Response to Meriden

We are writing in response to the letter from Terry Meriden, MD, FACP, regarding the position taken by the American Diabetes Association during the health care debate of the past 2 years. Dr. Meriden faults the Association for having taken a position on health care reform that, he asserts, "specifically endorsed the Clinton plan."

This principal assertion of Dr. Meriden, that the American Diabetes Association specifically endorsed all components of the Clinton health care plan, is simply incorrect. While it is true that much discussion took place about whether the Association should or should not endorse the specifics of the Clinton plan, in the end no such endorsement was made. The Principles on Health Care Reform, developed by the Association and endorsed by a number of other health care organizations involved with diabetes, were principles that the Association believed had to be incorporated in *any* health care reform package.

Let us be clear. We will continue to be advocates for the enactment of these principles, which would seek to ensure universal access to quality diabetes treatment; prohibit pre-existing condition exclusions; provide coverage for prescription drugs and insulin, as well as for diabetes-related supplies, equipment and education; and achieve a mandate for community rating. As with other issues, at times our advocacy will involve asking our constituents to promote the passage of a particular piece of legislation that provides significant benefits for people with diabetes.

Dr. Meriden also faults the Association for making "a political decision." In the overheated atmosphere of last year's health care debate, virtually any decision (including a decision not to take a position) could be labelled "political." To avoid taking a position because an issue is "too sensitive" and may have "negative consequences" because of changes in Washington's "political winds," as Dr. Meriden suggests, is no less "political" and far more calculating.

Finally, the mission of the Association does include, as Dr. Meriden asserts, finding a prevention and cure for diabetes. These goals correctly require our strong support for continued diabetes-related research. But that is only half of our mission. The other half is to improve the lives of people with diabetes. This requires us to be advocates for better health care delivery, more comprehensive insurance coverage, and for bringing an end to discriminatory laws and policies based on outdated information.

The Principles on Health Care Reform reflected precisely where the Association should have been during last year's debate. To have remained silent during this debate would have been to abdicate our responsibility to be advocates for people with diabetes.

DOUGLAS E. LUND
IMMEDIATE PAST CHAIR OF THE BOARD

KATHLEEN L. WISHNER, PHD, MD
IMMEDIATE PAST PRESIDENT

LINDA M. SIMINERIO, RN, MS, CDE
IMMEDIATE PAST SENIOR VICE PRESIDENT

Elevation and Fluctuation of Serum CA19-9 and SPAN-1 Levels After Administration of Sulfonylurea in a Diabetic Patient With Lewis(a−,b−) Blood Phenotype

It has been reported that poorly controlled diabetic subjects often show elevated serum CA19-9 levels in spite of there being no evidence of malignant diseases or other pathological conditions (1,2). However, Lewis (Le) blood phenotype is an important factor because type I carbohydrate antigens have the same structure as sialyated Lewis antigens (3). When serum CA19-9 concentrations are measured in diabetic subjects, the levels in Le(a+,b−) subjects are usually higher than those in Le(a−,b+) subjects (2,4,5). On the other hand, Le(a−,b−) subjects usually show normal levels of CA19-9, even when they have malignant tumors (6). In this report, we describe a rare case of a diabetic patient with Le(a−,b−) blood phenotype whose serum CA19-9 and SPAN-1 levels were markedly elevated and fluctuated after the administration of sulfonylurea.

HISTORY AND EXAMINATION — A 60-year-old woman with a 3-year history of NIDDM was referred to our hospital in June 1991. In January 1991, her glycemic control became aggravated and she was treated with insulin. After glycemic control was restored with daily administration of 12 U human NPH insulin and urinary excretion of C-peptide returned to normal (61 μg/day), insulin therapy was discontinued. This occurred 3 months before her visit to our hospital. Her height was 144 cm, body weight was 55 kg, and body mass index was 26.5 kg/m^2. No abnormal findings were recorded upon physical examination. Optic fundi were normal and peripheral neuropathy was not noted.

INVESTIGATIONS — Laboratory data showed a fasting plasma glucose (FPG) level of 102 mg/dl and HbA_{1c} of 5.3%. The serum CA19-9 level was elevated at 350 U/ml, but the serum carcinoembryonic antigen (CEA) level was 2.4 ng/ml. The serum amylase level was normal at 94 U. Liver function test, electrolytes, blood urea nitrogen, creatinine, and

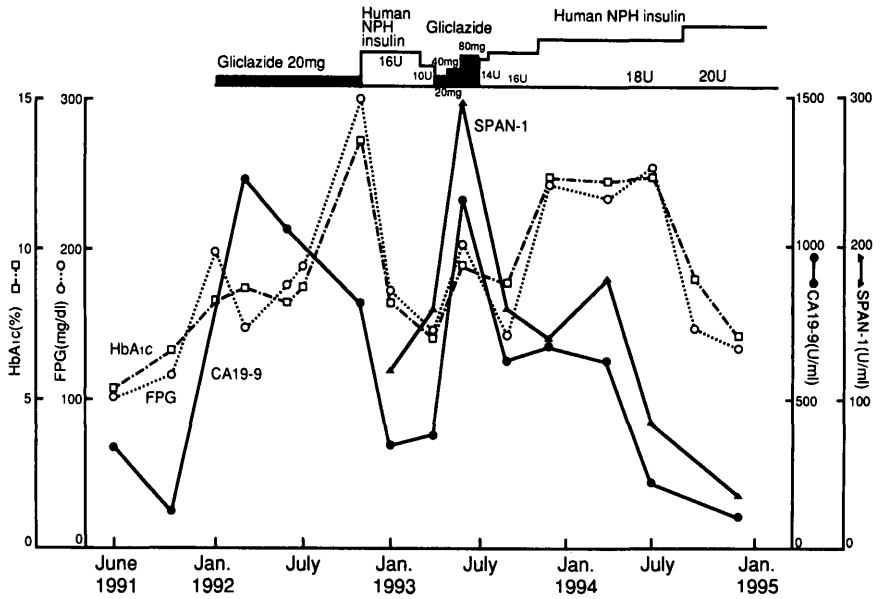

Figure 1—*Changes in the patient's FPG, HbA_{1c}, CA19-9, and SPAN-1 levels during a 4-year period.*

lipids were all within normal ranges. The patient belonged to the Le(a−,b−) blood phenotype. A chest X ray, ultrasonography and computed tomography of the abdomen, retrograde cholangiopancreatography, and barium enema were performed, showing no abnormal findings. A benign gastric polyp of 1.1 cm in diameter was detected by gastrifiberscopy. A gallium scintigram noted no abnormal accumulation.

Figure 1 shows the changes in the patient's FPG, HbA_{1c}, CA19-9, and SPAN-1 levels during a 4-year period. In October 1991, the FPG level was 117 mg/dl, HbA_{1c} was 6.6%, and the serum CA19-9 level was 133 U/ml (normal <50 U/ml). Because her FPG and HbA_{1c} levels were elevated at 198 mg/dl and 8.0%, respectively, the patient was administered 20 mg of gliclazide daily beginning in January 1992. The serum CA19-9 level markedly increased to >1,000 U/ml soon after the start of gliclazide administration. Because her glycemic control became aggravated (FPG 319 mg/dl; HbA_{1c} 13.6%) in November 1992, insulin therapy was started, resulting in an improvement in glycemic control (FPG 145 mg/dl; HbA_{1c} 7.1%). The serum CA19-9 level declined to 208 U/ml in April 1993. When the patient was readministered gliclazide, her serum CA19-9 and SPAN-1 levels (normal <30 U/ml) became markedly elevated again at 1,159 U/ml and 320 U/ml, respectively, in June 1993. Although insulin treatment was started again in December 1993, her glycemic control remained poor (FPG >200 mg/dl; HbA_{1c}: >10%) for 1 year, while serum CA19-9 and SPAN-1 levels gradually declined to 230 U/ml and 85 U/ml, respectively, in July 1994. After being admitted for 1 month in September 1994, the patient's glycemic control was restored (FPG 134 mg/dl; HbA_{1c} 6.5%). During the 4-year observation period, her serum amylase and CEA levels remained within normal ranges.

CONCLUSIONS — The elevation of serum CA19-9 levels has been reported in association with hyperglycemia in diabetic patients without malignant diseases (1,2). It is also known that the Lewis blood phenotype affects the serum CA19-9 levels (2,4,5) because Le(a−,b+) subjects synthesize less CA19-9 than do Le(a+,b−) subjects because of the competition for substrate between sialyltransferase (involved in the synthesis of the CA19-9) and secretor fucosyltransferase (involved in the synthesis of the Le(b) antigen) (3).

Our case is quite different from those in previous reports because the patient had Le(a−,b−) blood phenotype and there was no significant correlation between the serum CA19-9 levels and HbA_{1c} levels ($r = 0.31$, $P < 0.3$). In addition, the patient's serum CA19-9 and SPAN-1 level, which is not affected by Lewis blood phenotype, were markedly elevated and fluctuated after the administration of sulfonylurea. No malignant disease or chronic pancreatitis (her serum amylase levels were normal) was noted during the 4-year follow-up period. Although the precise mechanism remains to be elucidated, this is an uncommon case presenting marked elevation of serum CA19-9 and SPAN-1 levels after the administration of sulfonylurea.

KEIJI YOSHIOKA, MD

From the First Department of Internal Medicine, Matsushita Memorial Hospital, Osaka, Japan.

Address correspondence to Keiji Yoshioka, MD, First Department of Internal Medicine, Matsushita Memorial Hospital, 5-55 Sotojimacho, Moriguchi, Osaka 570, Japan.

References

1. Nakamura N, Aoji O, Yoshikawa T, Mori K, Kajiyama S, Kitagawa Y, Kanasuna T, Kondo M: Elevated serum CA19-9 levels in poorly controlled diabetic patients. *Jpn J Med* 25:278–280, 1986
2. Aoki Y, Yanagisawa Y, Ohfusa H, Kawa S, Oguchi H, Furuta S: Elevation of serum CA19-9 in parallel with HbA_{1c} in a diabetic female with Lewis (a+,b−) blood group. *Diabetes Res Clin Pract* 13:77–82, 1991
3. Hansson GC, Zopf D: Biosynthesis of the cancer-associated sialyl-Le^a antigen. *J Biol Chem* 260:9388–9392, 1985
4. Shimojo N, Naka K, Nakajima C, Ishizaki T, Okuda K, Murai J, Yamamoto M: The

effect of non-insulin-dependent diabetes on serum concentrations of tumor-associated carbohydrate antigens of CA19-9, CA-50, and sialyl SSEA-1 in association with Lewis blood phenotype. *Clin Chim Acta* 190:283–290, 1990
5. Tekemura Y, Kobayashi T, Ogino K, Itabashi H, Naito T, Sato A: The relationship between elevated serum CA19-9 and CA 50 concentrations and Lewis phenotype in diabetic patients. *J Jpn Diabetes Soc* 33:241–243, 1990
6. Koprowski H, Brockhaus M, Blaszcyk M, Magnani J, Steplewski Z, Ginsberg V: Lewis blood-type may affect the incidence of the gastrointestinal cancer. *Lancet* i:1332–1333, 1982

No Increase of IDDM Incidence Among Swiss Military Conscripts

A recent paper by Schoenle et al. (1) reports an increase in the incidence of insulin-dependent diabetes mellitus (IDDM) in Swiss men born from 1948 to 1972. Their analysis was based on data extracted from the medical files of the Swiss Army. Every Swiss man reaching the age of 19 years is legally obliged to appear before the Military Conscript Board. A person with IDDM is rejected unconditionally. According to Schoenle et al., cumulative incidence up to the age of 15 years has increased from 4.5/100,000 among those examined by the Board from 1967 to 1969 to 7.2/100,000 during the years 1989–1991 ($P < 0.005$). In addition, the authors found an urban-rural difference, with higher rates in urban areas.

We have also recently addressed the question of IDDM incidence among Swiss military conscripts, using the same army files (2). In contrast to Schoenle et al., we confirmed the diagnosis of IDDM by contacting the corresponding family physician. Accepted definitions for IDDM, introduced in Switzerland in 1971, were used (3). Diagnoses up to the age of 19 years were considered. In four surveys covering the period 1972–1993 and comprising a total of 162,607 conscripts, we were unable to confirm an increase in cumulative incidence of IDDM up to the age of 19 years (Table 1). There was no evidence for statistical heterogeneity in the proportion of conscripts with diabetes ($\chi^2 = 4.95$ on 3 df, $P = 0.18$). There was even a trend towards a decrease in the proportion of conscripts with IDDM; however, this did not reach conventional levels of statistical significance ($\chi^2 = 3.01$ on 1 df, $P = 0.08$).

Table 1—*Cumulative incidence of IDDM up to the age of 19 years among different birth cohorts of Swiss military conscripts*

	Year of examination				
	1972	1982	1987	1993	Total
Birth cohort	1953	1963	1968	1974	
Cases/conscripts	64/38,580	56/45,977	49/42,157	43/35,893	162,607
Cumulative incidence (per 100,000 per year)	8.7	6.4	6.1	6.3	6.8

We believe that the discrepant results between the two studies are explained by the inadequate case ascertainment used by Schoenle et al. The latter was entirely based on information derived from army files and not confirmed by another source. Our study indicates that overdiagnosis of IDDM has led to spuriously high rates in the later years. The same mechanism may well have produced an urban-rural difference.

In conclusion, contrary to Schoenle et al.'s assertions, analysis of Swiss Army files does not indicate that there was an increase in the incidence of IDDM in Switzerland over the past 20 years. Furthermore, the urban-rural difference described by the authors should be interpreted with great caution.

ADRIAN U. TEUSCHER, MD
PETER DIEM, MD
ARTHUR TEUSCHER, MD

From the Department of Medicine (A.U.T.), Regionalspital, Langenthal, and the Section of Diabetes, Department of Medicine (P.D., A.T.), University of Bern, Inselspital Bern, Bern, Switzerland.

Address correspondence to Adrian U. Teuscher, MD, Department of Medicine, Regionalspital, 4900 Langenthal, Switzerland.

References

1. Schoenle EJ, Molinari L, Bagot M, Semadeni S, Wiesendanger M: Epidemiology of IDDM in Switzerland: increasing incidence rate and rural-urban differences in Swiss men born 1948–1972. *Diabetes Care* 17: 955–960, 1994
2. Teuscher AU, Diem P, Thomas W, Janett J, Teuscher A: Häufigkeit des insulinabhängigen Diabetes mellitus in der Schweiz (1972–1993) bei 19 jährigen Männern. *Schweiz Med Wochenschr* 125:1041–1045, 1995
3. Teuscher A, Richterich N: Neue schweizerische Richtlinien zur Diagnose des Diabetes mellitus. *Schweiz Med Wochenschr* 101:345–352, 1971

Response to Teuscher et al.

Teuscher et al. disagree with our finding (1) of an increase of insulin-dependent diabetes mellitus (IDDM) incidence in young Swiss men born between 1948 and 1972 and see the source of disagreement in inadequate case