our belief that microproteinuria is not a prerequisite for the development of preeclampsia. Four of the five IDDM patients developing preeclampsia in our study had albuminuria <20 mg/24 h. An impaired endothelium-dependent relaxation in vitro in resistance arteries from women with gestational diabetes who are unlikely to exhibit proteinuria, similar to findings seen in vessels from women with preeclampsia, has recently been demonstrated (2). This speaks in favor of vascular pathophysiology in diabetes being independent of microalbuminuria.

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High Lipoprotein(a) Levels in Type 1 and Type 2 Diabetic Patients With Macroalbuminuria

Lipoprotein(a) [Lp(a)] is a subtype of the LDL molecule in which apoprotein(a), a large glycoprotein, is covalently bound to apolipoprotein B. Lp(a) serum levels are mainly under genetic influence. Besides the existing controversy about the recognition of high Lp(a) levels as an independent cardiovascular risk factor in diabetes, its association with diabetic kidney disease has also been debated (1–13). It has recently been stressed that short sampled studies could reconcile part of this controversy (12,13).

In an effort to detect a possible relationship between urinary albumin excretion and Lp(a) levels in both type 1 and type 2 diabetes, we consecutively studied 588 type 1 and 1,065 type 2 diabetic patients not presenting with any life expectancy–limiting condition and with triglyceridemia <400 mg/dl. After thorough clinical evaluation and routine chemistries, the urinary albumin excretion rate (UAER) was measured once in overnight urine collections using laser immunonephelometry, and patients were categorized as normoalbuminuric, microalbuminuric, or macroalbuminuric following current recommendations. Lp(a) was measured in fresh serum samples by means of an immunonephelometric assay [N antiserum to human Lp(a), Behring, Marburg, Germany, lower limit of detection: 9.5 mg/dl]. Because of nonadjustment to normality, Lp(a) levels were log-transformed for statistical calculations (analysis of variance [ANOVA] or *t* tests). To facilitate data interpretation, Lp(a) values are presented as non–log-transformed.

Lp(a) levels (mg/dl) were [median (range)] 17 (196), 16 (183), and 23 (468) for type 1 diabetic patients with normoalbuminuria, microalbuminuria, and macroalbuminuria, respectively (ANOVA, F = 2.27, P = 0.1), and 21 (272), 20 (236), and 28 (418) for type 2 diabetic patients with normoalbuminuria, microalbuminuria, and macroalbuminuria, respectively (ANOVA, F = 3.38, $P < 0.05$). In the latter case, a post hoc analysis (Student-Newman-Keuls test) showed statistically significant differences between patients with macroalbuminuria and patients with microalbuminuria, as well as between patients with macroalbuminuria and those with normoalbuminuria. A statistically nonsignificant trend toward greater Lp(a) levels in type 2 diabetes (versus type 1 diabetes) was observed [21 (418) vs. 18 (468), P = 0.1]. A statistically significant association between cerebrovascular disease and high Lp(a) levels was observed for type 2 diabetes [33.5 (211) vs. 20 (418), $P < 0.05$]. However, no association was found between Lp(a) levels and coronary heart disease or peripheral vascular disease in type 2 diabetes (data not shown). The number of type 1 diabetic patients with these complications was so scarce (n = 6, 13, and 15, respectively) that the data did not allow any statistical analysis. A current smoking habit was associated with lower Lp(a) levels in type 2 diabetes [13.5 (418) vs. 22 (272), $P < 0.01$], although such an association was not detected for type 1 diabetes (data not shown). A statistically significant association between hypertension and greater Lp(a) levels was found for type 2 diabetes [23 (418) vs. 19 (189), $P < 0.05$], and a borderline statistically significant association of the same kind was found for type 1 diabetes [23 (468) vs. 17 (256), P = 0.06]. Likewise, the presence of laser-treated retinopathy was associated with greater Lp(a) levels in both type 2 [25 (418) vs. 20 (261), $P < 0.05$] and type 1 diabetes [22 (468) vs. 16 (183), P = 0.08], although only borderline statistically significant differences were observed in the latter case. Borderline statistically significant associations between the female sex and greater Lp(a) levels were found for both type 2 [23 (261) vs. 20 (418), P = 0.06] and type 1 diabetes [22 (468) vs. 15 (256), P = 0.07]. Insulin therapy was associated with greater Lp(a) levels in type 2 diabetes [24 (418) vs. 19 (272), $P < 0.05$]. After considering the effect of age, duration of diabetes, and BMI in a multivariate ANOVA model with covariates, statistically significant associations were still observed for the UAER (F = 3.45, $P < 0.05$) and the current smoking habit (F = 4.35, $P < 0.05$) categories, while associations with cerebrovascular disease and type of diabetes were only borderline statistically significant; no associations of this type were observed for hypertension, sex, or laser-treated retinopathy.

These data prove the existence of an association between macroalbuminuria and high Lp(a) levels mainly in type 2 diabetes, although a similar trend might be observed for type 1 diabetes. The relationship between proteinuria and Lp(a) levels is not limited to diabetic kidney disease: it was recently found that after immunosuppressive treatment-induced remission of nephrotic syndrome, Lp(a) concentration dropped parallel to the reduction of proteinuria in 17 patients with primary kidney disease (14). Perhaps the elevation of Lp(a) occurs as part of nonspecific hepatic protein synthesis triggered by albumin loss to maintain constancy of plasma oncotic pressure. Hypothetically, raised levels of this and other substances could have a role in the accelerated atherogenesis commonly seen in overt diabetic nephropathy. An independent association of current smoking habit with lower Lp(a) levels was found in the present study. This association has previously been reported in other clinical settings (15,16). Further confirmation from longitudinal studies is necessary before considering this association established. Likewise, how the smoking habit influences

Lp(a) levels and how they interact in cardiovascular disease are issues that deserve to be investigated in future research.

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Noncardiogenic Pulmonary Edema in a Patient With Diabetic Ketoacidosis

Ketoacidosis is a common metabolic disturbance in patients with uncontrolled type 1 diabetes. Despite aggressive fluid replenishment in the initial management of the ketoacidotic state, pulmonary edema is a rare complication (1,2). We present an unusual case report of a patient with type 1 diabetes who has had recurrent episodes of noncardiogenic pulmonary edema during a 9-year period. A 49-year-old woman with a 5-year history of type 1 diabetes complicated by poor glucose control secondary to noncompliance and by neuropathy, nephropathy, neurogenic bladder, and chronic bronchitis initially presented in 1988 with the sudden onset of dyspnea and hypoxia (pH, 7.10; P_{O_2}, 94.4 mmHg; P_{CO_2}, 13.1 mmHg; HCO_3^-, 4.1 meq/l; and oxygen saturation, 94.7% on a 50% face mask). Her blood glucose level was 404 mg/dl, and acetone was present in her blood and urine. An electrocardiogram and the results of right heart catheterization were normal. She had a similar presentation in October of 1995. Medications at the time of most recent admission included NPH and regular insulin, metoprolol, omeprazole, estrogen, phenytoin, enalapril, cisapride, and furosemide. Initial examination revealed tachypnea. Initial laboratory studies showed a leukocyte count of 22,900/mm^3 with 19% band forms, blood glucose level of 490 mg/dl, 2+ acetone in the plasma, and 2% glycosuria and 4+ ketones on the urinalysis. An arterial blood gas study on room air showed a pH of 7.30, P_{O_2} of 119 mmHg, P_{CO_2} of 28 mmHg, HCO_3^- of 14 meq/l and an oxygen saturation of 98%. A chest X-ray examination (CXR) was unremarkable. On the fourth hospital day, the patient developed dyspnea and hypoxia. Arterial blood gas evaluation on 2 l of supplemental oxygen showed a pH of 7.53, P_{O_2} of 62.8 mmHg, P_{CO_2} of 29.4 mmHg, HCO_3^- of 24 meq/l, and an oxygen saturation of 94.5%. A CXR was consistent with pulmonary edema. An echocardiogram revealed normal systolic function with an ejection fraction of 60%. The patient appeared to be in noncardiogenic pulmonary edema, and her clinical condition improved with diuresis and oxygenation. Subsequent pulmonary function testing on follow-up revealed mild restriction and small-airways disease (3–6).

This case illustrates an uncommon presentation of the ketoacidotic state and is the first reported case of recurrence in the same patient. Sprung et al. (7) reported the occurrence of pulmonary edema in two such similar patients. In both instances, the patients suffered from type 1 diabetes and on presentation had ketoacidosis, normal results of right heart catheterization studies,