Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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REFERENCES

1. Ferastraoaru D, Hudes G, Jerschow E, Jariwala S, Karagic M, de Vos G, et al. Eosinophilia in asthma patients is protective against severe COVID-19 illness. J Allergy Clin Immunol Pract 2021;9:1152-62.e3.
2. Lindsley AW, Schwartz JT, Rothenberg ME. Eosinophil responses during COVID-19 infections and coronavirus vaccination. J Allergy Clin Immunol 2020;146:1-7.
3. Adamko DJ, Yost BL, Gleich GJ, Fryer AD, Jacoby DB. Ovalbumin sensitization changes the inflammatory response to subsequent parainfluenza infection. Eosinophils mediate airway hyperresponsiveness, m(2) muscarinic receptor dysfunction, and antiviral effects. J Exp Med 1999;190:1465-78.
4. Drake MG, Bivins-Smith ER, Proskocil BJ, Nie Z, Scott GD, Lee JJ, et al. Human and mouse eosinophils have antiviral activity against parainfluenza virus. Am J Respir Cell Mol Biol 2016;55:387-94.
5. Samarasinghe AE, Melo RC, Duan S, LeMessurier KS, Liedmann S, Surman SL, et al. Eosinophils promote antiviral immunity in mice infected with influenza A virus. J Immunol 2017;198:3214-26.
6. Sabogal Pineros YS, Bal SM, van de Pol MA, Dierdorp BS, Dekker T, Dijkhuis A, et al. Anti-IL-5 in mild asthma alters rhinovirus-induced macrophage, B-cell, and neutrophil responses (MATERIAL). A placebo-controlled, double-blind study. Am J Respir Crit Care Med 2019;199:508-17.
7. Prebensen C, Myhre PL, Jonassen C, Rangberg A, Blomfeldt A, Svensson M, et al. SARS-CoV-2 RNA in plasma is associated with ICU admission and mortality in patients hospitalized with COVID-19 [published online ahead of print September 5, 2020]. Clin Infect Dis. https://doi.org/10.1093/cid/ciaa1338.

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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 al[1] 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[2-4] and more importantly, how to speed the recovery of eosinophil counts to properly exhibit their antiviral effects.

Previous data show that bacterial, viral, and parasitic acute inflammation is associated with the decrease in circulating eosinophils due to egress inhibition from the bone marrow.[5] Eosinopenia in acute inflammation may also result from distribution of eosinophils in the inflamed tissues[5]; however, pulmonary samples from individuals with COVID-19 show a predominant mononuclear inflammatory infiltrate (mostly lymphocytic), without the presence of eosinophils.[6] Although eosinopenia is not unique to severe acute respiratory syndrome coronavirus (SARS-CoV-2), it was shown to be more prevalent in COVID-19 than it is in acute influenza infection.[7] Therefore, other mechanisms, perhaps specific to SARS-CoV-2 infection, may explain these findings. It is possible that differences in the cytokine profile of patients with COVID-19 might influence their circulating eosinophils. For example, among the proinflammatory cytokines that are elevated in patients with severe COVID-19,[8] IFN-γ/TNF-α have been associated with FasL-induced apoptosis of eosinophils.[9] However, it is not understood which patients are prone to severe disease, eosinopenia, or who are those individuals recovering their eosinophils faster and why. It also 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 released during COVID-19, gender differences, certain medications used for asthma control) are also of importance.

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REFERENCES

1. Drake MG, Fryer AD, Jacoby DB. Protective effects of eosinophils against COVID-19: more than an ACE(2) in the hole? J Allergy Clin Immunol Pract 2021;9:2539-40.
2. Ferastraoaru D, Hudes G, Jerschow E, Jariwala S, Karagic M, de Vos G, et al. Eosinophilia in asthma patients is protective against severe COVID-19 illness. J Allergy Clin Immunol Pract 2021;9:1152-62.e3.
3. Xie G, Ding F, Han L, Yin D, Lu H, Zhang M. The role of peripheral blood eosinophil counts in COVID-19 patients. Allergy 2021;76:471-82.
4. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy 2020;75:1730-41.
5. Bass DA. Behavior of eosinophil leukocytes in acute inflammation. II. Eosinophil dynamics during acute inflammation. J Clin Invest 1975;56:870-9.
6. Calabrese F, Pezzuto F, Fortarezza F, Hofman P, Kern I, Panizo A, et al. Pulmonary pathology and COVID-19: lessons from autopsy. The experience of European Pulmonary Pathologists. Virchows Arch 2020;477:359-72.
7. Tanni F, Akker E, Zaman MM, Figueroa N, Tharian B, Hupart KH. Eosinopenia and COVID-19. J Am Osteopath Assoc 2020;120:504-8.
8. Costela-Ruiz VJ, Illescas-Montes R, Puerta-Puerta JM, Ruiz C, Melguizo-Rodríguez L. SARS-CoV-2 infection: the role of cytokines in COVID-19 disease. Cytokine Growth Factor Rev 2020;54:62-75.
9. Luttmann W, Dauer E, Schmidt S, Marx O, Hossfeld M, Matthys H, et al. Effects of interferon-gamma and tumour necrosis factor-alpha on CD95/Fas ligand-mediated apoptosis in human blood eosinophils. Scand J Immunol 2000;51:54-9.

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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 Haga[1] about the possible explanation for why some