

- 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."