Fructosamine Concentrations in General Population of Kawerau

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We measured fructosamine concentrations in nonfasted serum from 7094 residents (82.8% of the estimated population) of Kawerau, New Zealand, including 65 known diabetic patients (prevalence of 0.92%). Fructosamine results showed a trimodal frequency distribution, with cutting points corresponding to 5th and 95th percentile values. Forty-two diabetic individuals had levels that exceeded the 95th percentile. These individuals had more severe metabolic abnormalities, characterized by lower plasma C-peptide and elevated fasting plasma glucose concentrations. Mean fructosamine values also showed a significant increase with age and a highly significant age-ethnic interaction that paralleled the higher frequency of diabetes in older age groups and among elderly Maori people. However, as a screening method in the general population, fructosamine measurement was diagnostically deficient because of a weak correlation with serum albumin. Arithmetic correction for albumin concentration in the sample did not increase the diagnostic usefulness of the test. ***Diabetes Care*** **11:239–45, 1988**

Diabetes mellitus is a serious public health problem; its high morbidity and mortality rates are secondary to coronary artery disease, peripheral vascular disease, and renal failure (1,2). Early detection of undiagnosed diabetes in the community would enable effective therapy and prevent some of the long-term effects of the disease (2,3). However, universal screening is not recommended because of the nonspecificity of traditional biochemical tests and the high cost of case detection (4,5).

We have reported a rapid automated assay for glycosylated serum proteins (fructosamines) (6) and have suggested that fructosamine measurement could provide a more specific screening test for diabetes than currently exists (7,8). Important advantages of the fructosamine test include low cost (7), ease of analysis with routine biochemical analyzers (6), and ready incorporation into existing external quality-assurance programs (9). We present data from a large community study and identify factors affecting fructosamine results in the general population.

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MATERIALS AND METHODS

Subjects. Kawerau is a small rural town in the Bay of Plenty hospital board district of New Zealand that was established in 1953 to service a large, integrated paper pulp, newsprint, and sawmill plant (Fig. 1). Kawerau was chosen for this study because of its relative isolation and its large population of Maori people, who are known to be a high-risk group for diabetes (10). There were 7094 participants in the study, comprising 82.8% of the estimated population. Characteristics of participants are compared with the population of the town from the 1981 census and with the general population of New Zealand in 1981 (Fig. 1).

The diabetes survey was performed in conjunction with a hepatitis B detection program (11). Households were identified from electricity department records, and both surveys were circulated in March 1984. All residents >6 mo old were invited to participate. Subjects

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gave informed consent, completed a questionnaire on age, gender, ethnic grouping, and previous history of diabetes, and provided a nonfasted sample of blood. Serum was separated promptly and stored at −20°C for later analysis of fructosamine and albumin concentrations.

Analytical techniques. We determined serum fructosamine concentrations with a Cobas Bio centrifugal analyzer (Hoffmann-La Roche, Basel). The reagent was carbonate buffer (0.1 M, pH 10.35) containing 250 μM nitro blue tetrazolium chloride, and the standards were glycosylated albumin (6). Long-term analytical errors, determined from normal and abnormal control sera with 2.05 and 4.37 mM mean fructosamine, were 3.0 and 3.2%, respectively. We measured plasma glucose concentrations with commercial reagents (Hoffmann-La Roche) and serum albumin concentrations with the bromocresol green method. C-peptide levels were determined with a commercial radioimmunoassay kit (Novo, Copenhagen). Statistical analysis was based on the 2 × 2 χ^2-test for comparison of groups, *t* tests for comparison of means, analysis of variance, and multiple regression with the Statistical Analysis System package (12).

RESULTS

Enrollment of participants. Population and numbers of dwellings in the Kawerau borough were obtained from the 1981 census. Of 2353 occupied dwellings, complete response was achieved from 1980 (84%), partial response from 297 (13%), and no response from 76 (3%). Residents responded to the survey at a rate of 93% (7901 responses received). A higher participation was not achieved despite strong support by community leaders, widespread publicity, and repeated attempts of follow-up. However, this response rate must be regarded as a conservative estimate because preliminary results of the 1986 census revealed 8118 people usually residing in the area, suggesting a net migration loss between 1981 and 1984.

Serum samples for fructosamine estimation were obtained from only 7094 residents (overall response rate of 82.8%), because of difficulty in obtaining the original specimen or because of leakage during transport. There were no known diabetic individuals among the missing group of 807 people, which included 398 children aged

	Kawerau 1984	Kawerau 1981	New Zealand
Population	7094	8568	3,143,307
Males	51.1% *	52.9%	49.7%
Age <20	43.9% **	46.6%	36.7%
20 - 39	34.1%	32.9%	29.8%
40 - 59	18.6% *	17.2%	19.6%
>60	3.4%	3.3%	13.9%
European	57.4% **	61.1%	85.8%
Maori	39.1% **	35.2%	8.9%

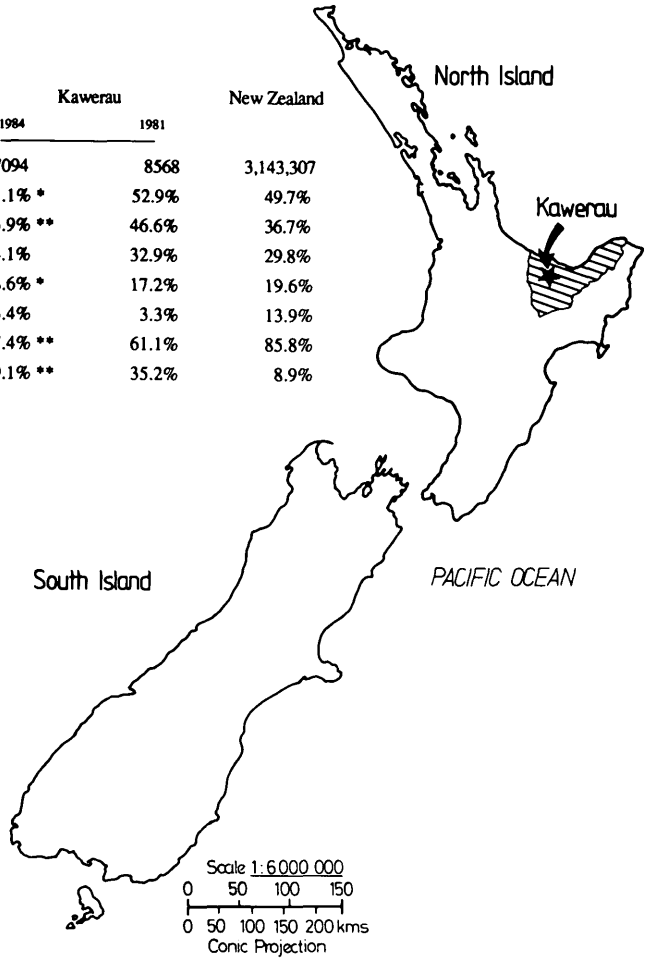

FIG. 1. New Zealand. Study group is compared with target population of Kawerau and population of New Zealand determined from 1981 census. Significant differences between survey and target populations are *$P < .05$ and **$P < .001$. *Hatched area* is Bay of Plenty hospital board district.

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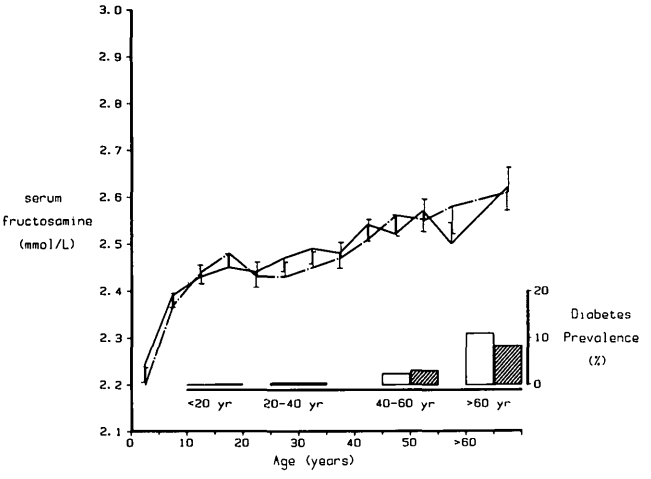

FIG. 2. Mean serum fructosamine concentrations for 7094 Kawerau residents showing effects of age and gender (males, *solid line*; females, *dashed line*). *Bars* are 95% confidence intervals. Histogram indicates prevalence of known diabetes for males (*open bar*) and females (*hatched bar*).

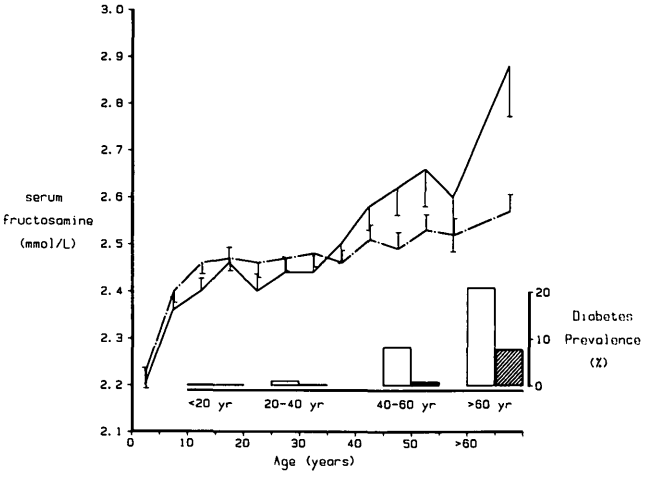

FIG. 3. Mean serum fructosamine concentrations for 7094 Kawerau residents showing effects of age and ethnic group (Maoris, *solid line*; Europeans, *dashed line*). *Bars* are 95% confidence intervals. Histogram indicates prevalence of known diabetes for Maoris (*open bar*) and Europeans (*hatched bar*).

<5 yr and 175 people aged 5–19 yr. Therefore, compared with the population of Kawerau on census night in 1981, the diabetes survey significantly underrepresented the <20-yr age group and Europeans (Fig. 1). This result was not expected to bias the results of the study because absolute differences were relatively minor.

Prevalence of known diabetes. Eighty subjects reported having diabetes mellitus in the questionnaire, and diagnosis was confirmed in 65 people from general-practitioner records. To check ascertainment of known diabetes mellitus, 154 adults with fructosamine >95th percentile and 246 adults selected at random from the remainder of the population were subjected to follow-up, which included oral glucose tolerance testing (OGTT) and plasma C-peptide measurement (5). No additional previously diagnosed cases of diabetes mellitus were detected.

Known diabetic patients comprised 32 men and 33 women whose mean age was 52.2 yr and of whom 38 (58.5%) were Maori. Distribution of known diabetic individuals among different age, ethnic, and gender groups in the community is shown in Figs. 2 and 3. Forty-four (67.7%) diabetic patients were located for follow-up.

Biologic variation of serum fructosamine concentration. Serum fructosamine concentrations ranged from 1.31 to 5.98 mM (median 2.45) and showed a trimodal distribution of results with cutting point corresponding to the 5th and 95th percentile of the fructosamine results (Fig. 4). The first mode contained 42 (64.6%) known diabetic individuals, whereas the third mode contained no diabetic individuals but did contain a high proportion (41.1%) of children aged <10 yr. Clinical details of diabetic subjects with elevated and with normal fructosamine results are in Table 1.

Effect of ethnic background, age, and gender. Using analysis of variance, we compared serum fructosamine concentrations between different age groups and found a highly significant increase after the first decade ($P < .001$; Fig. 2). There were no significant ($P > .05$) age-related changes between the second and fourth decades, although fructosamine concentrations increased significantly ($P < .05$) in subjects >40 yr old. There were no significant differences in fructosamine levels between males and females. Compared with Europeans, results in Maori subjects were lower during the first four decades and higher in the >40-yr-old age groups (Fig.

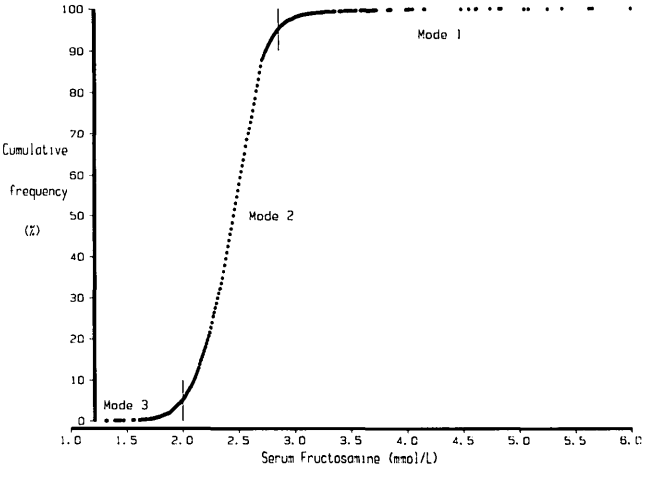

FIG. 4. Frequency distribution of serum fructosamine results from 7094 residents of Kawerau. Mode 1, upper 5th percentile; mode 2, 5th–95th percentiles (values 2.00–2.85 mM); mode 3, lower 5th percentile of results. *n* = 7094, mean ± SD 2.45 ± 0.30 mM, median 2.46.

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TABLE 1
Fructosamine levels in diabetic patients at follow-up

	Serum fructosamine (mM)	
	<2.85 (n = 14)	>2.85 (n = 30)
Glucose (mM)		
Fasting	6.7 ± 2.2	13.3 ± 5.5*
1 h	11.4 ± 3.6	20.6 ± 5.9*
2 h	9.4 ± 3.8	21.8 ± 6.8*
Plasma C-peptide (nM)		
Fasting	0.59 ± 0.21	0.43 ± 0.25†
2 h	2.09 ± 0.70	1.21 ± 0.77*

Data were obtained from plasma C-peptide and oral glucose tolerance tests and are means ± SD.
*P < .001, †P < .05.

3). Age-specific reference intervals for fructosamine and albumin concentrations are presented in Table 2.

Effect of serum albumin concentration. Serum albumin results among nondiabetic Kawerau residents [43.4 ± 4.2 g/L (mean ± SD)] were significantly elevated compared with albumin concentrations among diabetic individuals (41.0 ± 4.1 g/L, P < .001). Furthermore, fructosamine results (y) were significantly correlated with serum albumin concentrations (x) (i.e., $y = 1.3 + 0.03x$, $r = .38$, $P < .001$; Fig. 5).

Taken together, these findings imply that elevated albumin concentrations may have caused elevated fructosamine in a small proportion of healthy individuals. For example, 85 (25.4%) of 334 individuals represented in mode 1 (Fig. 4) had serum albumin >95th percentile albumin value for the population (Table 2). None of the 85 subjects had a previous diagnosis of diabetes mellitus.

Multivariate analysis. Multiple regression was used to determine the net association between serum fructosamine and age, ethnic group, gender, and serum albumin concentration. Modeling proceeded by forward selection to detect multicolinearity. Nonlinear relationships with fructosamine were investigated by transformations of the continuous dependent variables and with interaction terms. Gender had no significant ($P > .05$) relation to fructosamine, confirming Fig. 2. Table 3 shows regression coefficients for serum albumin, ethnic group, age, and the age-ethnic interaction term, with all four variables included in the same model. Age had a logarithmic relation to fructosamine, which is in agreement with Figs. 2 and 3. There was a significant ($P < .001$) age-ethnic interaction (confirming Fig. 3), with Maoris having lower fructosamine levels than Europeans in the younger age groups but higher values than Europeans in the older age groups. Albumin was linearly related to fructosamine concentrations, confirming Fig. 5.

Screening for diabetes in community. Clinical diagnostic tests are customarily assessed by their predictive value, i.e., the probability of disease or lack of disease in a subject with positive or negative test results, respectively (13). Predictive value of a positive fructosamine screening test was low because of a relatively high proportion of false-positive observations (Table 4).

To determine whether diagnostic performance was improved by correction for variation in serum albumin concentration, we adjusted all fructosamine results by the factor $43/x$, where 43 was the mean albumin concentration from the general population (Table 2) and x was the measured serum albumin concentration in grams per liter. Corrected fructosamine concentrations (y) were negatively correlated to serum albumin values ($y = 3.8 - 0.03x$, $r = .43$, $P > .001$) and yielded an even higher proportion of false-positive observations (not shown). Positive and negative predictive values and diagnostic efficiency of corrected fructosamine were 10.5, 98.2, and 94.6%, respectively.

DISCUSSION

Diabetes in population. Prevalence of known diabetes was low in Kawerau because it was a recently established community with relatively few elderly individuals (Fig. 1). However, when the population of Kawerau is standardized by direct age adjustment in 20-yr increments with figures from the 1981 census of the New Zealand population (14), the adjusted prevalence of di-

TABLE 2
Serum fructosamine and albumin concentrations from nondiabetic Kawerau residents

		Serum fructosamine (mM)				Serum albumin (g/L)			
Age (yr)	n	Mean ± SD	Median	5th percentile	95th percentile	Mean ± SD	Median	5th percentile	95th percentile
0–9	1419	2.32 ± 0.25	2.35	2.00	2.68	43.2 ± 3.8	44	36	48
10–19	1691	2.44 ± 0.24	2.45	2.14	2.81	44.0 ± 4.0	44	37	50
20–29	1245	2.44 ± 0.24	2.46	2.12	2.85	43.5 ± 4.5	44	35	50
30–39	1157	2.46 ± 0.25	2.49	2.12	2.85	43.3 ± 4.6	44	34	50
40–49	747	2.49 ± 0.26	2.50	2.15	2.90	42.9 ± 4.1	44	35	49
50–59	527	2.52 ± 0.26	2.55	2.16	2.83	42.5 ± 4.2	43	34	49
59+	213	2.52 ± 0.30	2.52	2.16	3.02	41.0 ± 4.0	42	35	48
Total	6999	2.44 ± 0.26	2.45	1.99	2.82	43.4 ± 4.2	44	36	49

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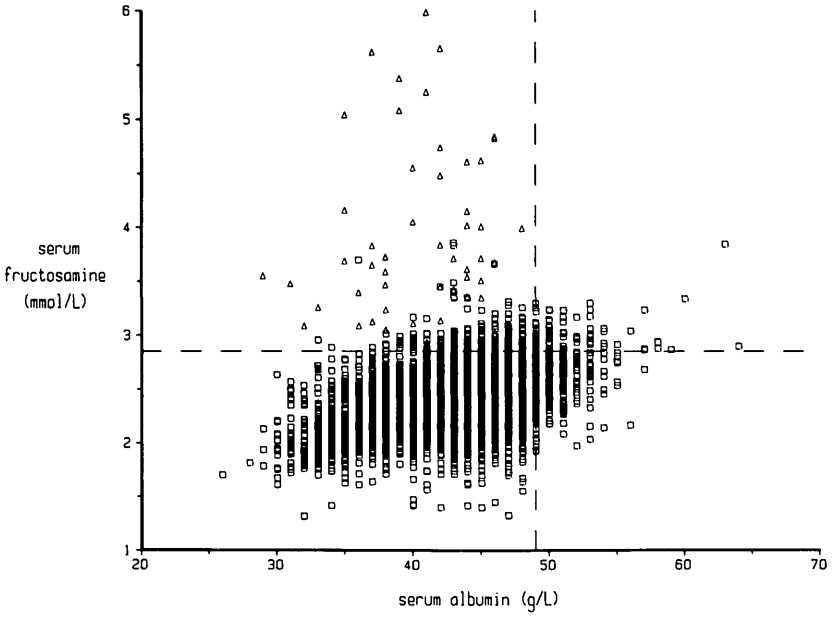

FIG. 5. Relationship between serum fructosamine and serum albumin concentration. △, Diabetic individuals; *horizontal dashed line*, 95th percentile fructosamine value; *vertical dashed line*, 95th percentile albumin value.

abetes is 1.8%. After correcting for ethnic group, the standardized prevalence of known diabetes among Maoris and Europeans was 2.6 and 1.3%, respectively.

The only previous total-community survey for diabetes in New Zealand, conducted in Rangiora in 1967 (15), reported a prevalence rate for undiagnosed and known diabetes of 3.6 and 1.7%, respectively, for an exclusively European population. However, the Rangiora survey covered only adults and a far higher proportion of people >60 yr old (29.2%) than the Kawerau survey (3.4%). Nevertheless, when the findings from Rangiora are standardized by age by 1981 census data, the adjusted prevalence of undiagnosed and known diabetes is 1.3 and 0.9%, respectively.

Prior and Davidson (10) investigated samples of the adult New Zealand Maori population in 1966 and reported a prevalence of diabetes mellitus of 8.1%. When similarly standardized by 1981 census results, this yields an age-adjusted prevalence rate of 4.1%, comprising 3.0% of newly diagnosed and 1.1% of known cases of diabetes mellitus. However, different criteria for diabetes were used in 1966 such that some of the "new" diabetic patients would be classified as having impaired glucose tolerance (5).

Based on this information, the rates of known diabetes mellitus among Maori and European people from Kawerau were not unreasonable. Improved public awareness of diabetes and better access to primary medical care may account for the higher proportions of people with known diabetes mellitus compared with previous studies in New Zealand (10,15).

Distribution of fructosamine concentrations. The frequency distribution of fructosamine results from the Kawerau population was trimodal (Fig. 2), with clear discrimination between first and second modes corresponding to the 95th percentile value of 2.85 mM. Diabetic patients were distributed between first and second modes such that patients with more severe diabetic abnormality had fructosamine results >2.85 mM (Table 1). From 14 known diabetic patients with normal fruc-

TABLE 3
Multivariate regression analysis of Maoris and Europeans

Variables	R^2	SE	Student's *t*
Intercept	.964	.037	25.98
Serum albumin	.028	.0007	37.23
Ethnic group	−.076	.023	−3.31
$\log_{10}$(age)	.206	.011	18.23
$\log_{10}$(age) × ethnic group	.079	.017	4.53

Ethnic group was entered as a dummy variable with Maoris 1, and Europeans 0. R^2 was .24, and F was 526.1 ($P < .001$). All variable estimates were significant ($P < .001$).

TABLE 4
Fructosamine test as screening method for diagnosing diabetes mellitus in the community

	Fructosamine result		
	Positive	Negative	Total
Diabetes mellitus			
Present	42 (A)	23 (B)	65
Absent	292 (C)	6737 (D)	7029
Total	334	6760	7094

Only diabetic patients with a previous diagnosis were considered. Discrimination value was 2.85 mM. Diagnostic usefulness of test was calculated as follows. Sensitivity [A/(A+B)], 65%. Specificity [D/(D+C)], 96%. Predictive value positive [A/(A+C)], 13%. Predictive value negative [D/(B+D)], 99%. Efficiency [(A+D)/(A+B+C+D)], 96%.

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tosamine results, OGTTs showed impaired glucose tolerance in 4 individuals and a nondiabetic curve in 4 more, supporting previous observations that elevated fructosamine concentrations primarily reflected fasting hyperglycemia (7,8).

Relationship between serum fructosamine and diabetes in population. If it is assumed that frequency of undiagnosed diabetes correlates with prevalence of known diabetes among different age and ethnic groups (Figs. 2 and 3), it is possible to explain some of the changes in mean fructosamine concentration. Such an assumption is not unreasonable in view of the findings of previous diabetes screening surveys in New Zealand (10,15) and in the United States (16). For example, the highly significant increase in fructosamine concentration after the first decade (Table 2 and Fig. 2) parallels the incidence of insulin-dependent diabetes (IDDM) in the New Zealand population, which Crossley and Upsdell (17) found to be constant at 1–9 yr of age, increasing to a sustained 2.2-fold–higher level from 11 yr.

The significant age-ethnic interaction for fructosamine results in Fig. 3 and Table 3 also reflects known ethnic differences in the prevalence of diabetes (9,18). IDDM is uncommon in Maoris (9) and other Polynesian peoples (18), possibly accounting for significantly lower serum fructosamine concentrations during the first four decades (Fig. 3). In contrast, non-insulin-dependent diabetes mellitus is common in Maoris >40 yr old (10) (prevalence of 9.1% in our study) compared with Europeans of similar age (prevalence of 1.9%).

Multivariate analysis. The contributions of age, ethnic background, and the age-ethnic interaction term in the multivariate model may be explained, at least in part, by undiagnosed diabetes in the community (Table 3). However, taking into account previous studies in nondiabetic (7) and diabetic (19) individuals, the association with serum albumin concentration was unexpected (Fig. 5 and Table 3). Although albumin is the most abundant serum protein with a long biologic half-life (20) and ample lysine residues available for glycosylation (21), previous studies had not demonstrated such a relationship without significant hypoalbuminemia (7) and clinical albuminuria (19).

This association, which may reflect sampling errors during specimen collection or storage, leading to altered albumin concentrations (22), constitutes a form of laboratory error. In applying the test as a screening tool, laboratory errors cause a broader reference interval, a blurring of the distinction between normal and abnormal, and an increased frequency of false-positive and negative observations (23).

Usefulness of fructosamine as screening method for diabetes. Despite the apparent high efficiency of fructosamine measurement on preliminary evaluation (7), the test appeared less satisfactory as a screening method when applied to unselected populations (Table 4). Clearly, some of the individuals with elevated fructosamine results and with normal or low albumin concentrations may have undiagnosed diabetes (Fig. 5). Nevertheless, even considering these patients, positive predictive value was low because of the magnification of false-positive errors by the relatively low prevalence of diabetes in the general population (24).

One method of circumventing this problem is to collect specimens carefully (22) and to preselect subjects with a recognized risk of diabetes to produce a higher prevalence of diabetes in the study population (24). For example, selective screening of >40-yr-old Maoris (prevalence of 9.1%) yielded positive predictive values of 61% and negative predictive values of 96%. Similarly, positive and negative predictive values of 58 and 98% were obtained in the selective screening of patients admitted to a coronary care unit (prevalence of diabetes 8.4%; 8).

Alternatively, Howey et al. (25) have suggested that sensitivity of fructosamine measurement may be enhanced by taking repeated measurements from the same patient. Because of the low biologic variation among individuals (7,25) and low analytical imprecision of the test (9), sequential measurements in the same patient would provide a sensitive means of detecting changes in glucose intolerance (9,26). Such an approach, which would minimize the effect of biologic variation in serum albumin concentration, is worthy of further investigation, particularly in pregnant women.

We conclude that fructosamine measurement in cross-sectional studies identifies diabetic patients with fasting hyperglycemia but not with lesser degrees of diabetic abnormality. Because of this reduced sensitivity, the test is not an attractive screening method for epidemiological surveys of the general population. However, among selected groups with a higher prevalence of diabetes, it may provide a cost-beneficial means of identifying patients who would benefit from therapy (4). In this context, fructosamine has the important advantage over OGTT that the fructosamine test is not affected by stress (8) and can be performed on casual blood samples without special patient preparation (7).

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REFERENCES

1. Fuller JH, Elford J, Goldblatt P, Adelstein AM: Diabetes mortality: new light on an underestimated public health problem. *Diabetologia* 24:336–41, 1983
2. Danowski TS, Ohlsen P, Fisher ER: Diabetic complications and their prevention or reversal. *Diabetes Care* 3:94–99, 1980
3. National Diabetes Advisory Board: The prevention and treatment of five complications of diabetes: a guide for primary care physicians. *Metabolism* 33:15–17, 1984

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4. Herron CA: Screening in diabetes mellitus: report of the Atlanta workshop. *Diabetes Care* 2:357–62, 1979
5. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 28:1039–57, 1979
6. Baker JR, Metcalf PA, Johnson RN, Newman D, Rietz P: Use of protein-based standards in automated colorimetric determinations of fructosamine in serum. *Clin Chem* 31:1550–54, 1985
7. Baker JR, O'Connor JP, Metcalf PA, Lawson MR, Johnson RN: Clinical usefulness of estimation of serum fructosamine concentration as a screening test for diabetes mellitus. *Br Med J* 287:863–67, 1983
8. Kyle C, Baker J, Metcalf P, Johnson R, Norris R: Serum fructosamine as a screening method for diabetes mellitus in patients with suspected acute myocardial infarction. *Aust NZ J Med* 17:467–71, 1987
9. Baker J, Metcalf P, Tatnell M, Lever M, Johnson R: Quality assessment of determinations of serum fructosamine in 33 clinical chemistry laboratories. *Clin Chem* 32:2133–36, 1986
10. Prior IAM, Davidson F: The epidemiology of diabetes in Polynesians and Europeans in New Zealand and the Pacific. *NZ Med J* 65:375–83, 1966
11. Milne A, Allwood GK, Moyes CD, Pearce NE, Lucas CR: Prevalence of hepatitis B infections in a multiracial New Zealand community. *NZ Med J* 98:529–32, 1985
12. SAS Institute Inc: *SAS User's Guide: Statistics*. 5th ed. Cary, NC, SAS Inst., 1985
13. Simel DL: Playing the odds. *Lancet* 1:329–30, 1985
14. *New Zealand Census of Population and Dwelling 1981. Birthplaces and Ethnic Origin*. Vol. 7. New Zealand Dept. of Statistics, 1982
15. Murray JT, Hannah EE, Laing JK, Cotter AP, Ferrar RH, Lovell-Smith HDJ, Thompson RL, Jepson LF, Beaven DW: Diabetes in European New Zealanders. *NZ Med J* 69:271–75, 1969
16. Harris MI, Hadden WC, Knowler WC, Bennett PH: Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. population aged 20–74 yr. *Diabetes* 36:523–34, 1987
17. Crossley JR, Upsdell M: The incidence of juvenile diabetes in New Zealand. *Diabetologia* 18:29–34, 1980
18. Zimmett P: Type 2 (non-insulin-dependent) diabetes in an epidemiological overview. *Diabetologia* 22:339–411, 1982
19. Johnson RN, Metcalf PA, Baker JR: Relationship between albumin and fructosamine concentration in diabetic and non-diabetic sera. *Clin Chim Acta* 164:151–62, 1987
20. Schultze HE, Heremans JF: *Molecular Biology of Human Proteins With Special Reference to Plasma Proteins*. Vol. 1. New York, Elsevier, 1966, p. 451–514
21. Peters T: Proteins. In *Chemical Diagnosis of Disease*. Brown SS, Mitchell FZ, Young DS, Eds. Amsterdam, Elsevier/North-Holland, 1979, p. 311–62
22. Pritchard NA: Collection and handling of patient specimens. In *Clinical Chemistry. Theory, Analysis, and Correlation*. Kaplan LA, Pesce AJ, Eds. St. Louis, MO, Mosby, 1984, p. 43–50
23. Krause RD, Anand VD, Gruemer HD, Willke TA: The impact of laboratory error on the normal range: a Bayesian model. *Clin Chem* 21:321–24, 1975
24. Vecchio TJ: Predictive value of a single diagnostic test in unselected populations. *N Engl J Med* 274:1171–73, 1966
25. Howey JEA, Browning MCK, Fraser CG: Assay of serum fructosamine that minimizes standardization and matrix problems: use to assess components of biological variation. *Clin Chem* 33:269–72, 1987
26. Baker JR, Johnson RN, Scott DJ: Serum fructosamine concentrations in patients with type 2 (non-insulin-dependent) diabetes mellitus during changes in management. *Br Med J* 288:1484–86, 1984

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