As shown in Fig 1, *A*, anti-HRV39 IgE could be detected in all samples to varying degrees. Importantly, this was specific and dose dependent (Fig 1, *B*). Significantly higher levels were found in the serum of subjects with neutralizing antibodies to HRV39 (OD, 0.62-2.95) than in those with no neutralizing antibodies (OD, 0.73-0.99, $P = .026$) or cord blood (OD, 0.43-0.62, $P = .0039$). It is interesting to note that patients with no known exposure to the virus generally had lower OD values than did those with reported exposure (note dotted line in Fig 1, *A*). Whether this is due to cross-reactivity between rhinovirus serotypes or distant exposure is unknown. There was no relationship between atopic status and the presence of HRV39 specific IgE (1.69 ± 0.29 [mean OD $\pm$ SEM] for nonatopic subjects vs 1.41 ± 0.43 for atopic subjects, $P = .60$; in Fig 1, compare triangles [atopic subjects] and circles [nonatopic subjects]). As shown in Fig 1, *B* (right panel), the ELISA is specific for HRV39 because the addition of HRV39 to subject's serum significantly inhibited binding to the level seen in subjects without an exposure history. We believe that OD values above 1.5 represent the presence of anti-HRV39 IgE, while those between 1.5 and 1.0 are indeterminate, and those below 1.0 indicate no evidence of anti-HRV39 IgE. Importantly, total IgE levels did not correlate with anti-HRV39 specific IgE (Fig 1, *C*, Pearson $P > .05$).

To our knowledge, this study is the first to show that IgE antibodies against rhinovirus (at least a laboratory strain) can be found in the sera of human subjects who have been exposed to that serotype, and adds to a growing body of evidence supporting a role for antiviral IgE as part of the natural antiviral immune response. It is important to stress that these data alone do not support the hypothesis that antiviral IgE is causative in the development of postviral atopic disease, but do begin to provide potential mechanistic explanations for why omalizumab might reduce asthma exacerbations outside of the pollen season. Furthermore, based on our studies in mice, these data support the model in which IgE against a respiratory virus drives the *de novo* development of postviral atopic disease (such as asthma), and provides some tantalizing evidence that the pathways identified in mice might be operative in humans.

These data provide the initial support for further investigations focusing on preexposure/postexposure to HRV (and other respiratory viruses) and the role of antiviral IgE in the immune response to respiratory viruses, as well as the development and exacerbation of atopic diseases. We acknowledge the limitation of the small sample size, as well as the issue of potential cross-reactivity of anti-HRV39 IgE with other HRV strains. It is interesting to note that anti–HIV-1 IgE has been shown to inhibit HIV-1 production in infected PBMC cultures.[10] Whether antiviral IgE is a purposeful or maladaptive immune response, it nonetheless appears to contribute to the exacerbation and perhaps development of atopic disease. Taken together, our study helps to shed light on the role viral infections might play in the development and exacerbation of atopic disease, and provides some additional rationale for future studies exploring therapeutic strategies to reduce or prevent the development of atopic disease.

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Deficient glucocorticoid induction of anti-inflammatory genes in nasal polyp fibroblasts of asthmatic patients with and without aspirin intolerance

To the Editor:

Nasal polyposis is a chronic inflammatory disease of the sinunasal mucosa frequently associated with asthma, particularly aspirin-intolerant asthma (AIA).[1] Patients with AIA have the most severe forms of upper and lower airway disease. Intranasal glucocorticoids are the first-line therapy for nasal polyposis.[2] Some patients, especially those with AIA, show incomplete response to maximal medical treatment and are submitted to endoscopic surgery. Glucocorticoids, via the glucocorticoid receptor (GR), reduce inflammation by inhibiting the expression of proinflammatory genes and transactivating anti-inflammatory genes, such as the mitogen-activated protein kinase phosphatase-1 (MKP-1), glucocorticoid-induced leucine zipper (GILZ), and tristetraprolin (TTP).[3,4] The objective of this study was to elucidate whether nasal polyp fibroblasts from patients with/without AIA have alterations in the GR signaling pathway that might explain the relative insensitivity of these patients to glucocorticoids.

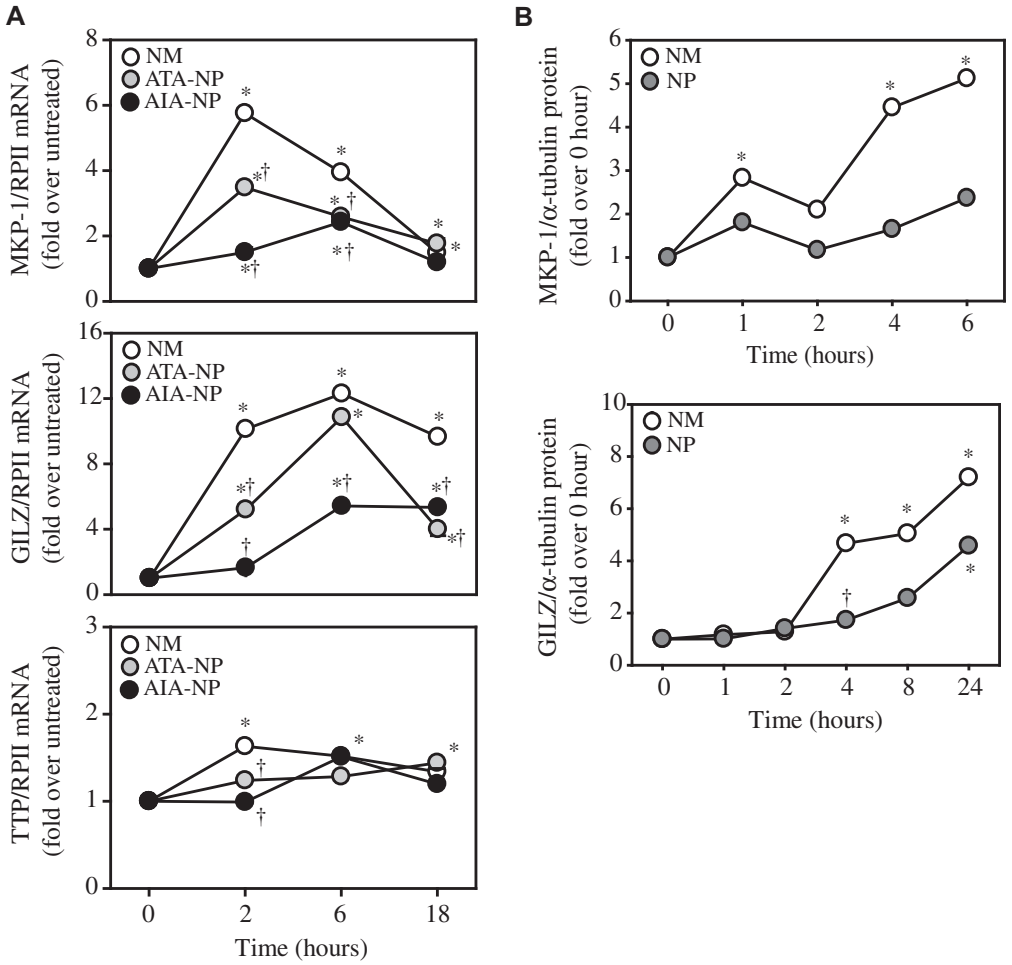

FIG 1. Effect of dexamethasone on MKP-1, GILZ, and TTP expression. **A,** RT-PCR analysis of nasal mucosa (NM; n = 10) and nasal polyp fibroblasts from aspirin-tolerant (ATA-NP; n = 5) and aspirin-intolerant (AIA-NP; n = 7) asthmatic patients. **B,** Immunoblot analysis of nasal mucosa (n = 5) and nasal polyp (NP; n = 5) fibroblasts. Fibroblasts were incubated with dexamethasone (10^{-7} mol/L) for the indicated times. **P* < .05 versus untreated/0 hour. †*P* < .05 versus NM.

Complete details are outlined in this article's Methods section in the Online Repository at www.jacionline.org. Briefly, nasal polyp fibroblasts from patients with aspirin-tolerant asthma (ATA, n = 5) and AIA (n = 7) and control nasal mucosa fibroblasts (n = 10; see clinical characteristics in Table E1 in this article's Online Repository at www.jacionline.org) were isolated and stimulated *in vitro* with dexamethasone. Expression of GRα, GRβ, MKP-1, GILZ, and TTP was analyzed by RT-PCR and immunoblotting, GR nuclear translocation by immunocytochemistry, histone H4 K5 acetylation by immunoblotting, GRα binding to glucocorticoid-responsive elements at the MKP-1 and GILZ promoters by chromatin immunoprecipitation, and IL-8 production by ELISA. Data are given as median and interquartile range unless otherwise specified. Nonparametric statistical analysis was performed by using the Friedman test and the Wilcoxon rank test for within-group comparisons and the Kruskal-Wallis test and the Mann-Whitney *U* test for between-group comparisons. Rho Spearman's analysis was used to assess the correlation between 2 numerical variables. The concentration of dexamethasone that resulted in 50% inhibition (IC_{50}) or stimulation (EC_{50}) of its maximal effect was calculated by using the GraphPad Prism software (GraphPad Software, La Jolla, Calif). Statistical analyses were performed with the SPSS software (IBM SPSS Statistics, Armonk, NY). Statistical significance was set at *P* less than .05.

GRα mRNA levels in nasal fibroblasts were much higher than those of GRβ (cycle threshold [C_T, median], 25.3 for GRα; 37.3 for GRβ). No significant differences in GRα and GRβ mRNA and protein levels were found between nasal mucosa and polyp fibroblasts (see Fig E1 in this article's Online Repository at www.jacionline.org). GRβ was detected in nuclear but not in total cellular protein extracts. GRα showed both nuclear and cytoplasmic localization in the absence of dexamethasone and nuclear localization after dexamethasone treatment (1-3 hours), without significant differences between nasal mucosa and polyp fibroblasts (see Fig E2, *A* and *B*, in this article's Online Repository at www.jacionline.org). Similarly, a marked increase in GRα nuclear levels was detected by immunoblot after incubation of nasal fibroblasts with dexamethasone for 1 hour (see Fig E2, *C* and *D*). GRβ nuclear levels were not altered by dexamethasone treatment.

Nasal polyp fibroblasts expressed higher baseline MKP-1 mRNA levels (without statistical significance for AIA) than did