Diabetes Incidence

A Two-year Follow-up of 10,000 Men in a Survey of Ischemic Heart Disease in Israel

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SUMMARY

In 1963, 10,059 men aged forty years and over were examined in an I.H.D. survey and 9,711 of them were re-examined two years later. At both these examinations suspect diabetics were screened out by a casual blood glucose value and/or a positive history of diabetes. Further information was collected on all these suspect diabetics to enable their classification into diabetic categories using similar criteria on both occasions.

Among 9,079 persons judged at risk of developing diabetes, 144 new cases of diabetes were discovered two years after the 1963 examination. The over-all two-year incidence rate for men over forty was 15.5 per thousand. Four regions of origin, Central Europe, Southeastern Europe, Israel and North Africa had incidence rates approximately equal to the over-all rate. The age adjusted incidence rate for men from Eastern Europe was lower (8.5 per 1,000) and from the Middle East higher (20.3 per 1,000) than the average. DIABETES *19*:938-43, December, 1970.

The prospective Israeli Ischemic Heart Study of a representative sample of male government employees aged forty and over[1] provided an opportunity for investigating the prevalence and incidence of associated conditions, one of which, diabetes mellitus, is reported here.

The prevalence of diabetes among the 10,059 men in 1963 was reported,[2] and this paper deals with the two-year incidence (from 1963 to 1965) of diabetes among those re-examined in 1965.

MATERIAL AND METHODS

Of the 9,711 subjects re-examined in 1965, 632 were excluded from the incidence study for various r (see table 1) leaving 9,079 subjects who made denominator. The numerator of the study was at as described below.

All subjects were asked during the course medical history about prior diagnosis of diabete time of diagnosis was listed as occurring either period before the initial examination in 1963, o that time, i.e. from 1963 to 1965. In addition, a blood sample was drawn into a vacutainer tube cc ing fluoride for a whole blood sugar determinati the Hoffman method using the AutoAnalyzer[3]— survey laboratory. As the subjects were examined times during the day, the blood sugar determin are "casual" ones.

All those reporting a history of diabetes sinc 1963 examination and those in whom the casual sugar equalled or exceeded 140 mg./100 ml. designated as positive screenees and investigated f (A whole blood sugar value of 140 mg. by the Analyzer was judged equivalent to the screening used in 1963.)

TABLE 1

Derivation of the denominator and numerator for di incidence (1963 to 1965)

Examined in 1963	
Reexamined in 1965	
Of these, excluded from incidence study:	
(a) Definite diabetics in 1963	
(b) Abnormal GTT in 1963	
(c) Inadequate data in 1963	
(d) 1965 examinees with no blood sugar estimation available	
Total excluded (a-d)	
∴ At risk for diabetes incidence (denominator)	
Positive screenees in 1965	
Of these, proved diabetics (numerator)	

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The 288 positive screenees consisted of

(a) 169 with a positive history of diabetes (Interestingly, only thirty of these subjects had a casual glucose value of 140 mg. per 100 ml., or greater); and

(b) 119 subjects with no history of diabetes, but whose casual sugar value was 140 mg. or over.

As in the 1963 survey, the next phase of the study was aimed at collecting sufficient information to permit a more precise classification of these 288 positive screenees. Information was obtained from the treating physician, laboratories, and/or diabetic clinics, in cases where the patient had been referred to a specialist. When neither the personal physician nor the specialist could provide satisfactory information, the subject was asked to report to the survey laboratory for an oral glucose tolerance test.

Classification of blood sugar levels is complicated and requires consideration of two main factors.

1. *Analysis of whole blood or plasma or serum.* The vast majority of our analyses were made on whole blood, which is about 10 to 15 per cent lower than those for plasma or serum.[4,5] The Committee on Statistics of the American Diabetes Association[5] suggests that the whole blood value be multiplied by 1.15 and 6 mg. per 100 ml. be added to bring the value into line with that of plasma or serum. In the present study, we did not use this formula but made a 10 per cent correction for the results on the rare occasion when the estimation was made on plasma or serum instead of whole blood.

2. *The chemical method used.* The tests used were grouped into two categories. The first included those tests which measure approximate true blood glucose values. This includes the Somogyi-Nelson, glucose-oxidase and Hoffman-AutoAnalyzer methods.[6,7] The second group consisted of the Hagedorn-Jensen method which was still commonly used at that time.

These two factors were taken into consideration and the results assigned points with the use of the principles of Remein and Wilkerson[8] with modification of their scheme as follows:

Evaluation of glucose tolerance test [blood sugar by "true blood glucose" methods (true B.G.) or Hagedorn-Jensen (H-J) methods]

	True B.G.	(H-J)	Points
Fasting	110 or more	130 or more	1
	100 to 109	120 to 129	½
	Less than 100	Less than 120	0 (normal)
One-hour level	170 or more	200 or more	½
	160 to 169	180 to 199	0 (abnormal)
	Less than 160	Less than 180	0 (normal)
Two-hour level	120 or more	140 or more	½
	100 to 119	120 to 139	0 (abnormal)
	Less than 100	Less than 120	0 (normal)

RESULTS

Classification of diabetic suspects

The criteria for the division into diagnostic categories remained the same as for the 1963 survey, and are given in abbreviated tabular form in table 2.

The classification of the suspected diabetics (positive screenees) is shown in table 3 and reveals 144 cases of diabetes among the 288 suspects. The distribution of these 144 incidence cases into their diabetic categories, and the criteria on which the diagnosis was based, are described in detail below and are shown in table 4.

1. *Definite diabetes.* This comprises a total of seventy-seven men of whom forty-one had glucose tolerance tests with definitely abnormal values at all three readings (2 points). The remaining thirty-six had two fasting blood sugar values of 130 mg. or more, plus one or more of the following: a third fasting sugar value of at least 150 mg.; a casual blood sugar value of at least 200 mg.; or a history of treatment with insulin or

TABLE 2

Summary of diagnostic criteria

Diagnosis	Glucose tolerance test criteria	Alternative criteria* Minimum blood sugar, mg. per 100 ml. Fasting (H-J)	Fasting (H-J)	Casual True B.G.
Definite diabetes	2 points	130 × 2 +	150 or	200 or Tabs/insulin
Probable diabetes	1½ points	130 × 2 +	130 or	160-199 or pos. hist.
Possible diabetes	1 point	130 × 1 +	130 or	160 or pos. hist.
Abnormal GTT	½ or abnormal			
Normal	Normal at all levels	Less than 120 mg. × 3		

*Diabetes diagnosed using the alternative criteria was almost always on the basis of three abnormal fasting blood sugar tests.

TABLE 3

Classification of 288 positive diabetic screenees in 1965 survey

Diabetes: Definite	77	
Probable	24	
Possible	43	
Total diabetics		144
Abnormal GTT	69	
Not diabetic	58	
Inadequate data for classification	17	
Total	288	

oral hypoglycemic agents.

2. *Probable diabetes.* This comprises a total of twenty-four men of whom twelve received 1½ points on the glucose tolerance test (ten with a moderate elevation on fasting and a definite abnormality on both later measurements, and two with a pronounced abnormality on fasting and one later measurement), and another twelve had two fasting blood sugar values of at least 130 mg. plus one or more of the following: a third fasting value between 130 and 150 mg.; a casual blood sugar value between 160 and 200 mg.; or a self-reported history of diabetes.

3. *Possible diabetes.* This comprises forty-three men of whom thirty-four received one point on the glucose tolerance test. (Twenty-eight had both abnormal one-hour and two-hour values, five were abnormal at only the one- or two-hour reading but had moderately abnormal fasting values, and one man was classified solely on an abnormal fasting value.) The other nine men had one fasting blood sugar value of 130 mg. or more, plus one or more of the following: a second fasting value of 130 mg. or more; a casual blood sugar value of at least 160 mg.; or a self-reported history of diabetes.

The positive screenees who were not found to have diabetes were distributed as follows.

Abnormal glucose tolerance test: Sixty-nine men had glucose tolerance test results in the zone between diabetic and not diabetic. Of these, forty received ½ point (abnormal at only one time), and twenty-nine received no points but had slightly elevated readings at one or two hours.

Not diabetic: Fifty-eight men were classified as definitely not diabetic. Of these, forty-seven had a normal glucose tolerance test, and eleven had two normal fasting levels and either a third normal value or a medical report that he was not diabetic.

Unclassified: There were seventeen men for whom we were unable to obtain enough data to permit us to classify them in one of the foregoing categories.

Incidence of diabetes by age and region of birth

For analyses of the incidence data by age and area of birth, the men in the categories of definite, probable, and possible diabetes have been combined. These three groups would be classified as diabetic by most diabetes surveys.[9,10] The diabetes incidence figures for the two years following the initial examination are given in table 5. To eliminate the possibility of a bias being introduced by individual differences in the length of the period of observation between the two examinations in 1963 and 1965 (average observation period 24.6 months), we have calculated incidence by person years of observation and our report is adjusted to a uniform period of two years. The two-year incidence of diabetes increases with age from 11.3 per thousand for men aged 40 to 49, to 19.7 for men aged 50 to 59, and to 25.2 for men over 60 in 1963. This increase with age is not so clearly seen in each of the groups relating to region of birth, presumably due to the smaller numbers in the groups.

TABLE 4

Diabetes incidence cases found in 1965

			1963-1965 History of diabetes			
Diabetic classification	Total		Negative		Positive	
Definitely diabetic	77		46		31	
Glucose tolerance		41		30		11
Other data		36		16		20
Probably diabetic	24		9		15	
Glucose tolerance		12		4		8
Other data		12		5		7
Possible diabetic	43		24		19	
Glucose tolerance		34		21		13
Other data		9		3		6
Total	144		79		65	

TABLE 5

Two-year incidence of diabetes from 1963 to 1965 by age and region of birth (age specific and age adjusted data)

Age in 1963	Eastern Europe		Central Europe		Southeastern Europe		Israel		Middle East		North Africa		Total	
	No. cases / No. at risk	Rate* per 1,000	No. cases / No. at risk	Rate* per 1,000	No. cases / No. at risk	Rate* per 1,000	No. cases / No. at risk	Rate* per 1,000	No. cases / No. at risk	Rate* per 1,000	No. cases / No. at risk	Rate* per 1,000	No. cases / No. at risk	Rate* per 1,000
40 to 49	4 / 725	5.5	9 / 700	12.5	7 / 783	8.8	5 / 680	7.1	15 / 1,334	11.1	18 / 826	21.3	58 / 5,048	11.3
50 to 59	10 / 783	13.0	9 / 464	19.0	11 / 640	26.9	12 / 465	24.7	19 / 646	28.7	4 / 253	15.4	65 / 3,251	19.7
60+	2 / 229	8.5	3 / 104	26.8	8 / 166	45.2	2 / 119	15.4	6 / 136	40.5	0 / 26	0	21 / 780	25.2
Total	16 / 1,737	9.2	21 / 1,268	16.1	26 / 1,589	16.0	19 / 1,264	14.4	40 / 2,116	18.5	22 / 1,105	19.4	144 / 9,079	15.5
Age adjusted rates		8.5		16.2		15.2		14.3		20.3		17.1		

*Rate obtained by dividing the number of new cases by the number of person years of observation and then multiplying by 2 (average observation period 24.6 months).

The over-all two-year incidence rate for men over 40 is 15.5 per thousand (S.E. = 4.1/1,000). Four regions, Central Europe, Southeastern Europe, Israel, and North Africa, have incidence rates approximately equal to the over-all rate. However, the age-adjusted incidence rate in Eastern Europe is lower (8.5 per 1,000), and in the Middle East it is higher (20.3 per 1,000) than the average.

For convenient comparison, table 6 shows the age-adjusted prevalence rates (from 1963) alongside the age-adjusted two-year incidence rates for six regions of birth. In our prevalence report we noted, surprisingly, higher age-adjusted prevalence rates in men from Israel, the Middle East, and North Africa as compared to those from Europe. This suggestive higher rate is noted at present only in men from the Middle East, on the one hand, while a lower rate is noted in those from Eastern Europe, on the other hand. These overall area differences in incidence rates are not statistically significant at the .05 level. It is to be noted, however, that there is a high incidence rate for the younger age group (40 to 49) from North Africa. We will await the results of our 1968 survey before drawing any conclusion.

DISCUSSION

The literature dealing with epidemiological surveys of the occurrence of diabetes refers almost exclusively to prevalence studies. There is still a dearth of literature dealing with the incidence of diabetes. Some of these problems encountered in prevalence and incidence studies are discussed by Newill.[11] Prevalence is, of course, easier to study. We simply observe what fraction of the group under study meets at one point in time our definition of disease. There is, however, the serious drawback that those who have died with (or because of) their disease, or may have been sick and then reverted

TABLE 6

Age adjusted prevalence and two-year incidence rates for 1,000 by region of birth

	Eastern Europe	Central Europe	South E. Europe	Israel	Middle East	North Africa	Total
Age-adjusted prevalence	40.5	37.8	42.5	62.5	56.5	59.5	49.5
Age-adjusted two-year incidence	8.5	16.2	15.2	14.3	20.3	17.1	15.5

to normal, are not identified in such a study. The incidence approach is more difficult, requiring an initial examination to identify those who are negative and therefore at risk of acquiring the disease, and then one or more subsequent examinations to determine which subjects have in fact acquired it. The objective of incidence studies is to learn what we can about the frequency with which new disease is occurring. It then becomes possible in further studies, to investigate some of the natural history of these new cases—such as death rates and spontaneous reversion to normality, and also the factors associated with new disease which are often distorted in prevalence studies because of changes in habits, physiology, etc., which are due to the presence of disease and not necessarily related to its pathogenesis.

For our general incidence calculations, we have deliberately excluded from the group at risk all those with possible, probable, or definite disease in 1963, as well as those with abnormal GTT or with unknown status, in order to present in the clearest form possible the risks of new disease in any form, symptomatic or not, in a population "known" to be disease free.

It might be argued that the best way of doing an incidence study would have been to offer a glucose tolerance test or a glucose-load test to all the study subjects under standard conditions. While agreeing that this might have been preferable, we found the logistic and other problems of doing this to be unrealistic and therefore relied on screening by history (from a study group that was completely covered by medical insurance and therefore readily available medical service) and a casual blood sugar determination. The positive screenees were examined and followed up more intensively, but the incidence figures are dependent first and foremost on the efficiency of the screening procedure. Overseas figures indicate that following mass screening for every diabetic previously known, another one is found. Our study shows similar findings in that 54.9 per cent of the 144 positive diabetics were newly discovered (table 7). Interestingly, the percentage of newly found cases was higher among the Israeli, Middle-East, and North African Europeans than among the three European groups, indicating some differential utilization of available medical services.

TABLE 7

The number of men previously known to have diabetes and the number discovered to have diabetes as a result of the survey grouped according to region of birth

Region of birth	Previously known	Newly discovered	Per cent newly discovered
Eastern Europe	9	7	43.8
Central Europe	11	10	47.6
Southeastern Europe	15	11	42.3
Israel	6	13	68.4
Middle East	15	25	62.5
North Africa	9	13	59.1
Total	65	79	54.9

Reports of the incidence of diabetes derived from hospital figures such as in the Oslo study[12] would considerably underestimate the true incidence of diabetes since they include neither diabetics who fail to report to hospitals, nor latent diabetics. For a long time it has been generally accepted that diabetes is more common among Jews than among other people.[13] This high incidence is reportedly limited to elderly Jews and believed to be associated with a high incidence of obesity. We could find a report of only one other incidence study based on an epidemiological survey. This study refers to the incidence of diabetes in Hiroshima and Nagasaki.[14] The incidence rates at comparable ages for the Hiroshima male population are more than double Israeli rates; however, the rates for Nagasaki men are similar to ours. In comparing the two studies we must emphasize that our incidence rates are based on those found normal in the original examination. Persons with an abnormal GTT or otherwise doubtful diabetes status in 1963 were excluded from the population at risk. It is not clear whether similar exclusions apply to the Japanese data. In addition, our criteria for the diagnosis of diabetes are somewhat more strict than theirs. For example, men who had a high two-hour level as their only abnormality on the GTT have not been classified as "diabetic" but are considered to have an abnormal GTT.

Our prevalence figures had shown, surprisingly, a higher prevalence of diabetes in men from Israel, North Africa, and the Middle East than those from Europe. Our two-year incidence figures tend to partly confirm our prevalence findings.

The largest difference is between the high incidence group (20.3 per thousand) from the Middle East and the low incidence group (8.5 per thousand) from East Europe. Next to immigrants from the Middle East, immigrants from North Africa show the highest incidence (17.1 per thousand). These area differences are not statistically significant and we are awaiting the results of our 1968 survey with its larger numbers to see whether these differences are maintained.

Additional Note: Sixty-seven subjects who in 1963 had an abnormal glucose tolerance test result and were ex-

cluded from those "at risk" for the incidence study were reinvestigated with the following results:

Diabetic proved	17	4 definite 2 probable 11 possible
Abnormal GTT	25	
Normal GTT	17	
Inadequate data for classification	8	
Total	67	

It is interesting to note that while seventeen (25.4 per cent of the sixty-seven) were definite diabetics two years later, a similar number had reverted to normal values.

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