COMMENTS AND RESPONSES

Response to Comment on: Riddle et al. Contributions of Basal and Postprandial Hyperglycemia Over a Wide Range of A1C Levels Before and After Treatment Intensification in Type 2 Diabetes. Diabetes Care 2011; 34:2508–2514

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We thank Monnier (1) for his interest in and comments on our article (2). We believe his original work on the relationships between fasting and postprandial hyperglycemia has opened discussion on various important questions, both physiological and clinical (3). In our present analysis, we aimed to extend this work by addressing two of the clinical questions in a larger population than has previously been studied (2). These were *1*) In a common clinical setting, when oral therapy is no longer successful in keeping A1C below 7%, which form of hyperglycemia is quantitatively most prominent? *2*) How does intensification of treatment affect hyperglycemic patterns? Our results show that in this population of patients basal hyperglycemia is by far the main contributor independent of the A1C range at baseline and that intensification of treatment greatly alters the relative contributions from basal and postprandial hyperglycemia. Moreover, the way treatment is intensified affects the patterns seen after intervention. Because treatment intensification usually employs agents (such as basal insulin) that mainly improve basal glycemia, it is not surprising that residual postprandial hyperglycemia is more evident when A1C is lower after intervention. However, other questions remain. Regarding Monnier's concern about how best to calculate the contribution from postprandial increments, we believe an important way our methods differed from those in other studies was that, in keeping with the American Diabetes Association's stance, we assumed fasting values higher than 100 mg/dL were abnormal rather than considering values up to 110 mg/dL as normal (4). By doing this, we avoided underestimating the contribution from basal hyperglycemia. Over 24 h, this difference in basal glycemic exposure of tissues is not trivial and, most importantly, potentially correctible. Another question of interest concerns patterns of hyperglycemic exposure in patients who are early in the natural history of type 2 diabetes—before pharmacological treatment is started and when A1C is below 7%—for whom postprandial hyperglycemia has been proposed to precede fasting elevations (5). Unlike Monnier's earlier studies, our study did not include such individuals, and we found fasting and postprandial hyperglycemia increased nearly in parallel at rising A1C levels above 7%. We agree that future studies using continuous glucose monitoring will help us to get beyond debates about calculating glycemic exposure from self-measured profiles and to define patterns in untreated persons early in the course of type 2 diabetes. Despite the unanswered questions, we believe our findings provide specific clinical guidance that was not provided by the earlier reports from smaller and heterogeneous populations. Clinicians can assume that when A1C is above 7% on oral therapy, basal hyperglycemia is the main contributor, and the relative contribution of basal versus postprandial hyperglycemia after treatment is intensified will be determined more by the main effects of the treatments used than by the level of A1C achieved. We also agree that careful attention to both basal and postprandial abnormalities, including the use of newer therapies, will often be needed to achieve glycemic goals.

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