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COMMENTS AND  
RESPONSES

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**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**

We read with great interest the article by Lin et al. (1), who performed a cohort study and concluded that Ad36 seropositivity was associated with greater adiposity and less deterioration of glycemic control. They reported that seropositive individuals had a higher percentage of body fat coupled with lower fasting insulin levels. Their results are considered important because of the long follow-up period of the study, and the findings help us gain a better understanding of whether this virus plays a role in the etiology of human obesity and metabolic diseases.

However, their data do not correspond with the results of our latest meta-analysis (2). We performed a meta-analysis of

10 observational studies ( $n = 2,870$ ) from around the world, which demonstrated that Ad36 infection in humans was associated with the risk of obesity and weight gain (an estimated BMI increase of  $3.19 \text{ kg/m}^2$ ). However, we found no significant association for blood glucose, total cholesterol, triglycerides, HDL, waist circumference, and systolic blood pressure.

Ideally, these results should be confirmed in prospective clinical trials, but ethical considerations preclude experimental infection of humans with candidate viruses to unequivocally define their contribution to obesity and metabolic diseases. Accordingly, we cannot exclude the possibility that the association of Ad36 with obesity results from greater susceptibility of obese individuals to infection compared with nonobese individuals (3).

Moreover, we should consider the clinical significance of their findings. Although Lin et al. concluded that Ad36 seropositivity increases adiposity and attenuates the deterioration of glycemic control, most of their analyses were not statistically significant, and the differences in BMI and fasting glucose between the groups were subtle.

Next, the biological mechanism of the relation between Ad36 and obesity or glycemic control is unclear. Ad36 infection is typically cleared after formation of neutralizing antibodies, so Ad36 seropositivity only indicates past exposure, and the virus does not insert its genome into human DNA (unlike retroviruses, etc.).

In our opinion, Ad36 infection might be associated with obesity, but it seems too early to discuss the clinical implications or the development of new approaches for prevention and treatment.

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