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NIDDM, non-insulin-dependent diabetes mellitus.

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Response to Giugliano

Dr. Giugliano's work is an interesting contribution to the literature on combination therapy, a combination withdrawal study. As we noted in our review, some patients in almost all of the studies respond much better than the average patient to combination therapy. The problem is finding identifying characteristics for prediction of that response. The current work suggests that a parallel group is present who deteriorate to a greater degree when sulfonylurea is withdrawn.

We disagree with Dr. Giugliano about what is scientifically known regarding the best therapy for NIDDM. Although we hope the ongoing United Kingdom Study will help in this regard, human experiments have not made clear whether low dose insulin is preferable to sulfonylurea or whether combination therapy is preferable to high dose insulin (>1 U $\cdot$ kg^{-1} $\cdot$ day^{-1} as defined by Dr. Giugliano) in prevention of complications if the same degree of glycemic control is achieved. We do agree that combination therapy is worth a try in individual patients on large doses of insulin with poor glycemic control. If minimal response is seen, the sulfonylurea can be withdrawn.

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NIDDM, non-insulin-dependent diabetes mellitus.

Measurement of Subcutaneous Glucose Concentration

Influence of the method on the result

In 1992, Schmidt et al. (1) used a microdialysis-based enzyme sensor, calibrated in vitro, for the estimation of the subcutaneous glucose concentration and recently extended their investigations using the same sensor technique and two additional methods: subcutaneous filtrate collection and an equilibration method using ultrafiltration (2). The subcutaneous glucose concentration appeared to be 44–46% of the corresponding blood glucose.

We have some concerns about the methods used for estimating subcutaneous glucose concentration. From microdialysis studies in the brain, it is known that the recovery of the microdialysis (=dialysate concentration of a substance/concentration in the undisturbed surrounding) is considerably lower in vivo than in vitro (3), because the mass transport of substances in the tissue differs from the situation in aqueous solutions. According to Bungay et al. (4), the recovery in vivo is considerably lower because of local drainage of the analyte leading to a concentration gradient in the surrounding of the microdialysis probe. The theoretical predictions have been verified in practice (3,5). Similar results were obtained by Benveniste et al. (6)—theoretically and practically—using a different mathematical approach.

Considering the theory of microdialysis, the subcutaneous glucose concentration might be underestimated when measured by a microdialysis-based glucose sensor, calibrated in vitro. The ultrafiltration technique removes glucose from the subcutaneous space, and thereby local drainage occurs, leading to underestimation of the subcutaneous glucose concentration. This view is supported, because the volume of the ultrafiltrate decreased and reached a constant level of 40 μl after 6 h (1).

The divergent results of Schmidt et al. (7) compared with the wick technique cannot be attributed to contamination of the wicks with blood, because wicks stained with blood were not used to measure the glucose concentration. On the other hand, implanting the wicks

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