Table 2—*Clinical characteristics and respiratory function in the diabetic patients investigated and in control subjects*

	N	AGE (YUR)	BMI (KG/M^2)	FVC	FEV_1 (% PREDICTED)	FEV_1/FVC
DIABETIC PATIENTS	27	23.2 ± 6	18.7 ± 1.8	93.5 ± 9.1	95.8 ± 9.5	100.2 ± 10.5
CONTROL SUBJECTS	15	21.7 ± 5.0	19.7 ± 1.3	106 ± 10	103.5 ± 10.5	97.3 ± 9.5

Data are means ± SD.

minuria was <30 μg/ml, Doppler examination was normal, and eye examination revealed only minimal changes of the retinal vessels. As shown in Table 1, the diabetic subjects presented values of respiratory function slightly but not significantly lower than control subjects. In 7 diabetic patients, lung volumes were lower than those of the remaining 20 diabetic patients (FVC, 85.5 ± 7.4; FEV_1, 86.1 ± 7.8; $P < 0.05$). Duration of known disease was the only variable that discriminated patients with low or normal lung volumes (9.8 ± 5.0 vs. 5.8 ± 3.2 yr, $P < 0.05$).

In studies that demonstrated reduced lung volumes in diabetic patients, the mean duration of disease was >10 yr on average. The diabetic patients we studied were younger, and the duration of disease was shorter. This suggests that chronic hyperglycemia or some metabolic variable associated with it may be related to pulmonary function. Consistent with this, long-term near-normoglycemia achieved with insulin pumps may be beneficial in preventing the deterioration of lung function associated with diabetes mellitus (6). Whatever the mechanism involved, the functional significance of the reduction of lung volumes reported in some diabetic patients is not known, but is probably small.

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IDDM, INSULIN-DEPENDENT DIABETES MELLITUS; FVC, FORCED VITAL CAPACITY; FEV_1, FORCED EXPIRATORY VOLUME IN 1 S.

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More Concerns Regarding Methodology in Hypoglycemia Study

We note with interest the discussion of the paper by Muehlhauser et al. (1) regarding hypoglycemia symptoms and the incidence of severe hypoglycemia in patients treated with human and animal insulin (1–5). As clinicians involved in the recruitment of patients into this study (center no. 7), we feel compelled to comment on the criticisms raised and on the authors' response.

First, the authors fail to clarify the procedures used for patient selection and matching on diabetes duration. The study protocol states that "about 800 to 1000 patients with type I diabetes, who had been informed about their diabetes by a doctor, shall be interviewed" (1). Indeed, no exclusion criteria or matching procedures are mentioned in the study protocol, and the participating centers were presented with the results of the study, based on a total of 551 patients, in February 1990. This analysis indicated no difference in symptoms and frequency of hypoglycemia between human insulin– and animal insulin–treated patients, but a clear difference was noted in the mean duration of diabetes—13 yr in 297 human insulin–treated patients compared with 18 yr in 254 animal insulin-treated patients. When the data were presented later at the annual meeting of the German Diabetes Association, we realized that patients (3 from our center) had been excluded to balance the groups for diabetes duration. This had neither been foreseen in the study protocol, nor was it described in the study published in *Diabetes Care* (1).

Furthermore, with regard to our patients, we noted numerous inaccuracies. Five of 29 (17%) patients were actually taking a different insulin species

than is stated in the study. The figures given in Table 2 relating to the frequency of severe hypoglycemia in the preceding year are also incorrect for our center and are likely to be incorrect for other centers as well. The table states that there were three episodes of severe hypoglycemia during the last year on human insulin compared with 25 on animal insulin. Among the 25 events attributed to animal insulin, however, 14 actually occurred during treatment with human insulin. Patients were transferred back to porcine insulin precisely because they had suffered severe hypoglycemia with human insulin! The first discrepancy illustrates that patients are an unreliable source of information for the assessment even of current insulin species. The latter discrepancy is explained by the design of the questionnaire. Patients were asked for the species (human, porcine, or bovine) of the insulin they were currently using and for the number of severe hypoglycemia episodes over the last year. The questionnaire, however, did not assess the insulin species used at the time of the hypoglycemic events. The data were then analyzed assuming that insulin species had not changed over the past year. As demonstrated by our patients, this assumption clearly is invalid.

These critical comments were related to the authors at the end of August 1990, but they were not taken into account. Instead, the authors stated that ". . . it will be the reviewers' task to evaluate the data and decide if, and in which form, they should be published and thus made public." But how could the reviewers possibly decide without the information we report here?

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Response From Authors

The comments raised by Dr. Kriegstein are repetitive of those put forward by Dr. Teuscher in a letter to the *Lancet* (1) and another letter by Dr. Teuscher to *Diabetes Care* (2), the latter one being an almost verbatim repetition of the first one. We have answered Dr. Teuscher's comments (3). We do not think Dr. Kriegstein raises any issues that have not been addressed already in our paper (4) and in the subsequent correspondence.

Like all other heads of the participating centers, Dr. Kriegstein agreed to the study protocol (including the questionnaire as the principal assessment method) before initiation of the study in September 1989; but he raised his concerns about the protocol only in August 1990, 3 mo after preliminary results had been communicated at the Annual German Diabetes Meeting. During the course of the study it turned out to be impossible to recruit 1000 type I diabetic patients as planned in the protocol, mainly because the vast majority of patients in Germany had already been switched to human insulin at that time. In this context, matching of both patient groups, i.e., those on human insulin and those on animal insulins, with respect to the duration of diabetes, had become indispensable in order to avoid a selection bias in favor of human insulin. The fact that the patient groups were matched has been stated in our paper (METHODS)—in contrast to Dr. Kriegstein's allegation—and the procedure used for matching has been reported in further detail in our response to Dr. Teuscher's letter.

The discrepancies between the data assessed by the structured patient interview technique according to the study protocol and the data given by Dr. Kriegstein concerning 5 of 29 patients have been mentioned already in the acknowledgement section of our original publication and again in the letter by Dr. Teuscher and our response. The patient interviews conducted by the two students on 19 September 1989 at the diabetes center of Dr. Kriegstein were supervised by Dr. Kriegstein. In fact, some missing data were supplemented by Dr. Kriegstein himself, and the protocols were later sent to us by him. We are astonished by Dr. Kriegstein's statement in his most recent letter that this "discrepancy illustrates that patients are an unreliable source of information for the assessment even of current insulin species." In fact, based on our experience and those from other diabetes centers, we believe that patients do know what type of insulin they use, including the insulin species. If Dr. Kriegstein were right in that his patients do not know the