tion, and worsened glycemic control, which might be related to the cytochrome P450–mediated metabolic pathway (4,5). The results in this study are an important observation for patients with diabetes and are consistent with another report that pitavastatin, which is metabolized with little involvement of cytochrome P450 isoenzymes (4), did not show these major adverse effects (6). Because pitavastatin has been marketed for only a few years, further studies with a greater number of subjects and a longer duration are needed to establish the safety of this agent.

In conclusion, pitavastatin is effective in lowering LDL cholesterol and triglyceride levels without affecting glycemic control in patients with diabetes. We believe that this agent must also help prevent the development of macrovascular disease in diabetic patients, as has been seen with other statins, but this still requires confirmation in a controlled clinical trial.

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Twelve-Hour Glycemic Profiles With Meals of High, Medium, or Low Glycemic Load

Diets of low glycemic load may dampen the postprandial glycemic response, thereby avoiding high blood glucose concentrations that could be detrimental to health (1). We compared blood glucose profiles of two nondiabetic subjects (A and B) consuming meals of high (baguette, strawberry jam, and maltose), medium (baked potato, cheese, and Coca Cola), or low (chickpeas, tuna, vinegar, and oil) glycemic load at regular intervals throughout the day.

Three test meals contained the same calorie content but different glycemic load for each subject (A: glycemic load = 92, 49, and 19; B: glycemic load = 115, 66, and 24). For each glycemic load category, three full portions of the test meal with a 4-h interval in between and six half-portions with a 2-h interval in between were consumed on 2 different days. For each subject, six 12-h blood glucose profiles deduced from the interstitial glucose in subcutaneous abdominal tissue measured by MiniMed continuous glucose monitoring system were obtained.

A relatively stable blood glucose profile was observed throughout the day with low–glycemic load meals for both subjects (Fig. 1). Consumptions of high– and medium–glycemic load meals were usually followed by peaks of blood glucose. However, there did not appear to be an obvious dose-response effect between the actual glycemic load and the height of the peaks (either full portion versus half portion or high glycemic load versus medium glycemic load), suggesting a possible "threshold" effect (2). Nibbling diets with small frequent meals may only help avoid hyperglycemia when the meal glycemic load is below a certain threshold level. Compared with the glucose response of the first meal, some of those triggered by each subsequent but identical meal appeared to be lower. This apparently greater "breakfast" glycemic response may be due to higher ACTH and glucocorticoid levels before awakening. Since glycemic index values of food are derived in the fasting state, the glycemic load formula may give better prediction of the postprandial glucose response for breakfast than those for lunch or dinner.

Calculated meal glycemic load may deviate from the actual glycemic response of food combinations. Potential limitations of the continuous glucose monitoring system also need to be considered when interpreting our glycemic profiles (3). In this study, 25% of the sensor-deduced blood glucose concentrations deviated by ≥15% from the corresponding fingerstick glucometer values (for calibration) among 48 paired values.

Our pilot study suggests that a stable blood glucose profile can be maintained by consuming a low–glycemic load diet. However, meal glycemic load may need to be below a certain threshold to be of benefit. Identical meals may produce different blood glucose responses at different times of the day, indicating that the glycemic load formula may not predict the postprandial glucose response for meals eaten in the nonfasting state.

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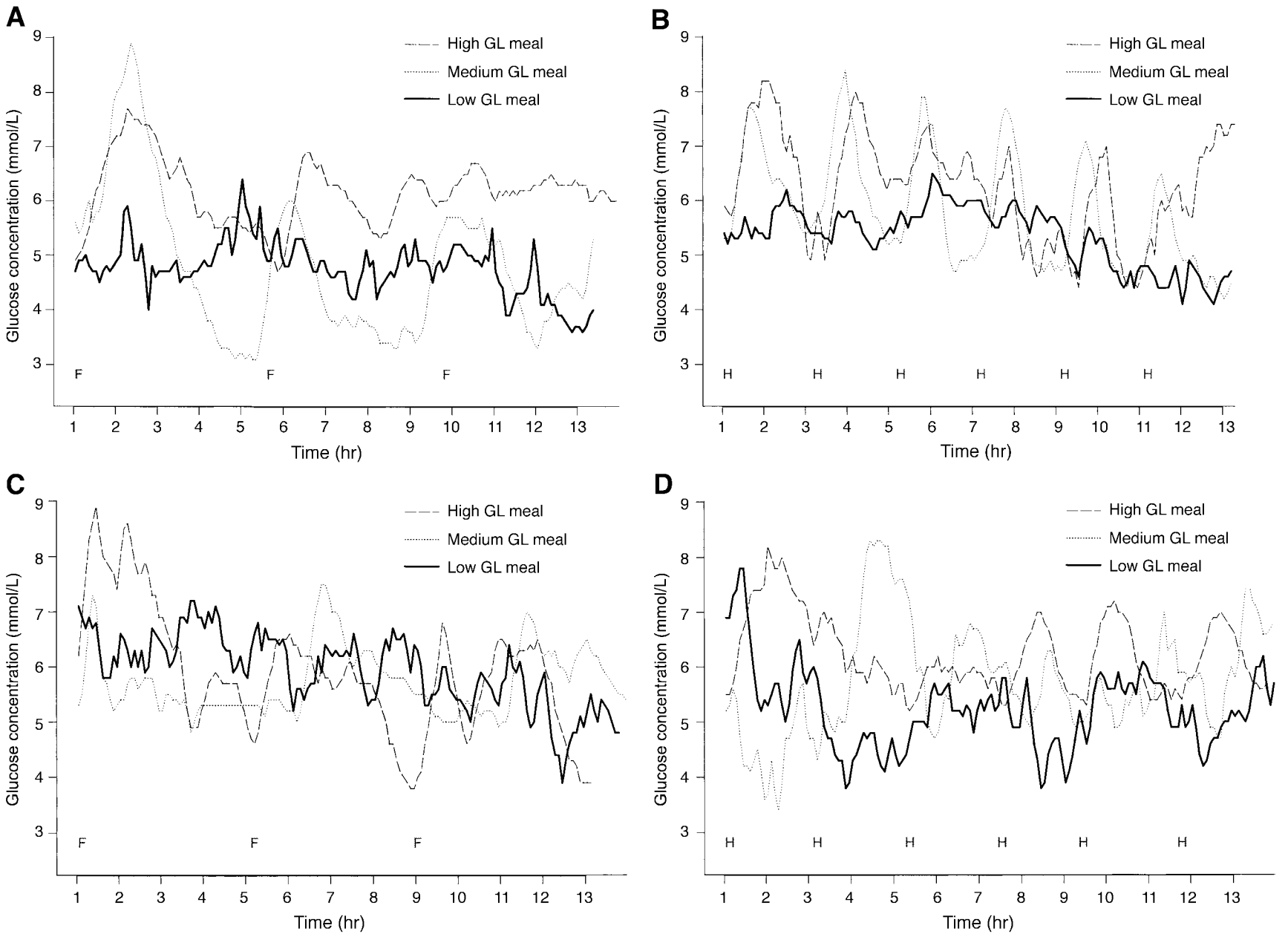

Figure 1—*Twelve-hour glucose profiles reported by continuous glucose monitoring system on the 6 experimental days for subject A consuming high–, medium–, and low–glycemic load (GL) meals as full portions* (A; *three meals*) *or as half portions* (B; *six meals*) *and subject B consuming high–, medium–, and low–glycemic load (GL) meals as full portions* (C; *three meals*) *or as half portions* (D; *six meals*).

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A Case of Lipoatrophy With Insulin Glargine

Long-acting insulin analogs are not exempt from this complication

Lipoatrophy as a cutaneous complication of insulin therapy became extremely rare since the introduction of recombinant human insulin. Recently, some cases of lipoatrophy were reported in association with the use of rapid-acting insulin analogs, like lispro insulin, in combination with pump therapy (1,2). If long-acting insulin analogs are exempt from this, the complications are not known.

We report the case of a 39-year-old type 1 diabetic Caucasian woman (weight 50 kg, BMI 21.4 kg/m^2) with diabetes duration of 8 years. She began intensified insulin therapy with two premixed insulin injections before breakfast and dinner and regular insulin before lunch (20 IU/day, 72% neutral protamine Hagedorn insulin). In January 2004, she agreed to participate in a 6-month randomized study comparing different multiple daily insulin therapies, all using bedtime insulin glargine as basal insulin. No specific instructions about the preferred injection area for both insulins were given, but it is a common practice in our country to inject rapid-acting insulin into the abdomen and long-acting insulin into the buttock or thigh.

At follow-up, a lipoatrophic area appeared at study end in the outside, upper third of the right thigh (Fig. 1). Asking the patient about the possible causes, she recognized that she didn't change pen needles frequently and, even more importantly, she had used the right thigh for glargine injection almost exclusively. She was prompted to avoid the right thigh for insulin injection shifting to buttock or left thigh areas and changing the area every day. However, 12 months later the lipoatrophy area persisted with the same extent.

This case confirms that any insulin preparation, even insulin analogs, may induce lipoatrophy. Insulin glargine, a diarginyl insulin analog, is a new long-acting insulin analog soluble at acid pH (4.0) but less soluble at neutral pH because

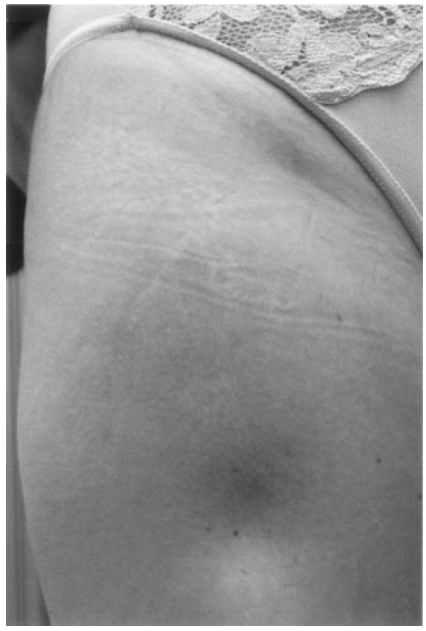

Figure 1—*Lipoatrophic area on the outside, upper part of thigh where insulin glargine was injected.*

isoelectric point is at a pH level of ~6.4–6.6. After subcutaneous injection, precipitation or crystallization of glargine at the site of injection delays absorption and prolongs the effect of insulin, allowing a peakless, nearly 24-h duration of action (3).

Insulin glargine is now being used extensively as basal insulin in both type 1 and type 2 diabetes. To our knowledge, this is the first description of lipoatrophy induced by insulin glargine. Certainly, the frequent use (up to 14 times) of the same pen needle and the repeated injection into the same area were relevant to the appearance of lipoatrophy in this case. Under such circumstances, we did not know if in this case the injection of an acid insulin solution and the subsequent formation of crystals in the subcutaneous tissue could have played a role in lipoatrophy formation. It has been suggested earlier that lipoatrophy results from a local immune reaction to insulin crystals (4). The inflammatory response includes local hyperproduction of tumor necrosis factor α from macrophages that led to dedifferention of adipocytes (lipoblastoma-like lipoatrophy) (4).

In conclusion, daily pen needle change and frequent switching of injection area are even more important with insulin glargine to avoid lipoatrophy.

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COMMENTS AND RESPONSES

A Comparison of Lipid and Glycemic Effects of Pioglitazone and Rosiglitazone in Patients With Type 2 Diabetes and Dyslipidemia

Response to Goldberg et al.

The study by Goldberg et al. (1) in the July issue of *Diabetes Care* concluded that, compared with rosiglitazone, pioglitazone was associated with improvements in triglycerides, HDL cholesterol, LDL concentration, and LDL particle size.

It should first be noted that 4,410 subjects were screened to obtain 735 eligible subjects. This was a highly selective