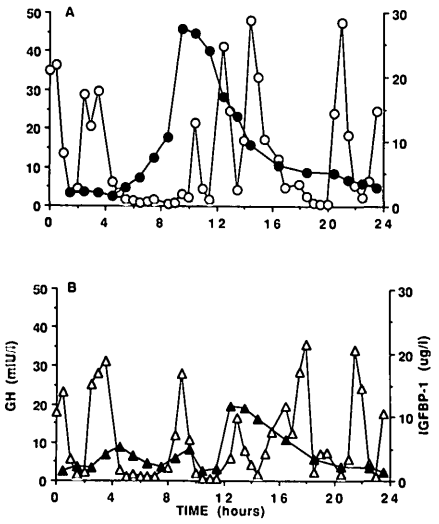

Figure 1—*A: GH (○) and IGFBP-1 (●) profiles on subcutaneous insulin. B: GH (△) and IGFBP-1 (▲) profiles on intraperitoneal insulin.*

hypothalamus (4). The IGF-I levels were not statistically different between regimens and, if anything, tended to be lower on intraperitoneal insulin making it highly unlikely that IGF-I would be mediating any decrease in our patient's GH profile.

IGFBP-1 appears to have an inhibitory effect on IGF-I action in various tissues (6), and it has been suggested that increased amounts of this binding protein inhibit the detection of IGF-I by the hypothalamus and/or pituitary gland (5). Suppressing IGFBP-1 levels with direct intraperitoneal (intraportal) insulin administration may allow improved detection of IGF-I by the pituitary or hypothalamus and subsequently lead to a decreased GH secretion.

This case report highlights a possible benefit of insulin delivery via the intraperitoneal route. These preliminary findings need, however, to be examined in larger studies and over longer time intervals. If the marked increase of IGFBP-1 known to occur in type I diabetes can be more effectively suppressed by using intraperitoneal insulin this may provide particular benefit to adolescent diabetic patients as elevated levels of IGFBP-1 have been postulated to play a role in the growth impairment seen in these patients (7).

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GH, growth hormone; IGF-I, insulin-like growth factor-I; IGFBP-1, insulin-like growth factor binding protein-1; type 1 diabetes, insulin-dependent diabetes mellitus; BMI, body mass index; IRMA, immunoradiometric assay; RIA, radioimmunoassay.

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Prospective Study of Asymmetric Retinopathy as a Predictor of Brain Infarction in Diabetes Mellitus

Usually retinopathy develops symmetrically in diabetic patients, unless local ophthalmic abnormalities are apparent such as branch vein occlusion, optic nerve atrophy, and glaucoma (1–3). However, the stenosis of extraocular artery could elicit a unilateral ischemic retinopathy (4), the fundoscopic finding of which is similar to that of diabetic retinopathy. Therefore, laterality of retinopathy in diabetic patients may reflect the existence of arteriosclerosis in arteries perfusing the ophthalmic artery and may predict the development of brain infarction.

To elucidate this possibility, we conducted a prospective study of diabetic patients with or without laterality of retinopathy for the development of brain infarction. We followed 142 outpatients with diabetes mellitus, including 9 IDDM patients, from 1981 to 1989. Patients treated with photocoagulation or with a history of brain infarction were excluded. They were divided into 3 groups fundoscopically: 12 patients with asymmetric retinopathy, 65 with symmetric retinopathy, and 65 without retinopathy.

Optic fundi examinations were repeated >1 time/yr in each patient. Ophthalmologists in our university hospital performed the examinations. The severity of retinopathy was graded according to Scott's classification (5). The

Table 1—*Incidence of brain infarction in 3 groups of diabetic patients with and without retinopathy*

Retinopathy type	Brain infarction
Asymmetric	5*/12 (41.7%)
Symmetric	5/65 (7.7%)
Negative	5/65 (7.7%)

*$P < 0.005$, patients with asymmetric retinopathy vs. those with symmetric retinopathy and without retinopathy by χ^2 analyses.

presence of laterality in retinopathy was defined when >2 grades difference were found between eyes in a patient. Fluorescent angiography was made in some cases to determine whether retinopathy was preproliferative or proliferative.

A total of 15 patients developed brain infarction during the follow-up period. As shown in Table 1, the percentage of brain infarction in patients with asymmetric retinopathy was 41.7% (5 of 12), which was significantly higher than 7.7% in patients with symmetric retinopathy or 7.7% in patients without retinopathy. The laterality of brain infarction determined by CATscan coincided with that of the worse side of asymmetrical retinopathy in 4 of 5 patients.

No differences were observed in sex, age, duration of diabetes, BP, BMI, fasting blood glucose, HbA_1 or serum lipid levels among the 3 groups in 1981. In some cases, asymmetry of retinopathy disappeared during the follow-up period. The asymmetry of retinopathy significantly persisted in 42% of patients who had asymmetry at the starting point and throughout the follow-up period. This contrasted with the 4% of patients who had a new appearance of asymmetry in symmetric retinopathy ($P < 0.001$).

By the multiple regression analysis for the incidence of brain infarction in 77 patients with retinopathy, male sex and fundoscopic laterality indicated a significantly high risk for brain infarction (t values are 1.76 and 2.24, respectively). However, age, sBP, and HbA_1 were not associated with the incidence of brain infarction.

The laterality of retinopathy in our cases was observed significantly more repetitively compared with symmetric retinopathy patients. Therefore, some extraocular factors such as arteriosclerosis or anomaly of carotid-brain vasculature may persist in diabetic patients with asymmetric retinopathy and may accelerate the diabetic retinopathy. This acceleration may be uneven in each side of the eyes, because in our cases the site of brain infarction coincided with that of retinopathy. We conclude that laterality of diabetic retinopathy is one of the predictors for brain infarction development in patients with diabetes mellitus.

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BP, blood pressure; sBP, systolic blood pressure; BMI, body mass index; IDDM, insulin-dependent diabetes mellitus.

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Effect of Eicosapentaenoic Acid Ethyl on Urine Albumin Excretion in NIDDM

Fish oil, rich in n-3 fatty acid (EPA and DHA), has properties that help prevent development of atherosclerosis and thrombosis (1). Dietary cod-liver oil partially normalized increased microvascular albumin leakage in diabetic patients with albuminuria (2). EPA is useful in stopping the progression of IgA nephropathy (3). The effect of purified EPA on albuminuria was examined in NIDDM patients with albuminuria.

The subjects in this study were 10 male and 14 female NIDDM patients with albuminuria. The average age was 63.9 ± 2.8 yr. The average duration of diabetes mellitus (after diagnosis) was 9.8 ± 1.2 yr. Patients were treated with diet therapy only (8.3%), oral sulfonylurea administration (58.4%), or conventional insulin therapy (33.3%). Diabetic retinopathy was found in 41.7% of patients and 16.7% of the patients combined with diabetic neuropathy. In 37.5% of the patients, hypertension was observed and BP levels were controlled by antihypertensive agents. The dose of these agents and diet composition were not changed. According to the average UAI (mg/g Cr) of two timed collections obtained at the same time, all patients were divided into two groups: group 1: 30 mg/g Cr<UAI<300 mg/g Cr, group 2: UAI>300 mg/g Cr.

The capsule of EPA-E, 900 mg/