finger blood test after a carbohydrate load, were analyzed. After excluding persons with known diabetes or incomplete data, 250,938 had the initial screening test and 9,682 or 3.9 per cent screened "positive." Approximately 75 per cent of the "positive" screenees returned for a confirmatory carbohydrate tolerance test. Five thousand, three hundred and seventy persons, or approximately 74 per cent of those who returned, had "positive" confirmatory tests. Since only persons who were "positive" in both tests were considered to have diabetes, the prevalence rate for previously undetected diabetes was 2.1 per cent.

When allowance was made for "positive" screenees who failed to return by assuming that they would confirm "positive" at the same rate as the returnees, the estimated prevalence rate for previously undetected diabetes was 2.8 per cent.

A representative sample of 100,077 persons showed very similar test results which were further analyzed by sex, race, weight and family history in relation to decades of age. The prevalence rate of undetected diabetes and the rate of "positive" confirmation for "positive" screenees varied markedly with age. The importance of considering the other variables in relation to age for planning detection programs is discussed; 60 per cent of the persons with diabetes detected in this program had a negative family history for diabetes.

Information from return postcards sent to "positive" screenees from three months to three years after their initial test showed that a very high percentage of screenees had consulted their physicians as a result of the test; 62 per cent of the confirmed "positives" who replied stated that the diagnosis of diabetes had been confirmed by their physicians. DIABETES *17*:274-80, May, 1968.

The results of recent studies indicate that the prevalence of diabetes in the general population is much greater than was formerly believed.[1] As the observed prevalence increases, the subclinical, latent or "prediabetic" states are probably also on the rise. From the point of view of public health, it is becoming increasingly necessary to devise and practice mass screening programs to detect persons with diabetes in its unrecognized, early stages in order to recommend treatment and prevent complications if possible.

Such a program, called the "DAC" Detection Program for Diabetes, has been used very successfully in the metropolitan area of Greater Cleveland, Ohio, and has been reported previously.[2] This paper presents the further results of this program during a four-year period. This is not a statistical study per se, but an attempt to reflect the experience gained in the groups studied.

Presented at the Sixth Congress of the International Diabetes Federation in Stockholm, Sweden, on July 31, 1967.

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METHODS

Persons were given the screening test[2] at their place of employment or in such neighborhood settings as shopping centers. Whites and nonwhites were included in the proportion in which they occurred in the groups studied. Both males and females were tested.

Each screenee was asked to fill out an IBM type of identification card with name, address, phone numbers, age, sex, race, height, weight, religion, family history of diabetes and physician's name with signed permission to release the result to him. Several questions were included to ascertain whether the individual had previously diagnosed diabetes.

The screenee ingested 7 oz. of a carbonated, cola or cherry flavored, partial hydrolysate of cornstarch (commercially available as corn syrup) to drink. As pre-

viously reported,[3] this solution is designed to contain the equivalent of 75 gm. of glucose. It is palatable, does not provoke nausea and can be tolerated by young and old persons. It can be given with or without preliminary fasting.

No attempt was made to determine the relation of the carbohydrate load to the last feeding, but the screenee was told not to eat for two hours after its ingestion. Two hours later a drop of finger blood, 0.075 cc., was drawn into a calibrated, disposable pipette and added to a 1.15 cc. solution of 1 per cent sodium fluoride in a small plastic vial. The ferricyanide method for blood sugar was used with an AutoAnalyzer.[2] No test was judged valid if the two-hour interval varied by more than plus or minus ten minutes.

A screening blood glucose level over 140 mg. per 100 ml. was called "positive." The screenee was notified by letter and given an appointment to return, after at least a two-week interval, for a confirmatory carbohydrate tolerance test. With the use of the same technic, blood glucose determinations were then obtained in a fasting state of at least four hours' duration and one hour and two hours after the ingestion of the carbohydrate load. The confirmatory test was called "positive" if the blood glucose levels were one or more of the following: above 120 mg. per 100 ml. in the fasting state, or over 190 mg. per 100 ml. at one hour, or above 140 mg. per 100 ml. two hours after carbohydrate ingestion.

For purposes of analysis, only persons who were "positive" on both the screening and confirmatory carbohydrate tests were judged diabetic; persons known to have diabetes before testing were excluded.

The exact results for both tests on each person judged to be diabetic were sent by letter to the designated physician. A letter was also sent to the screenee indicating that his tests were abnormal and advising him to consult his physician. "Positive" screenees, who failed to return for a confirmatory test, in spite of repeated efforts over a three to six-month period, and their designated physician were sent similar letters.

Finally, a follow-up postcard survey on all patients who screened "positive" was carried out from three months to three years after the initial tests.

RESULTS

General

The initial screening test was performed on 253,190 persons over a four-year period. After elimination of 274 persons known to have diabetes prior to screening and 1,978 persons with data incomplete for various reasons, i.e., omission of age, etc., data on 250,938 persons were analyzed. This included the previously reported early pilot study[2] on 8,790 persons which represented 3.5 per cent of the total (see table 1).

Of the total, 67.8 per cent were screened at places of employment and were referred to as the industrial group; the remaining 32.2 per cent were screened in neighborhood settings and are referred to as the community group. This 2:1 ratio for the total survey differs from the pilot study which was almost equally divided between the industrial and community groups.

The industrial group was a predominately male, active, healthy, working group with the majority between twenty and fifty-nine years of age. The community group contained a larger number of women and older people, many of whom were not gainfully employed, but almost all were healthy and active. Except in the early pilot study, relatively few very elderly patients were tested.

As shown in table 2, 9,682 persons (3.9 per cent) of the total 250,938 had an initial "positive" (abnormal) screening test; such persons are hereafter referred to as "positive" screenees. Of the "positive"

TABLE 1

Summary of diabetes detection program

Persons	Pilot study	1964	1965	1966	1967 June	Grand total
Total persons screened	8,790	76,279	79,537	63,576	22,756	250,938
Persons with positive screen tests	709	3,019	2,455	2,865	634	9,682
Positive screen and positive confirmatory test	407	1,668	1,412	1,548	335	5,370
Positive screen and negative confirmatory test	153	539	471	603	152	1,918
Positive screen but no confirmatory test	149	812	572	714	147	2,394

screenees, 7,288, or 75.3 per cent, returned for the confirmatory carbohydrate tolerance test. Of these, 5,370, or 73.7 per cent, had a "positive" confirmatory test and are hereafter referred to as confirmed "positives"; 1,918 had a negative (normal) confirmatory test. There were 2,394 "positive" screenees who failed to return for a retest.

Only the 5,370 confirmed "positive" were considered to have diabetes, giving a known prevalence rate for previously undetected diabetes of 2.1 per cent in the population screened. Since 24.7 per cent of the "positive" screenees did not return for a confirmatory test, the actual prevalence rate was obviously higher. If we assume that the "positive" screenees who did not return would have confirmed "positive" at approximately the same rate (74 per cent) as those who did return, then an estimated additional 1,772 persons, or a total of 7,142, confirmed "positives" from the total 250,938 persons screened would give an estimated prevalence rate for previously undetected diabetes of 2.8 per cent.

DISCUSSION

Analyses of representative sample

For more detailed evaluation, a sample of 100,077 of the 250,938 individuals screened was analyzed by age, sex, race, weight, and family history of diabetes in relation to the test results. This sample was made up of persons selected in the order in which they were screened, following the completion of the pilot study, after excluding those known to have diabetes and whose personal data card was incomplete. It was held to be representative of the total (population screened), since the percentage of persons in the industrial group (67.1 per cent) and the community group (32.9 per cent) in the sample corresponded very closely to the percentage of these categories, 67.8 per cent and 32.2 per cent respectively, in the total study.

The analysis of the total results for the screening and confirmatory tests in the sample are also shown in table 2. When compared with the results for the total study, the percentages derived in a like manner for the sample are very similar, thus substantiating the validity of the sample representative of the total study. Of the 100,077 persons screened, 4,292 or 4.3 per cent of the sample had a "positive" screening test initially. Of the "positive" screenees, 75.5 per cent, a per cent almost identical to that for the total study, returned for the confirmatory carbohydrate tolerance test. Of these, 2,400, or an almost identical 74.1 per cent, had a positive confirmatory test giving an established known prevalence rate for previously undetected diabetes of 2.4 per cent for the sample. With the use of the same assumption discussed above, 74 per cent of the 1,051 who failed to return, or an additional 778 persons, were estimated to confirm "positive" for a total of 3,178 estimated confirmed "positives" from the total 100,077, which gave an estimated prevalence rate for previously undetected diabetes of 3.2 per cent for the sample.

TABLE 2

Analysis of screening and confirmatory test results for total study and representative sample

	Total study	Representative group
Persons who had initial screening test		
Total screening tests	250,938	100,077
Positive screening tests	9,682	4,292
As per cent of total screening tests	3.9 per cent	4.3 per cent
Persons with positive screening test who returned for confirmatory test		
Total confirmatory tests	7,288	3,241
As per cent of positive screening tests	75.3 per cent	75.5 per cent
Positive confirmatory tests	5,370	2,400
As per cent of total screening tests	2.1 per cent	2.4 per cent
As per cent of total confirmatory tests	73.7 per cent	74.1 per cent
Persons with positive screening test who did not return for confirmatory test		
Total confirmatory tests not done	2,394	1,051
Estimated additional positive confirmatory tests (74 per cent of those not done)	1,772	778
Estimated prevalence of previously undetected diabetes		
Known positive plus estimated additional positive confirmatory tests	7,142	3,178
As per cent of total screening tests	2.8 per cent	3.2 per cent

As illustrated in the bar graph (figure 1), 87 per cent of the persons in the sample were in the age decades of 20-59 yrs.

Distribution of the test results by age decade in table 3 reveals that the per cent of confirmed "positive,"

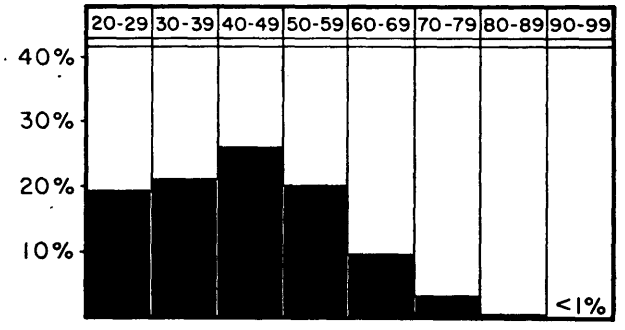

FIG. 1. Screenees distribution by decades of age.

in relation to the total number screened in each age group, increased with each succeeding decade (column $g = \frac{\text{column d}}{\text{column a}}$). However, the majority of persons in the older decades still had normal tolerance tests (column b).

The per cent of confirmed "positive," in relation to the number of "positive" screenees in each age group who returned for retesting, also increased with age since it was only 37 per cent in the 20-29-yr. decade and over 75 per cent after fifty years of age (table 3, column $h = \frac{\text{column d}}{\text{column d} + \text{e}}$). Comparison of the confirmation rate by sex revealed no significant difference.

Therefore, since age is an important variable in the occurrence of diabetes, the other variables were also related to the test results by decades of age. For these analyses, the sample was divided into the "diabetic group" (table 3, column d) which was composed of only the confirmed "positives" and the "nondiabetic" group which was composed of all the remaining screenees (table 3, column b, e, f).

Since the prevalence rate of confirmed "positives" as well as the rate of "positive" screenees who confirmed "positive" varies with age, "positive" screenees who failed to return for retest were included in the "nondiabetic" group for simplification. However, as stated above, the arbitrary exclusion of all "positive" screenees who failed to return makes the figures for the "diabetic" group falsely low.

Comparison of the "diabetic" and "nondiabetic" groups by race according to age (table 4) reveals that the rate of previously undetected diabetes was slightly higher for each age decade in the nonwhite group than for the white group, except in the ninth decade which had too few persons to be statistically significant.

When compared in a similar manner by sex (table 5), females showed a slightly higher rate of confirmed diabetes than males in all age groups.

Forty per cent of the "diabetic" group had a positive family history compared to 28 per cent in the "non-"diabetic group." Relating the incidence of positive family history to age decade, there was not much variation in the "nondiabetic" group, but the percentages decreased significantly as age increased in the "diabetic" group (table 6). However, since the rate of previously undetected diabetes increased with age, the number of

TABLE 3

Analysis of testing results by age groups for representative sample

Age (yrs.)	Total persons screened	Screening test results		Confirmatory test on positive screenees			Confirmed positive tests	
		Negative	Positive	Positive	Negative	Not Done	As per cent of total screening tests done	As per cent of total confirmatory tests done
	a	b	c	d	e	f	g	h
20-29	18,907	18,807	100	25	42	33	0.1	37
30-39	21,996	21,683	313	123	128	62	0.6	49
40-49	27,088	26,301	787	409	192	186	1.5	68
50-59	19,673	18,435	1,238	709	217	312	3.6	76
60-69	8,989	7,886	1,103	673	172	258	7.5	79
70-79	2,959	2,346	613	373	67	173	12.6	84
80-89	436	312	124	77	20	27	17.7	79
90-99	29	15	14	11	3	0	38.0	78
20-99	100,077	95,785	4,292	2,400	841	1,051	2.4	74.1

TABLE 4

Comparison of race by decade for diabetic and nondiabetic groups in sample

Age (yrs.)	White male and female			Nonwhite male and female		
	Diabetic group	Nondiabetic group	Per cent diabetic	Diabetic group	Nondiabetic group	Per cent diabetic
20-29	22	16,401	0.1	3	1,930	0.2
30-39	92	18,537	0.5	24	2,461	1.0
40-49	340	23,292	1.4	52	2,091	2.4
50-59	601	16,539	3.5	59	1,144	4.9
60-69	578	7,076	7.5	39	474	7.6
70-79	316	2,182	12.6	20	126	13.7
80-89	72	288	20.0	1	29	3.3

TABLE 5

Comparison of sex by decade in diabetic and nondiabetic groups in sample

Age (yrs.)	Male			Female		
	Diabetic group	Nondiabetic group	Per cent for Diabetic group	Diabetic group	Nondiabetic group	Per cent for diabetic group
20-29	12	10,502	0.1	13	7,829	0.7
30-39	63	13,160	0.5	53	7,839	0.7
40-49	196	14,704	1.3	196	10,679	1.8
50-59	309	9,756	3.1	351	7,927	4.2
60-69	264	3,714	6.6	353	3,836	8.4
70-79	116	981	10.6	220	1,327	14.2
80-89	17	138	11.0	56	179	23.8

TABLE 6

Comparison by decades of age for family history

Age yrs.	Diabetic group			Nondiabetic group		
	Positive history	Negative history	Per cent positive history	Positive history	Negative history	Per cent positive history
20-29	16	9	64	5,433	13,449	28
30-39	69	54	56	6,951	14,922	32
40-49	212	197	50	8,078	18,601	30
50-59	283	426	40	4,986	13,978	26
60-69	261	412	39	2,066	6,250	25
70-79	108	265	29	547	2,039	21
80-89	14	63	18	53	306	15
90-99	2	9	18	2	16	12
20-99	965	1,435	40	28,116	69,561	28

persons with positive family history was larger in proportion to the total screened in the older age groups.

Of the "diabetic" group, 64 per cent were twenty-five pounds or more overweight compared to 42 per cent of the "nondiabetic" group.

Follow-up survey

A double postcard was mailed to "positive" screenees from three months to three years after their initial test asking the following questions:

1. Did you visit your doctor because of diabetes?
2. Do you have diabetes?
3. Are you under your doctor's prescription for diet, tablets, or insulin?

From the 7,116 cards sent, 3,127 replies were received and grouped into three categories for analysis (table 7).

A. Positive screenees who failed to return for a confirmatory carbohydrate tolerance test but did see their physician. Out of 698 persons who replied, 256, or 37 per cent, stated that they had diabetes in comparison to 74 per cent of those who returned to the "DAC"

TABLE 7

Post card follow-up (October 1963 through December 1966)

Persons with positive screening test	Number sent	Number returned	Has diabetes	Has no admitted diabetes
A— Did not return to detection program for confirmatory test	1,186	698 (58.8 per cent)	256 (37 per cent)	442
B— Negative confirmatory test	1,028	458 (44.5 per cent)	29 (6 per cent)	429
C— Positive confirmatory test	4,272	1,971 (46 per cent)	1,233 (62 per cent)	738
Totals	7,116	3,127 (44 per cent)	1,518 (48 per cent)	1,609

program and were judged to have diabetes because of a positive confirmatory test.

B. Positive screenees who returned for a confirmatory carbohydrate tolerance test which was normal. Out of 458 persons, 29, or 6 per cent, reported that they had diabetes. However, in a similar group of 72 persons who were requested by the program to return at a much later date for a repeat confirmatory test, 22 per cent had positive results.

C. Positive screenees who had a positive confirmatory carbohydrate tolerance test. Out of 1,971 persons who replied, 1,233, or 62 per cent, considered that they had diabetes.

DISCUSSION

Since the prevalence of diabetes increases with age, the detection rate of previously undiagnosed diabetes will be influenced by the age composition of the population which is screened. Two thirds of the persons screened in the study were in age groups from 20-49 yrs. of age and two thirds were actively working in industry. In considering high risk factors, table 3 is of particular interest and shows the relationship between age and abnormal carbohydrate tolerance. It should be noted that while approximately 60 per cent of the total screenees were age forty or over, nearly 94 per cent of the "diabetics" were in this age group. Therefore, an even higher prevalence rate would be expected in a more representative cross-section of the adult population which included a larger number of elderly, inactive persons.

By restricting the diagnosis of diabetes to those persons who had a "positive" screening test followed by a "positive" confirmatory test for calculation of the prevalence rate, several additional factors must be considered in its interpretation. First, the rate will be falsely lowered by eliminating the "positive" screenees who failed to return for confirmatory testing so that the size of this group, which was 25 per cent in this study is an important factor. To allow for this, an estimated prevalence rate was projected by assuming that the rate of "positive" confirmation would be the same for the nonreturnees as for the returnees, but no data are available to support this. Second, as shown in a small follow-up study, some of the "positive" screenees who had a negative confirmatory test had a "positive" confirmatory test at a later date which would tend to increase the prevalence rate. Third, a few of those who screened negative undoubtedly would have had a "positive" confirmatory test, had one been done, which would also tend to increase the prevalence rate, but no data are available to support this assumption.

Approximately one fourth of the "positive" screening tests were not confirmed by the repeat carbohydrate tolerance test. This can be explained by several factors: (1) possibility of error in either the original screening procedure or in the confirmatory test, (2) more inconsistent results in young individuals as was indicated by study figures which showed that the abnormal tests were more consistently reproducible in the older age groups, (3) variations in carbohydrate tolerance particularly in early stages of diabetes.[4] (As mentioned above, some persons with negative confirmatory tests had "positive" tests at a later date.)

Since juvenile diabetes is usually symptomatic and easily diagnosed early in the course of the disease, a factor in the very low frequency rate in the youngest

age group may be that most of the diabetics in this group were already diagnosed and therefore excluded from the analysis.

Several proposals have been made to change the diagnostic criteria because of the marked increase in the frequency of occurrence of diabetes in older age groups.[5] Although the results showed that each ascending decade of age had a higher per cent of persons who were considered to have diabetes, the majority of persons, even in their eighties, had normal tests. This would support the theory that diabetes is associated with but not necessarily caused by aging.

We have no explanation for the slightly greater prevalence of diabetes in nonwhites than whites and females than males.

The fact that 60 per cent of the "diabetic" group found in this program did not have a family history of diabetes suggests that detection programs should not be restricted to persons with a positive family history. Perusal of table 6 shows that after the age of fifty years, 40 per cent or less of the people with abnormal glucose tolerance curves have a family history of diabetes. Therefore, 60 per cent of the positive group, or more, would be missed if this criteria for selection of screenees were used. However, if programs have to be restricted for economic reasons, persons under fifty with a positive family history should certainly be included since the percentage of persons with a positive family history is higher in the younger age groups. Correct and more frequent diagnoses of diabetes in recent years probably are factors in the higher frequency of positive family history in the younger age groups. No attempt was made to correlate the degree of carbohydrate tolerance impairment with family history.

Since a number of the "nondiabetic" group become diabetic in future years, it is interesting to note that more than 25 per cent of this group had a family history of diabetes.

The higher rate of obesity in the diabetic group is in accord with the knowledge that people who are overweight are more apt to develop diabetes.

The postcard follow-up survey revealed that a high percentage of persons consulted their physicians as a result of the detection program. The fact that only 62 per cent of those who were classified as diabetic in the program subsequently admitted to having diabetes in the postcard replies may indicate the reluctance of many diabetics to identify themselves as such.

In summary, this study has shown that the prevalence rate of previously undiagnosed diabetes is influenced by many factors which should be considered in planning detection programs and evaluating the results.

ACKNOWLEDGMENT

This study was supported by The Diabetes Association of Greater Cleveland and United States Public Health Service Grant CH37-16.

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