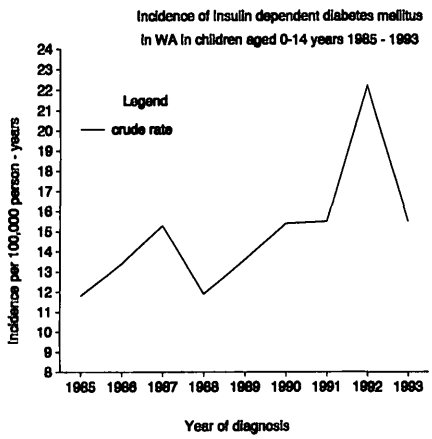

Figure 1—*Incidence (1985–1993) of IDDM in Western Australian children 0–14 years of age.*

with a population base of 1.7 million, where IDDM is not a notifiable disease, a dramatic increase in the incidence of IDDM in the 0–14 year age-group in 1992 has been recognized. This increase was not sustained in 1993. Because ascertainment of cases is prospective in Western Australia, the change in incidence has been documented as it has occurred. Between 1985 and 1989, there was a mean incidence of IDDM in the 0–14 year age-group of 13.2 per 100,000 person-years, but there was no significant change in incidence over the 5 years (3). This trend continued for the next 2 years, but in 1992, a change occurred with a 50% increase in the number of children 0–14 years diagnosed with IDDM. Although the expected number of children diagnosed in 1992 would have been 52, based on previous years' experience, the observed number was 84, and the incidence had risen to 22.2 per 100,000 person-years ($P < 0.0001$) (4). In 1993, the incidence of IDDM in the 0–14 year age-group was 15.5 per 100,000 person-years, of the order of the years before 1992 (Fig. 1). Because of prospective data collection, with ascertainment rates of at least 99% (3, 4), changes in incidence can be recognized as they occur.

Although Fig. 1 may have the appearance of an epidemic curve, with a small epidemic occurring in 1992 above a substantial background incidence of disease, the use of the term epidemic to describe changes in incidence in a disease with a prodromal period of many years (5) needs to be questioned. Indeed, the prodromal period may be longer than the period for which the increased incidence has been observed. The concept of an epidemic, which was developed for acute rather than chronic diseases, comes from infectious diseases' epidemiology and conventionally refers to an increased incidence of disease above that expected, but the concept also assumes that the incidence will return to a baseline level after the epidemic has finished, when a susceptible population is no longer exposed to an environmental antigen at the rate at which it was exposed during the epidemic.

To date, no environmental antigen has been proven to be involved in the expression of IDDM, and the comparison of an increased incidence of IDDM with an infectious disease epidemic, given our current understanding of the pathogenesis of IDDM, is tenuous. While one can point to changes in incidence in IDDM, a suggestion of an epidemic is, at this stage, inappropriate. Moreover, for any timely investigation to be made of an increased disease incidence, data collection must also be timely.

HEATH A. KELLY, FAFPHM
ROBERT J. CONDON, FAFPHM
GEOFFREY C. BYRNE, FRACP

From the Department of Diabetes and Endocrinology, Princess Margaret Hospital for Children, Perth; the Public Health Unit, Southern Health Authority, Albany; and the West Australian Research Institute for Child Health, Subiaco, Western Australia.

Address correspondence to Heath A. Kelly, MD, Public Health Unit, Southern Health Authority, P.O. Box 1411, Albany 6330, Western Australia.

References

1. Dokheel TM: An epidemic of childhood diabetes in the United States?: evidence from Allegheny County, Pennsylvania. *Diabetes Care* 16:1606–1611, 1993
2. World Health Organization DIAMOND Project Group on Epidemics: Childhood diabetes, epidemics and epidemiology: an approach for controlling diabetes. Am J Epidemiol 135:803–816, 1992
3. Kelly H, Byrne GC: Incidence of IDDM in Western Australia in children aged 0–14 years from 1985 to 1989. *Diabetes Care* 15:515–517, 1992
4. Kelly H, Russel M, Jones TW, Byrne GC: A dramatic increase in the incidence of insulin-dependent diabetes mellitus in Western Australia. *Med J Aust.* In press
5. Bonafacio E, Bingley PJ, Shattock M, Dean BM, Dunger D, Gale EM, Botazzo GF: Quantification of islet cell antibodies and prediction of insulin-dependent diabetes. *Lancet* 335:147–149, 1990

Lipoprotein(a) and Silent Myocardial Ischemia in IDDM

Diabetic subjects are predisposed to silent myocardial ischemia (1). It has been suggested that silent ischemia might be associated with increased plasma lipoprotein(a) [Lp(a)] concentration in diabetic subjects (2). The results of studies in subjects with non-insulin-dependent diabetes mellitus and insulin-dependent diabetes mellitus (IDDM) show that the role of Lp(a) in predisposition to myocardial infarction, angina, and mortality is not clear (2–4). We were specifically interested in the relationship between plasma Lp(a) and silent ischemia in IDDM.

RESEARCH DESIGN AND METHODS— Eighty-five IDDM subjects (60 men) were ascertained through the diabetes and lipid clinics at St. Michael's Hospital. Each person gave informed consent to participate. Subjects

Downloaded from http://ada.silverchair.com/care/article-pdf/17/11/1365/515018/17-11-1365.pdf by guest on 10 April 2024

Table 1—*Biochemical features in diabetic subjects with and without silent myocardial ischemia*

	Silent ischemia	No silent ischemia	2P (Student's *t* test)
n	18	67	
M/F	17/1	43/24	0.01
Age (years)	58.4 ± 9.3	53.5 ± 10.0	0.06
Lp(a) (mg/dl)	17.8 ± 21.7	13.9 ± 14.4	NS
Total cholesterol (mmol/l)	5.50 ± 0.80	5.22 ± 1.24	NS
Triglycerides (mmol/l)	2.19 ± 0.71	2.22 ± 1.57	NS
LDL cholesterol (mmol/l)	3.35 ± 0.84	3.02 ± 0.96	NS
HDL cholesterol (mmol/l)	1.15 ± 0.45	1.16 ± 0.32	NS
Apolipoprotein Al (g/l)	1.44 ± 0.32	1.41 ± 0.25	NS
Apolipoprotein B (g/l)	1.38 ± 0.31	1.28 ± 0.40	NS
HbA_{1c} (% of total)	10.4 ± 1.09	9.88 ± 1.21	NS

Data are means ± SD.

had no evidence of heart disease, were not taking digoxin, and had normal resting electrocardiograms. Biochemical analyses were performed in the J. Alick Little Lipid Research Laboratory using established methods (5).

A graded exercise stress test was performed according to the Bruce protocol, as described previously (1). Ambulatory electrocardiographic monitoring was performed for 48 h, as described previously (1). Subjects with significant ST segment depression on either stress testing or ambulatory monitoring underwent exercise thallium-201 scintigraphy for corroboration of silent ischemia using established criteria (1).

Comparison between subjects with and without silent ischemia was performed with an unpaired Student's *t* test. Because of its non-normal distribution, Lp(a) was logarithmically transformed for analysis.

RESULTS— Eighteen subjects were found to have silent ischemia as defined by a perfusion defect on exercise thallium scintigraphy. Mean plasma concentrations of lipoproteins and Lp(a) are shown in Table 1. There was a significantly higher proportion of men in the group with silent ischemia. The age of subjects with silent ischemia also tended to be higher. No biochemical variable was significantly different between subjects with or without silent ischemia. Nonsignificant trends toward higher total and low-density lipoprotein cholesterol, apolipoprotein B, and Lp(a) were seen in subjects with silent ischemia ($P = 0.18$, 0.18, and 0.32, respectively).

CONCLUSIONS— These results suggest that Lp(a) is not elevated in IDDM subjects with silent ischemia. Although a trend toward higher levels of Lp(a) was observed in subjects with silent ischemia, this difference was not significant. To be 85% certain of detecting a significant difference between two groups with these means and SDs, more than 800 subjects would be required. Such a study would be challenging to coordinate. Lp(a) might be associated with silent ischemia in a larger sample, but our results suggest that it would not be useful as a predictor of silent ischemia in a particular diabetic subject.

These results suggest that the biological mechanism for the excess risk of silent ischemia in IDDM is related to factors other than Lp(a). The relationship between Lp(a) and other aspects of disease severity in diabetes is not straightforward (6). At present, there is no definitive evidence that Lp(a) is a risk factor for coronary heart disease, including silent myocardial ischemia, in diabetes. More studies are required to address this issue. In the meantime, an increased plasma concentration of Lp(a) in a diabetic subject should not itself be a target for treatment. However, if elevated Lp(a) is present, traditional reversible risk factors should be managed aggressively, as they would be in any diabetic subject.

ROBERT A. HEGELE, MD
PHILIP W. CONNELLY, PHD
PAUL W. ARMSTRONG, MD
ANATOLY LANGER, MD

From the Divisions of Endocrinology and Metabolism (R.A.H., P.W.C.) and Cardiology (P.W.A., A.L.), Departments of Medicine (R.A.H., P.W.C., P.W.A., A.L.) and Clinical Biochemistry (R.A.H., P.W.C.), St. Michael's Hospital and University of Toronto, Toronto, Ontario, Canada.

Address correspondence to Robert A. Hegele, MD, DNA Research Laboratory, St. Michael's Hospital, 30 Bond St., Toronto, Ontario M5B 1W8, Canada.

Acknowledgments— This work was supported by an operating grant from the Heart and Stroke Foundation of Ontario (A-2356). R.A.H. is a McDonald Scholar of the Heart and Stroke Foundation of Canada.

References

1. Langer A, Freeman MR, Josse RG, Steiner G, Armstrong PW: Detection of silent myocardial ischemia in diabetes mellitus. *Am J Cardiol* 67:1073–1078, 1991
2. Velho G, Erlich D, Turpin E, Neel D, Cohen D, Froguel P, Passa P: Lipoprotein(a) in diabetic patients and normoglycemic relatives in familial NIDDM. *Diabetes Care* 16:742–747, 1993
3. Maser R, Usher D, Becker DJ, Drash AL, Kuller LH, Orchard TJ: Lipoprotein(a) concentration shows little relationship to

Downloaded from http://ada.silverchair.com/care/article-pdf/17/11/1365/515018/17-11-1365.pdf by guest on 10 April 2024

IDDM complications in the Pittsburgh Epidemiology of Diabetes Complications Study cohort. *Diabetes Care* 16:755–758, 1993
4. Haffner SM, Moss SE, Klein BEK, Klein R: Lack of association between plasma lipoprotein(a) concentrations and coronary heart disease mortality in diabetes: the Wisconsin Epidemiologic Study of Diabetic Retinopathy. *Metabolism* 41:194–197, 1992
5. Jenkins DJA, Wolever TMS, Rao V, Hegele RA, Mitchell SJ, Ransom TPP, Boctor D, Spadafora PJ, Jenkins AJ, Mehling C, Relle LK, Connelly PW, Story JA, Furumoto EJ, Corey P, Wursch P: Effect on blood lipids of very high intakes of diets low in saturated fat and cholesterol. *N Engl J Med* 329: 21–26, 1993
6. Haffner SM: Lipoprotein(a) and diabetes: an update. *Diabetes Care* 16:833–840, 1993

Reliability of Driving Performance During Moderate Hypoglycemia in Adults With IDDM

Numerous studies have demonstrated that experimentally induced hypoglycemia results in cognitive-motor deficits in insulin-dependent diabetes mellitus (IDDM) subjects (1–4). However, these deficits are not uniform across subjects, even when blood glucose (BG) levels are similar (5). A recent report suggests that there may be central nervous system (CNS) adaptation to recurrent low BG episodes, such that less cognitive-motor disruption occurs during a subsequent low BG episode within the next 12 h (6). Therefore, it is possible that some of the individual differences seen in cognitive-motor vulnerability, previously reported, may reflect differences in subjects' BG profiles shortly before testing.

However, it is also possible that these individual differences reflect stable, but idiosyncratic, differences in cognitive-motor vulnerability to hypoglycemia. A recent report has demonstrated that cognitive-motor disruptions with moderate hypoglycemia were relatively stable for individuals over a 3-month period (7). No studies, however, have investigated whether driving impairments due to hypoglycemia are stable for individuals over time.

The present study investigated whether individual driving performance during induced moderate hypoglycemia (2.6 mmol/l) was consistent over 3 months. Subjects had been previously tested on a driving simulator four times at euglycemia during a control day and four times on an experimental day at euglycemia (6.4 ± 0.67 mmol/l), mild hypoglycemia (3.6 ± 0.33 mmol/l), moderate hypoglycemia (2.6 ± 0.28 mmol/l), and again at euglycemia (6.3 ± 0.89 mmol/l). While moderate hypoglycemia resulted in significantly more swerving and spinning, and in more time driving off-road and across the midline, there were large individual differences (8).

Because of costs and an exclusive focus on reliability, only 15 of the original 25 IDDM subjects (9 females, 6 males) were randomly selected to repeat the experimental day 3 months later. Repeat day participants did not significantly differ from the original subject population in terms of age, diabetes duration, mean glycosylated hemoglobin levels, number of years driving, or number of miles driven. One individual experienced spontaneous moderate hypoglycemia (2.3 mmol/l) ~2 h before testing began on the repeat day and was consequently excluded from data analysis.

The procedure for the repeat testing was identical to the original experimental day (8). Participants were admitted to the University of Virginia General Clinical Research Center the evening before the study. After eating dinner, subjects fasted until completing the following day's testing, receiving intravenous regular human insulin through the night to maintain euglycemia. Subjects were kept blind to BG levels while driving the Atari simulator (Atari Games, Milpitas, CA). They drove for 4 min at euglycemic baseline (6.1 ± 0.63 mmol/l), mild hypoglycemia (3.5 ± 0.28 mmol/l), moderate hypoglycemia (2.6 ± 0.27 mmol/l), and again at euglycemia (5.3 ± 1.64 mmol/l).

In the original study, each subject's experimental day performance was compared with control day performance. Similarly, at 3 months' follow-up, repeat day performance was compared with the control day data from the original study. Eight driving variables related to steering and speed control were calculated by the simulator (8). The total number of variables that exceeded each subject's control day mean performance by two SDs was computed for the experimental and repeat days. Using this criteria, the four trials were ordinally ranked for both the experimental and the repeat day based on the total number of disrupted driving variables. In other words, if moderate hypoglycemia (trial 3) resulted in the greatest number of disrupted driving variables, it was ranked 4. If, however, moderate hypoglycemia resulted in the least disruption in driving performance, it was ranked 1. If two trials resulted in the same number of disrupted driving variables, they were assigned the mean of the two rankings. For example, if mild (trial 2) and moderate hypoglycemia (trial 3) had an equal number of disrupted driving variables, and these trials were the most disrupted, then each was assigned a rank of 3.5 (mean, 3 ± 4). This procedure allowed relative determinations of each subject's driving performance.

Relative ranks of driving performance at moderate hypoglycemia during the experimental and repeat days were compared. Five subjects had identical ranks, six subjects had ranks that differed by only 0.5, and three subjects had ranks that differed by one position, resulting in a Spearman correlation of $r = 0.65$ ($P = 0.012$).

Driving performance during

Downloaded from http://ada.silverchair.com/care/article-pdf/17/11/1365/515018/17-11-1365.pdf by guest on 10 April 2024