COMMENTS AND RESPONSES

Comment on: Chen et al. Utilizing the Second-Meal Effect in Type 2 Diabetes: Practical Use of a Soya-Yogurt Snack. Diabetes Care 2010;33: 2552–2554

Chen et al. (1) recently reported that a high protein, low carbohydrate "snack" taken 2 h before breakfast leads to a reduction in the postbreakfast glycemic excursion of some 40% in patients with well-controlled type 2 diabetes. The suggested mechanism was suppression of plasma free fatty acids, with a concomitant increase in the storage of glycogen in muscle. We agree that the dramatic improvement in postprandial glycemia following a protein "preload" has substantial implications for the dietary management of type 2 diabetes, but take issue with the authors' assertion that this is the first time that such an effect has been demonstrated, and wish to draw attention to other mechanisms that are likely to contribute to this phenomenon.

We reported in *Diabetes Care* in 2009 that 55 g whey protein, when consumed in soup 30 min before a high-carbohydrate mashed potato meal, markedly reduced the glycemic response in type 2 diabetic patients (2). This was associated with the stimulation of gut hormones, including glucagon-like peptide 1 (GLP-1) and cholecystokinin as well as insulin, in advance of the meal and slowing of gastric emptying. We attributed the increase in insulin secretion after whey, at least in part, to reflect direct pancreatic stimulation by absorbed amino acids.

The central role of the gastrointestinal tract, particularly gastric emptying and the secretion of the incretin hormones GLP-1 and glucose-dependent insulinotropic polypeptide in determining postprandial glycemia has often been neglected (3), although it has recently achieved increasing prominence with the availability of pharmacological therapies for type 2 diabetes that appear to act predominantly by modifying gut function, including GLP-1 analogs (4) and the amylin analog, pramlintide. The relative contribution of the various factors in determining postprandial glycemia is likely to vary with the composition of the "preload" and the timing of its administration. For example, the effects of a fat "preload" on postprandial glycemia in type 2 diabetic patients differ substantially from those of protein (5). Gastric emptying is now well recognized as a major determinant of postprandial glycemia, particularly the initial rise in glucose, and usually occurs at a closely regulated overall rate of about 1–4 kcal/min in health, but is often abnormally delayed in long-standing diabetes (3). Moreover, acute changes in the blood glucose per se influence the rate of gastric emptying (3). Although the energy content of the "snack" used in the study by Chen et al. (1) was not specified, given that it comprised 30 g soya beans and 75 g yoghurt, we assume that emptying would not have been complete at the time of ingestion of breakfast and, accordingly, phenomena that result from nutrient-gut interactions, including peptide secretion, would still have been active. Only by evaluating the potentially relevant mechanisms simultaneously, including gastrointestinal peptide responses and gastric emptying, will it be possible to understand and then refine the "preload" concept on a rational basis.

Christopher K. Rayner, mbbs, phd
Jing Ma, md, phd
Karen L. Jones, phd
Michael Horowitz, mbbs, phd

From the Discipline of Medicine, University of Adelaide, Royal Adelaide Hospital, Adelaide, Australia, and the Centre of Clinical Research Excellence in Nutritional Physiology, Interventions and Outcomes, University of Adelaide, Adelaide, Australia.

Corresponding author: Christopher K. Rayner, chris.rayner@adelaide.edu.au.

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