

overproduction or not. The further increase in serum IL-5 observed during treatment with mepolizumab has been described in other studies.^{2,9}

In summary, our observation suggests that mepolizumab may represent a novel suitable therapeutic option in refractory CSS. The marked, sustained clinical and biological improvement observed by using mepolizumab also highlights the pivotal role of IL-5 and eosinophils in ANCA-negative CSS, probably underestimated to date. Although further studies are needed to confirm these preliminary data, a new therapeutic approach in CSS based on antieosinophil drugs may be promising.

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Persistent rotavirus vaccine shedding in a new case of severe combined immunodeficiency: A reason to screen

To the Editor:

Rotavirus infections in the United States have decreased as a result of vaccination efforts. Before 2006, when the vaccine was implemented, the burden of disease was high, with approximately 27,000 to 70,000 children under 5 years of age hospitalized with

rotavirus infection and about 20 to 60 reported deaths annually according to the Centers for Disease Control and Prevention and other studies.¹⁻⁵ Since the introduction of vaccination, rotavirus rates in the United States have diminished by more than 50%, translating to the prevention of 48,000 hospitalizations and 30 deaths.^{2,4,5} Studies have also shown a delay in the seasonal onset of the disease by 2 to 4 months.^{4,7} Cost savings to the medical community with the vaccines are estimated to be as much as \$198,000 per life-year.⁸ The question arises, however, as to the unforeseen costs on a population of patients with undiagnosed immune deficiency. In March 2009 there were 2 reported cases by Patel et al⁹ of rotavirus infection from RotaTeq (Merck and Co, Inc, Whitehouse Station, NJ) vaccine strains in unknown cases of SCID (severe combined immune deficiency) with adenosine deaminase deficiency and IL-2 receptor- γ deficiency. Werther et al¹⁰ also recently described a 9-month-old girl with a new diagnosis of unspecified SCID who shed the RotaTeq virus strain for 7.5 months and finally cleared it posttransplant. All 3 of these patients presented with gastrointestinal symptoms and failure to thrive. Vaccine strains were identified by RT-PCR.

The patient reported here is a 5-month-old boy born to non-consanguineous parents who presented with lethargy, dehydration, and failure to thrive. He had developed chronic diarrhea beginning at 2 months of age and had poor weight gain over the month before admission. He had been vaccinated with RotaTeq at 2 and 4 months. Before his admission, a stool sample had grown *Salmonella*. His blood cultures on admission grew *Salmonella* that was promptly treated with antibiotics. Further testing of his stool revealed *Rotavirus* antigen as well as persistent *Salmonella*. A diagnosis of SCID was suspected and then confirmed (T^B NK⁻, IL-2RG mutation). He quickly decompensated after 48 hours of admission with onset of respiratory distress and was diagnosed by bronchoscopy to have *Pneumocystis jirovecii*. A stool sample was assessed by RT-PCR for the genes *VP6* and *NSP1*. They matched the RotaTeq vaccine strain exactly. One month later, he continued to demonstrate rotavirus antigen in his stool. He is currently awaiting stem cell transplant by an unrelated matched donor. RotaTeq virus shedding is expected from 1 to 15 days in 9% after first dose and in 0.3% after the third dose in healthy children.¹¹

This case and the previously reported cases bring into question current vaccination practices. The updated American Academy of Pediatrics guidelines pose vaccination of immunocompromised children as a precaution. They clearly state that immunodeficient children might be at risk for severe or prolonged gastroenteritis.⁸ However, the timing of the vaccination does not allow patients with congenital immune deficiency sufficient time to declare themselves. There is no question about the substantial benefit from the vaccine in reducing morbidity as well as health care costs in the United States for the general population. Risks of the vaccine to immunocompromised hosts do not negate its widespread use, but rather reinforce the need for neonatal screening measures of SCID in particular.

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Cardiorespiratory fitness, adiposity, and incident asthma in adults

To the Editor:

Available large-scale prospective studies on adiposity and asthma used body mass index as an indicator of adiposity.¹ Studies involving more accurate measures of adiposity, such as body fat percentage (BF%), are needed to confirm or contrast body mass index–related results. Cardiorespiratory fitness is a strong predictor of morbidity and mortality,² and the available literature suggests that moderate-high cardiorespiratory fitness reduces many of the health hazards associated with obesity.³ The current study aimed (1) to examine whether cardiorespiratory fitness and/or BF% are associated with subsequent acquisition of asthma in adults, and (2) to test the hypothesis that a high cardiorespiratory fitness level can reduce the risk of incident asthma in individuals with excess adiposity.

To address these issues, we selected 9810 individuals free of asthma at baseline (7712 men) age 20 to 82 years from the Aerobics Center Longitudinal Study.^{2,4} Baseline asthma was reported by the participants using a standardized medical questionnaire. Participants completed a baseline examination⁴ and a follow-up survey by which self-reported physician-diagnosed asthma was identified. The study protocol was approved annually

by the Institutional Review Board of the Cooper Institute. The endpoint was defined as a participant report of a physician diagnosis of asthma. (See this article's [Online Repository](http://www.jacionline.org) at www.jacionline.org for further information about the study sample, design, baseline examination and ascertainment of asthma.)

Cardiorespiratory fitness was defined as the total time of a symptom-limited maximal treadmill exercise test by using a modified Balke protocol.⁴ Low fitness, moderate fitness, and high fitness were defined as the lowest 20%, the next 40%, and the remaining 40% of individuals in each age-specific and sex-specific distribution of treadmill time. BF% was assessed with hydrostatic weighing, with the sum of 7 skinfold measures, or with both assessments, following standardized protocols.⁵ On the basis of the standard clinical definitions, overfat was defined as having a BF% $\geq 25\%$ in men and $\geq 30\%$ in women.

Information on smoking (never smoker, exsmoker, and current smoker), leisure time physical activity (physically inactive or active), and respiratory symptoms was obtained from a standardized medical questionnaire. A respiratory symptoms index was defined as the presence of 1 or more of the following respiratory symptoms: chronic cough or phlegm, tuberculosis, bronchitis, pneumonia, emphysema, coughed up blood, or unexplained shortness of breath while sleeping, sitting, or exercising. Participants had complete and valid data for all the study variables mentioned. Pulmonary function assessment was carried out in a subset of the participants (86% of the total study sample), and FEV₁ was obtained with a Collins 421 Survey spirometer (Collins, Mass). Hankinson et al⁶ predictive equations for FEV₁ specific for sex, age, and height and derived from healthy National Health and Nutrition Examination Survey (NHANES) III participants were used.

Associations of cardiorespiratory fitness and BF% at baseline with incident asthma, after adjustment for a set of confounders (ie, age, sex, height, physical activity, smoking, and respiratory symptom index) were analyzed by binary logistic regression. Interaction terms for sex were entered into the logistic regression models. No significant sex interaction was found in the associations between the exposures and the outcome. We find that cardiorespiratory fitness reduces some of the health hazards associated with obesity.³ To test this hypothesis for asthma, the associations between cardiorespiratory fitness and asthma were analyzed in the subset of overfat individuals after adjusting for the confounders. Finally, the main logistic regression models were also adjusted for FEV₁ to examine how pulmonary function could affect the associations of fitness and fatness with asthma. The analyses were performed by using SAS (Version 9.1; SAS Institute, Cary, NC). For all analyses, the statistical significance level was 5%.

We found an incidence of asthma of 5% over a mean follow-up period of 11.5 years. Both low cardiorespiratory fitness and high BF% were associated with subsequent acquisition of asthma (Table I). However, whereas BF% was associated with asthma independent of cardiorespiratory fitness, the association between cardiorespiratory fitness and asthma did not persist after adjusting for BF% (Table I). When the association between cardiorespiratory fitness and asthma was also adjusted for FEV₁ (data not shown), it became nonsignificant, suggesting that this association was also mediated by FEV₁. High adiposity remained associated with higher risk of asthma after adjustment for FEV₁ though, suggesting that factors other than pulmonary function may explain this association. Further research on this topic is needed to confirm these findings. (See the [Online Repository](http://www.jacionline.org) for further