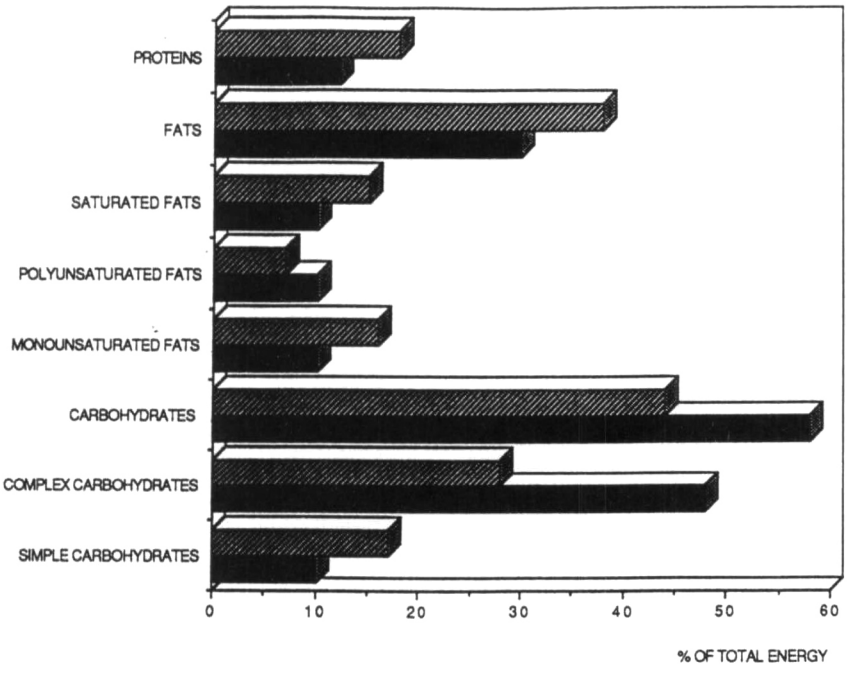

Figure 1—*Nutritional intake of Belgian diabetic children.* ▨, *diabetic children;* ■, *recommended intake.*

tions. The dietary consumption habits have nearly not changed over the past 15 years.

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References

1. Randecker GA, Smiciklas-Wright H, McKenzie JM, Shannon BM, Mitchell DC, Becker DJ, Kieselhorst K: The dietary intake of children with IDDM. *Diabetes Care* 19:1370–1374, 1996
2. Dorchy H, Bourguet K, Pieters S, Mozin MJ: Déséquilibres alimentaires importants chez les enfants diabétiques et nondiabétiques belges. *Percentile* 1:45–50, 1996
3. Dorchy H, Roggemans MP, Willems D: Glycated hemoglobin and related factors in diabetic children and adolescents under 18 years of age: a Belgian experience. *Diabetes Care* 20:2–6, 1997
4. Dupin H, Abraham J, Giachetti I: *Apports nutritionnels conseillés pour la population française*. 2nd ed. Paris, Tec & Doc Lavoisier, 1992
5. Souci SW, Fachmann W, Kraut H: *La composition des aliments: tableau des valeurs nutritives*. 5th ed. Stuttgart, Germany, Medpharm, 1994
6. *Nevo tabel*. Den Haag, The Netherlands, Stiching nederlands voedingsstoffen bestand, 1993
7. Dorchy H, Mozin MJ, de Maertelaer V, Toussaint D, Loeb H: Relations entre ingesta lipidiques (cholestérol, graisses saturées et polyinsaturées), cholestérolémie, contrôle métabolique (HbA_{1c}) et rétinopathie des enfants diabétiques. *Rev Pédiatr (Paris)* 18:259–270, 1981

Mixing Insulin Lispro and Ultralente Insulin

We read with interest the recent article by Torlone et al. (1). In their conclusion, the authors do not favor mixing insulin lispro with ultralente insulin. Instead, they suggest that NPH insulin is a better therapeutic option, because "zinc-retarded insulin . . . may blunt the rapid-acting component of the mixture to an unpredictable extent" (2).

In contrast to Torlone's conclusion, we have shown that insulin lispro can be mixed with ultralente insulin without any effect on its rapid onset of activity. In a glucose clamp study (Eli Lilly, unpublished observations), insulin lispro and ultralente insulin were administered separately and as a 1:2-ratio mixture in trials with 12 healthy volunteers. The absorption rate of insulin lispro was not delayed, as evidenced by no change in *1*) the maximum serum insulin concentration, *2*) the time to maximum serum insulin concentration, *3*) the area under the curve of serum insulin versus time, *4*) the maximum glucose infusion rate, *5*) the time to maximum glucose infusion rate, or *6*) the total glucose infused (Table 1).

These findings highlight another advantage of insulin lispro: it can be mixed with an ultralente insulin preparation without a change in insulin absorption when injected within 5 min of mixing.

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References

1. Torlone E, Pampanelli S, Lalli C, Del Sindaco P, Di Vincenzo A, Rambotti AM,

Table 1—*Results of a glucose clamp study of insulin lispro and ultralente insulin administered mixed and separately*

	C_{max} (ng/ml)	t_{max} (min)	AUC (ng · min · ml^{-1})	R_{max} (mg/min)	T_{rmax} (min)	G_{tot} (g)
Humalog plus Humulin U, separate	2.49	51	364	467	126	79.5
Humalog plus Humulin U, mixed	2.56	44	437	466	144	81.6
P values	0.720	0.519	0.124	0.990	0.524	0.833

Data are means. C_{max}, maximum serum insulin concentration; t_{max}, time to maximum serum insulin concentration; AUC, area under the curve; R_{max}, maximum glucose infusion rate; T_{rmax}, time to maximum glucose infusion rate; G_{tot}, total glucose infused.

Modarelli F, Epifano L, Kassi G, Perriello G, Brunetti P, Bolli G: Effects of the short-acting insulin analog [Lys(B28),Pro(B29)] on postprandial blood glucose control in IDDM. *Diabetes Care* 19:945–952, 1996
2. Heine RJ, Bilo HJ, Fonk T, Van der Veen EA, Van der Meer J: Absorption kinetics and action profiles of mixtures of short- and intermediate-acting insulins. *Diabetologia* 27:558–562, 1984

Reply to Bastyr et al.

In their letter, Bastyr et al. argue that the insulin analog lispro can be mixed with ultralente insulin without any loss of the rapid onset of activity of lispro. While the data of Bastyr et al. cannot be questioned, we would, nevertheless, like to make a comment on its relevance to the treatment of IDDM.

Bastyr et al. have studied normal nondiabetic subjects. Their conclusions do not necessarily apply to C-peptide–negative IDDM. For example, the nonsuppressed endogenous insulin secretion of nondiabetic subjects during a euglycemic clamp might confuse the pharmacokinetics and pharmacodynamics of the mixture, compared with separate injections. On the other hand, it is well known that the trapping effect of any zinc-retarded insulin on soluble insulin mixed in the same syringe is largely dependent on a number of factors (e.g., ratio of soluble to retarded insulin, time elapsed between preparation and injection, site of injection, temperature of insulin). In this regard, what the data of Bastyr et al. really show is that the fast-acting insulin lispro maintains nearly intact its property of fast absorption when the ratio with ultralente insulin is 1:2 and when the injection is made immediately after preparation. But what about IDDM patients who use different ratios of insulin lispro and ultralente insulin or patients who for personal reasons need to prepare the mixture in advance, as opposed to at the time of injection? There is no doubt that the real chemical stability of a mixture of soluble (or lispro) insulin is with protamine-retarded insulin (NPH). In fact, insulin manufacturers market soluble (or lispro) insulins that are premixed with NPH, not zinc-retarded insulins.

Even assuming that the data of Bastyr et al. can be transferred to IDDM patients, we would discourage the use of ultralente insulin with insulin lispro. Insulin lispro is a sophisticated insulin preparation that clearly improves immediate postprandial blood glucose levels. It makes no sense simply to substitute human regular insulin with insulin lispro without changing the overall strategy of insulin therapy into that of the intensive management of IDDM. And, in intensive therapy (four injections of regular insulin at each meal and restarting insulin at bedtime), ultralente insulin is not the preparation of choice because of its high variability in absorption and unpredictable effect on blood glucose; multiple small daily doses of NPH mixed with insulin lispro at each meal do a better job in terms of quality of control. At present, this is a hypothetical model of IDDM treatment. Convincing, long-term data will be presented at the 1997 meetings of the American Diabetes Association and the International Diabetes Federation.

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Erratum

Pyörälä K, Pedersen TR, Kjekshus J, Faergeman O, Olsson AG, Thorgeirsson G, the Scandinavian Simvastatin Survival Study (4S) Group: Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease: a subgroup analysis of the Scandinavian Simvastatin Survival Study (4S). *Diabetes Care* 20:614–620, 1997

The authors of the above article wish to make two corrections. In Table 1 on page 615, the data in the row "Men" under the column "Diabetic" should read 158 (78) instead of 158 (72) [*n* (%)]. On page 619, column 1, lines 2–6 should read "Simvastatin treatment of 100 CHD patients for 6 years would prevent an expected major CHD event in 9 out of 19 nondiabetic patients, compared with 24 out of 49 diabetic patients expected to have an event."