COMMENTS AND RESPONSES

Comment on: Lin et al. Long-Term Changes in Adiposity and Glycemic Control Are Associated With Past Adenovirus Infection. Diabetes Care 2013;36:701–707

The innovative article by Lin et al. (1) raises the possibility that certain infections may modulate not only obesity but also diabetes risk. Obesity is currently regarded as an imbalance between food intake and physical exercise, modulated by endocrine and genetic factors. Nonetheless, evidence is available that environmental infections, and notably adipogenic adenoviruses in humans, are associated with obesity, being causative factors of obesity in animals (1–3). How obesity relates to type 2 diabetes is still a mosaic of information and more comprehensive approaches may help advance effective and cost-effective interventions for both conditions, including more tailored therapy (4). The conjectural model that an improvement in glycemic control via the expansion of adipose tissue, as documented in animal models, is attractive and is the suggested way by which Ad36 may mediate its effect on glycemic control by increasing adiposity (1). Investigations into the pathogenesis of these and others coexistent conditions are needed and more focus to neglected or novel roads should be the challenge of translational and clinical research.

Since major contributors to insulin resistance are excess food intake, genetic predisposition, and physical inactivity, we used insulin resistance as a boundary in our case records (3,5) for investigating if the link with obesity (BMI >30 kg/m^2) was differently associated with lone Ad36 seropositivity. In nondiabetic subjects with insulin resistance (n = 100), defined as homeostasis model assessment >1.7, Ad36 seropositivity has a greater risk of obesity (odds ratio 1.547 [95% CI 0.692–3.462]) in comparison with Ad36 seropositive subjects without insulin resistance (n = 79; odds ratio 0.539 [95% CI 0.061–4.798]). The two groups (outpatients assessed for nutritional counseling) were not different for age, sex, and physical exercise level, and these effects were seemingly independent from the quality of nutritional profile, defined by adherence to Mediterranean diet score, which is used as a proxy of healthy nutrition (5). Many questions remain to be answered: the effects of Ad36 directly on hepatic glucose metabolism and hepatic glucose output, fatty acid synthesis and triglycerides formation within the liver, and the interplay of competing cytokines within the liver.

In humans, Ad36 increases adiposity and attenuates deterioration of glycemic control (1), and we observed a possible beneficial metabolic effect of Ad36 seropositivity, seemingly facilitating weight and fatty liver loss by dietary intervention in obesity (5). This is a further challenge to the concept of systematic unfavorable effects of all virus infections on the liver and other body organs. Human microbiome cannot be considered just the gut bacterial milieu, but it is the totality of microbes and their genetic elements and environmental interactions within an individual in all the organs and systems. The novel study of Lin et al. (1) empowers and supports the concept that a more comprehensive model of microbiome should be considered, including viruses and past virus infection effects. This field of clinical research deserves a greater integration of knowledge regarding the link of metabolic and nutritional disease and the relationship of adipocytes and hepatocytes with the microbiome.

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