

2. Yuen KC, Day JL, Flannagan DW, Rayman G: Diabetic neuropathic cachexia and acute bilateral cataract formation following rapid glycaemic control in a newly diagnosed type 1 diabetic patient. *Diabet Med* 18:854–857, 2001
3. Kihara M, Zollman PJ, Smithson IL, Lagerlund TD, Low PA: Hypoxic effect of exogenous insulin on normal and diabetic peripheral nerve. *Am J Physiol* 266:E980–E985, 1994

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## COMMENTS AND RESPONSES

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### **Influence of Glycemic Index/Load on Glycemic Response, Appetite, and Food Intake in Healthy Humans**

Response to Alfenas and Mattes

In their recent article, Alfenas and Mattes (1) conclude that the glycemic index values of individual foods do not predict glycemic response to mixed meals, nor influence measures of hunger. Because the observed glycemic response did not differ between diets, the lack of effect on appetite is not surprising. Thus, the potentially important aspect of the study pertains to the prediction of glycemic index in mixed meals.

The authors' approach was to validate published glycemic index values in a pretest, selecting 48 of 79 foods with consistent glycemic responses. However, their methods do not conform to standard procedures (2–4). Only 3 subjects were used for each food instead of the recommended minimum number of 10 (3). Blood glucose was measured by glucometer, a device that is not sufficiently accurate in the normal range for research purposes (4). With such a small subject number, CIs around the mean would likely overlap for most foods on both diets. From a statistical perspective, the selection of foods with an underpowered pretest using inaccurate methods would produce regression to the mean.

It is important to emphasize that published values for specific foods cannot be used for a study such as this without careful validation because published values

may not have been determined correctly, the composition or manufacturing procedures of individual products may change over time, and shelf life and preparatory methods may also affect glycemic index. Such concerns are not unique to studies of glycemic index. One cannot assume, for example, that a published value for vitamin C content of Valencia orange will apply to every piece of fruit, at all times of year, from any location.

Major categories of food differ in glycemic index with reasonable consistency; most fruits, legumes, minimally processed grain products, and pasta prepared from hard wheat have low- to moderate-glycemic index, whereas highly processed grains products and pasta previously prepared and canned have a high-glycemic index. Most of the foods used by Alfenas and Mattes for the low-glycemic index diet included highly processed grain products (quick pizza, quiche, pita, bagel, etc.).

There are many studies demonstrating that the glycemic index of individual foods predicts a response to mixed meals when appropriate methodology is utilized (5–7). With regard to the authors' description of our study, two of the test meals did have identical macronutrient composition and solid food components, and the measured glycemic response corresponded closely with prediction (8).

Clearly, research into the relationship between glycemic index and glycemic response merits study. To advance the dialogue, adequately powered studies employing accepted methodology will be needed. A more fundamental question is whether diets comprised of low-glycemic index foods improve important clinical end points related to obesity, diabetes, heart disease, and cancer.

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#### References

1. Alfenas RCG, Mattes RD: Influence of glycemic index/load on glycemic response, appetite, and food intake in healthy humans. *Diabetes Care* 28:2123–2129, 2005
2. Wolever TM, Vorster HH, Bjorck I, Brand-Miller J, Brighenti F, Mann JI, Ramdath DD, Granfeldt Y, Holt S, Perry TL,

Venter C, Xiaomei Wu: Determination of the glycaemic index of foods: interlaboratory study. *Eur J Clin Nutr* 57:475–482, 2003

3. Brouns F, Bjorck I, Frayn KN, Gibbs AL, Lang V, Slama G, Wolever TMS: Glycaemic index methodology. *Nutr Res Rev* 18: 145–171, 2005
4. Velangi A, Fernandes G, Wolever TM: Evaluation of a glucose meter for determining the glycemic response of foods. *Clin Chim Acta* 356:191–198, 2005
5. Wolever TM, Bolognesi C: Prediction of glucose and insulin responses of normal subjects after consuming mixed meals varying in energy, protein, fat, carbohydrate and glycemic index. *J Nutr* 126: 2807–2812, 1996
6. Chew I, Brand JC, Thorburn AW, Trusswell AS: Application of glycemic index to mixed meals. *Am J Clin Nutr* 47:53–56, 1988
7. Bornet FR, Costagliola D, Rizkalla SW, Blayo A, Fontvieille AM, Haardt MJ, Letanoux M, Tchobrousky G, Slama G: Insulinemic and glycemic indexes of six starch-rich foods taken alone and in mixed meal by type 2 diabetics. *Am J Clin Nutr* 45:588–595, 1987
8. Ludwig DS, Majzoub JA, Al-Zahrani A, Dallal G, Blanco I, Roberts SB: High glycemic index foods, overeating, and obesity. *Pediatrics* 103: e26, 1999

### **Influence of Glycemic Index/Load on Glycemic Response, Appetite, and Food Intake in Healthy Humans**

Response to Alfenas and Mattes

Recently, Alfenas and Mattes (1) concluded that the differential glycemic responses of foods tested in isolation are not preserved under conditions of chronic ad libitum consumption of mixed meals (1). This conclusion is unwarranted because of serious methodological problems that undermine the validity of their results.

Foods were classified as low- or high-glycemic index by the investigators; the glycemic index of each food was determined in three subjects by measuring glucose four times with a glucose meter and discarding means with inconsistent values. Since white bread was used as the reference, all glycemic index values discussed here are adjusted accordingly. We commend the authors for wanting to mea-