to the Editor:

We read with great interest the recent publication by Ferstraarou et al.1 in the January 2021 issue of JACI: In Practice that reported type 2 high asthma with eosinophilia is protective against severe coronavirus disease (COVID-19). As the authors note, this protective effect may be due to reduced viral binding and propagation in type 2 high asthmatic airways as the result of downregulated expression of the severe acute respiratory syndrome coronavirus (SARS-CoV-2) receptor, angiotensin-converting enzyme 2 or ACE(2), on airway epithelium. It is notable, however, that many prior studies have reported antiviral and immunomodulatory functions of eosinophils in humans and in animal models, which in light of the present findings, are potentially complementary or alternative mechanisms that explain this effect. Eosinophils express a variety of pattern recognition receptors capable of detecting viral RNA genomes, including Toll-like receptors 3 and 7, RIG-like receptors, and NOD-like receptors.2 Once activated, eosinophils release mediators with direct antiviral activity such as eosinophil cationic protein and eosinophil-derived neurotoxin, whose ribonuclease activity degrades viral RNA genomes, and nitric oxide, which has been shown to reduce infectivity of 2 other RNA respiratory viruses, parainfluenza virus and respiratory syncytial virus.3 Eosinophils also produce TH1-related cytokines involved in antiviral defense, including IFNγ and IL-12, and they express major histocompatibility complex class 1 and 2 molecules that enable antigen presentation and recruitment of viral-specific CD8 T cells to the lung.2

Although much of our mechanistic understanding of eosinophil’s antiviral effects is derived from in vitro studies of human and mouse eosinophils, several experimental observations support the concept that eosinophils are antiviral in vivo as well. For example, mice and guinea pigs with allergen-induced airway eosinophilia have lower titers of parainfluenza virus in the lung 4 days after infection,4,5 and transgenic mice with eosinophilia due to IL-5 overexpression also exhibit accelerated viral clearance.4 In influenza-infected mice, adoptive transfer of eosinophils into airways reduces viral titers,5 whereas double transgenic eosinophil-deficient mice that overexpress IL-5 lack this antiviral response, indicating that eosinophils specifically, not IL-5, mediate the antiviral effect.4 Similarly, in a study of experimental rhinovirus infection in humans, mild asthmatics treated with the anti-IL5 antibody mepolizumab had higher nasal viral titers than placebo-treated individuals, suggesting that eosinophils’ antiviral functions are conserved between animals and humans.6

As both eosinophils and viral infections are important causes of asthma attacks, eosinophil activation in virus-infected airways is likely a double-edged sword capable of causing both harm during asthma exacerbations triggered by seasonal respiratory viruses and protection against serious and fatal infections from pandemic SARS-CoV-2. Indeed, despite a common evolutionary lineage with seasonal coronavirus variants, SARS-CoV-2 and prior SARS, share unique genomic features that account for their immunogenicity. Given that higher SARS-CoV-2 titers are immunogenic. Given that higher SARS-CoV-2 titers are associated with increased mortality,7 eosinophil’s ability to directly and indirectly attenuate viral replication may protect against development of a runaway inflammatory response that underlies the onset of severe COVID-19 disease.

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Protective effects of eosinophils against COVID-19: More than an ACE(2) in the hole?

To the Editor:

We read with great interest the recent publication by Ferstraarou et al.1 in the January 2021 issue of JACI: In Practice that reported type 2 high asthma with eosinophilia is
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The rest of the authors declare that they have no relevant conflicts of interest.

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Reply to “Protective effects of eosinophils against COVID-19: More than an ACE(2) in the hole?”

To the Editor:

We would like to thank Drake et al1 for their valuable comment regarding the antiviral effect of eosinophils, which may explain why patients with type 2 high asthma were protected against severe disease (COVID-19) in our study.2 An important aspect that warrants further investigation is to find a mechanistic explanation for high rates of eosinopenia in hospitalized patients with COVID-19.3 Moreover, it remains to be determined if this is an asthma-specific protective effect or a more generalizable finding extending to other conditions.

We show in our study that patients with asthma with prior eosinophilia are more likely to recover their circulating eosinophils during COVID-19 hospitalization, and these patients had subsequently less risk of dying from SARS-CoV-2 infection.2 Therefore, individuals with type 2 high asthma appear to have the advantage of pre–COVID-19 eosinophilia. However, it is unclear if this is their main tool in fighting against severe COVID-19 disease, or if other characteristics of these patients (eg, prior Th2 cytokine predominance that might influence the cytokine milieu during COVID-19, gender differences, certain medications used for asthma control) are also of importance.

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Patient variability in severity of COVID-19 disease. Main suspect: vascular endothelium

To the Editor:

We read with care and interest the original article from Ballow and Haga1 about the possible explanation for why some...