other surrogates and are comparable to those of clamp (6). Finally, changes in QUICKI after therapeutic interventions are significantly correlated with changes in \( S_{\text{clamp}} \) (5, 7, 8), whereas changes in \( S_{\text{AM}} \) are unrelated (5). A metaanalysis of insulin-resistant subjects demonstrates that QUICKI is the best fasting surrogate index for predicting onset of diabetes (9). Thus, discordance between QUICKI and \( S_{\text{AM}} \) likely reflects problems with the minimal model rather than QUICKI. Others find excellent correlations between QUICKI and glucose clamp in normal, obese, and diabetic populations (6–8, 10, 11). Previous studies of peripubertal children have validated QUICKI against the glucose clamp in populations similar to that studied by Brandou et al. (12, 13).

Brandou et al. (1) inaccurately use the term “accuracy.” An “accurate” surrogate reflects the true value of the variable being measured. Brandou et al. examine only correlations. When we evaluated the accuracy of QUICKI to predict insulin sensitivity determined by glucose clamp (14), we found that it is much more accurate than \( S_{\text{AM}} \). In summary, finding that QUICKI and \( S_{\text{AM}} \) do not correlate well has been documented previously. However, the conclusion that QUICKI has limited accuracy in peripubertal children is incorrect. If anything, Brandou et al. (1) provide confirmation of the limited utility of the minimal model for assessing insulin sensitivity.

Rajaram J. Karne, Hui Chen, Gail Sullivan, and Michael J. Quon

Diabetes Unit
National Center for Comprehensive and Alternative Medicine
National Institutes of Health
Bethesda, Maryland 20892

References


doi: 10.1210/jc.2005-0528

Authors’ Response: Limited Accuracy of Surrogates of Insulin Resistance during Puberty in Obese and Lean Children at Risk for Altered Glucoregulation

To the editor:

In response to the comments of Karne et al. (1), the purpose of our study (2) was not to demonstrate that quantitative insulin sensitivity check index (QUICKI) and other surrogates of insulin sensitivity (SI) are meaningless. On the contrary, we have reported their accuracy in adults (3) and proposed a simplified version (SI = 40/Ib) (4).

However, the biologic method is above criticism because the glucose clamp has some methodological limits (5, 6). Actually, none of those methods cited by Karne et al. (1) for the minimal model (MM) has been recognized as a major flaw, and a huge body of literature demonstrates the robustness of this approach (7, 8). The concerns about glucose effectiveness have no influence on SI calculations (9). Our reduced sampling procedure has been validated (10). No serious scientist would easily believe that the MM (which has been extensively investigated and used in studies published in leading journals over the past 25 yr) provides a less accurate measurement than simple indexes based on baseline values.

Despite the statement of Karne et al. (1), SI-MM usually correlates as closely as SI-clamp with all surrogates in adults (11, 12). However, this correlation disappears in certain populations. We do not understand why Karne et al. (1) so angrily dispute the fact, which is evidenced by many investigators (13, 14), that surrogates (including QUICKI) have limits to their validity, as is the case for any physiological model.

It is clear that during puberty insulinemia mirrors SI less closely. It is not appropriate to conclude that our findings are false only because Uwaifo et al. (15) have found a correlation in prepubertal children between QUICKI and SI, as others found in healthy pubertal children (16). Those reports do not mean that similar correlations are to be found in pubertal children at risk of disturbed glucoregulation, in whom the feedback loop between SI and insulinemia is even more disturbed.

QUICKI and homeostasis model assessment can safely be used as predictors of SI in lean and obese sedentary individuals, but in other populations (e.g., diabetics, athletes, individuals with high SI, puberty, etc.), serious concerns have been raised about their use that argue for caution. Our hope is that further study will extend the range of populations in which surrogates can be employed. However, to deny the relevance of studies that point out their limits of validity is probably not the best way to reach this goal. The potential consequences of such a “rigid” position may unfortunately be that surrogates will lose much of their credibility in the near future. Our purpose in this study was just the opposite.

F. Brandou, J. F. Brun, E. Raynaud, and J. Mercier
Equipe d’Accueil EA 701 Physiologie des Interactions
Service Central de Physiologie Clinique
Centre d’Exploration et de Réadaptation des Anomalies du Métabolisme Musculaire (CERAMM)
Centre Hospitalier Universitaire Lapeyronie, 34295 Montpellier Cedex 5, France

References


doi: 10.1210/jc.2005-0649

Letter re: The Biological Variation of Testosterone and Sex Hormone-Binding Globulin (SHBG) in Polycystic Ovarian Syndrome: Implications for SHBG as a Surrogate Marker of Insulin Resistance

To the editor:

We read with great interest the paper by Jayagopal et al. (1) published in 2003 in the Journal for Clinical Endocrinology and Metabolism. In this paper, the authors assess the biological variability of two markers of insulin resistance, the homeostasis model assessment method (HOMA-IR) and the serum concentrations of SHBG. Thereby, fasting blood samples were collected at 4-d intervals on 10 consecutive occasions from 12 overweight patients with the polycystic ovary syndrome (PCOS) and 11 age- and weight-matched healthy controls. The authors found that, in contrast to the HOMA-IR, the infradian individual variation in SHBG was lower in patients with PCOS compared with controls. However, in healthy regularly menstruating controls, we and others

Received April 12, 2005. Address correspondence to: Jardena J. Puder, Division of Endocrinology, Diabetes and Clinical Nutrition, University Hospital Basel, Petersgraben 4, 4031 Basel, Switzerland. E-mail: Puderj@uhbs.ch.

A response to this letter was invited, but the authors of the original article chose not to provide one.