



Editorial

Atopy and viral infections

Could polyomaviruses be to blame?



Respiratory viruses have been associated with the development of asthma and possibly even allergic disease.¹ Key among these have been respiratory syncytial virus (RSV) and rhinovirus (RV). Both of these viruses have been associated with the development of asthma, whereas RV has been associated with exacerbations of disease. Although these viruses drive development or exacerbation of disease, it is possible that other viruses would be protective of asthma or even other atopic diseases. Perhaps, this might demonstrate a difference between RNA viruses (such as RSV and RV) and DNA viruses (such as herpesviruses and Epstein-Barr virus). Indeed, in the current issue of the *Annals of Allergy, Asthma & Immunology*, Karachaliou et al² have evaluated the linkage between DNA viruses and atopic disease, focusing on childhood eczema, asthma, and allergic rhinitis. Unique to this study was the focus on a relatively newly identified group of small, nonenveloped DNA viruses, the polyomaviruses. These widespread viruses consist of 117 species and have been associated primarily with clinical disease only in those who are immunocompromised.^{3,4} Several of these viruses have skin tropism, and their genomic sequences have been associated with malignancy and autoimmune conditions. In immunocompetent individuals, infection with polyomaviruses is usually asymptomatic, and most children have been infected by these viruses early in life. Until this study, little was known of the association of these ubiquitous viruses and atopic disease.

In this report, the authors used seropositivity (ie, the presence of immunoglobulin G [IgG] against the virus) as evidence of a previous infection. Using this criterion, they found 2 polyomaviruses (KIPyV and HPyV6) associated with protection from eczema at 4 years of age. A similar protection from eczema was found in those children who had Epstein-Barr virus seropositivity. Unlike the case of eczema, evidence of infection with the WUPyV polyomavirus associated with the development of asthma by 4 years of age. Furthermore, the authors noted that there were additional effects with evidence of infection from multiple viruses, and this risk was very much dependent on tissue specificity of the virus. Those with seropositivity to 2 or more skin polyomaviruses had lower odds of developing eczema, whereas those with seropositivity to any respiratory polyomavirus had an increased risk of developing asthma. This risk of asthma further increased with evidence of infection with more than one respiratory polyomavirus.

Together, this study suggests that a viral infection could be protective or detrimental depending on the tissue specificity of the pathogen. The authors raise the question as to whether these effects are due directly to infection by the virus or indirectly through alteration of the microbiome in the target tissue. This is an important distinction, and one that future studies will need to evaluate. In addition, the presence of IgG against a virus does not provide any information on the severity of the initial infection (or the viral load). There remains a question of cross-reactivity between the antiviral IgG and how specific the presence of anti-polyomavirus IgG is for a given species. Finally, there is the question of the “chicken or the egg.” Although the authors suggest that the viruses drive the development or protection from atopic disease, it is quite possible that the opposite is occurring—that the presence of atopy (or lack thereof) makes an individual more susceptible to infection with a given polyomavirus. Perhaps the antiviral immune response is different in those with eczema or asthma compared with those without, and this differential response can be found in the robustness of the IgG antiviral immune response.

These limitations only indicate the need for further investigations into the potential role of polyomaviruses and atopy. Although the authors focused on IgG, it would be interesting to see if the individuals made other antibodies against the viruses and whether they correlated with disease. The production of antiviral IgE has been documented for RNA respiratory viruses, such as RSV and RV.¹ There is evidence that this antiviral IgE can be pathologic, possibly leading to asthma exacerbations, and in a mouse model, antiviral IgE is associated with the development of postviral airway disease.^{5,6} Whether DNA viruses are capable of driving similar antibody responses that could be either pathologic or protective remains to be determined.

Therefore, the study by Karachaliou et al² shines the first beam of light on the potential role of DNA viruses in development of or protection from atopic diseases. Much work remains to better understand this relationship and determine whether this is just a correlative or causative association. Nevertheless, the potential here for novel therapeutics is great—imagine using specific polyomaviruses to prevent the development of eczema or measuring specific IgG to these viruses to gauge the risk of developing eczema or asthma. The role of these unique DNA viruses in understanding allergic disease is just beginning!

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