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Letters to the Editor

Hyperproinsulinaemia in cirrhosis

Dear Sir

Taylor and Alberti, confirming our finding of hyperproinsulinaemia in patients with cirrhosis, at the same time questioned the correctness of the selection of the group of healthy subjects serving as controls in this study [1, 2]. In particular, they stressed the difference between levels of blood glucose after oral loads of 50 and 100 g glucose and the prolonged maintenance of raised serum immunoreactive insulin (IRI) and C-peptide levels after 100 g glucose in these subjects. Their remarks require a response.

Our study was begun before the WHO proposal of modifying the oral glucose tolerance test to a 75-g glucose load and at that time a 50-g load served as the basis for the selection of subjects, as was described in detail in our study. The oral 100-g glucose load was used for stimulation of the secretion of insulin, C-peptide and proinsulin in order to obtain results comparable with those of other investigators, who generally used this dose of glucose.

The problem of blood glucose curve patterns in healthy subjects after ingestion of 50 and 100 g glucose has not been clarified so unequivocally as suggested by Taylor and Alberti. In a study of 50 healthy subjects, a significant difference in the course of blood glucose curves was found between 90 and 180 min of oral glucose loading [3] and in another study a similarly significant difference was observed as early as 30–120 min following oral administration of 50 and 100 g glucose [4].

In healthy subjects evident differences are observed in IRI and C-peptide (and proinsulin) concentrations in serum following oral loads of 50 and 100 g glucose. In tests prolonged to 300 mins it could be shown that after 50 g glucose – in agreement with the remarks of Taylor and Alberti – the maximal increases in serum IRI and C-peptide occurred between 45 and 60 min and the levels of these peptides fell rapidly after that time. On the other hand, after a load of 100 g glucose the rise in serum IRI levels persisted as a plateau or as a double peak between 30 and 120 min, and returned to the initial value only between 240 and 300 min. A similar shape was observed in the serum C-peptide curve in these subjects [3]. This finding shows that the prolongation of raised IRI and C-peptide levels observed in our control subjects after an oral load of 100 g glucose is a phenomenon which is normally found in healthy subjects.

Although two of our healthy subjects had borderline blood glucose levels (exceeding the upper normal limit) 60 min after a 50-g oral glucose tolerance test, we do not think this of real significance for the interpretation of our results. Discussion of the definition of health in relation to carbohydrate metabolism is obviously very difficult, since at this juncture we enter a field where from time-to-time borderlines are arbitrarily changed and frequently questioned:

"Grammatici certant et adhuc sub iudice lis est"

(Horatius: Ars Poetica, line 78)

Yours sincerely,

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References

1. Taylor R, Alberti KGMM (1984) Hyperproinsulinaemia in cirrhosis. Diabetologia 26: 392 (Letter)
2. Kasperska-Czyżykowa T, Heding LG, Czyżyk A (1983) Serum levels of true insulin, C-peptide and proinsulin in peripheral blood of patients with cirrhosis. Diabetologia 25: 506–509
3. Czyzyk A (1974) Frühdiagnose des Diabetes mellitus. In: Bibergeil H, Fiedler H, Poser U (eds) VIII Karlsburger Symposium: Frühdiabetes – Pathogenese, Diagnose, Prävention. Zentralinstitut für Diabetes, Karlsburg, pp 187–199
4. Heding LG, Kasperska-Czyżykowa T (1981) B-cell response to 50- and 100-g oral glucose in non-diabetic persons. Diabetologia 21: 280 (Abstract)

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Diet and insulin-dependent diabetes in the BB rat

Sir,

We would like to comment on the Short Communication from Elliott and Martin [1]. The authors fed diabetes-prone BB rats four diets from weaning as follows: chow (control); group 1: semi-synthetic diet in which protein was replaced with l-amino acids; group 2: contained 1% gliadin in addition to the aforementioned; and group 3: contained 1% skim milk powder instead of gliadin. The incidence of diabetes was 19/39, 3/19, 7/20 and 11/21, respectively. From these results they concluded, "Accordingly, the presence of intact protein appears necessary for the full expression of the genetic susceptibility to develop diabetes in this colony of BB rats".

The finding that animals fed skim milk powder, in addition to the base diet, developed diabetes in numbers comparable to heavier chow-fed rats is interesting but the authors' conclusion that the effect was due solely to protein is clearly open to debate since skim milk powder contains many other constituents besides protein as shown in their Table 1 [1]. Furthermore, since the chow "control" diet was not isocaloric with respect to the test diets, intake of *all* nutrients in chow-fed rats would differ from that of animals on the test diets.

Since there is probably an interaction of environment and genetic background in development of the syndrome [2, 3], the authors should have distributed littermates equally among all groups, including the chow control group. Were there litter effects – how many of the seven litters in group 3 produced diabetic rats? How many litters were in the chow-fed control group?

The use of a closed formula diet, such as chow, as the sole control was unfortunate since this mixture of chemicals is not only ill-defined but varies with changes in the market place. It is preferable to use standard, purified diets, such as the AIN-76 diet, which consist of commercially refined protein, carbohydrates, fat and defined mineral and vitamin mixtures [4]. The diet constituents reported by Elliott and Martin were described only as "carbohydrates, fat, salt mixture and vitamins", etc. What was the source of carbohydrate and fat and which salt and vitamin mixtures were used? The "control" chow diet contained 50.0% carbohydrate, 5.0% fat and 5.2% fibre, compared with 64.2% carbohydrate, 10.0% fat and no fibre in the "semi-synthetic base". The 5.2% fibre reported in the "control" chow diet must have been crude fibre; the actual dietary fibre content of this diet was probably 15%. Whether or not these major differences can account for the more than 40% greater body weight of chow-fed rats is difficult to determine without more detailed diet information and data on food and water intake. It is clear that other purified diets, such as AIN-76, give equal or even better growth rates compared with chow [4], strongly suggesting that the semi-synthetic base diet used by Elliott and Martin was nutritionally inadequate. To date we have fed more than 300 BB rats using modified AIN-76 diets with growth rates equal to or better