The course of COVID-19 is divided into multiple phases relying on the viral load and symptoms that occur over time. Insistent symptoms and long-term problems long than 5 weeks from SARS-CoV-2 infection are defined as long COVID-19.[2] It is estimated that 31% to 69% of patients with SARS-CoV-2 infection will have long COVID-19 symptoms after the initial recovery from SARS-CoV-2 infection.[3] SARS-CoV-2, a respiratory virus, causes pulmonary system dysfunction in long-term COVID-19. SARS-CoV-2 first infects the alveolar epithelium, causing a chronic inflammation response that triggers the constant creation of inflammatory cytokines and reactive oxygen species. In the article, second, fourth, and fifth patients (three of six patients) received a diagnosis of asthma 33, 42, and 27 days, respectively, after SARS-CoV-2 infection. Although long COVID-19 has been described, it is thought-provoking that asthma is diagnosed in these patients within such a short period after COVID-19.[1]

Moreover, FeNO greater than 25 ppb is seen as evidence of type 2 inflammation. It is also found in some types of asthma and nonasthmatic conditions, such as allergic rhinitis and eosinophilic bronchitis. In the article,[1] FeNO greater than 20 ppb is considered positive, and this value is incompatible with the literature. For healthy adults, the upper limit of normal values is 39 to 88 ppb.[4] In addition, although a decrease in FeNO level is expected after asthma treatment, the increase in FeNO level after treatment in the fourth and fifth patients is thought-provoking. Unexpectedly, although the fourth patient was also a smoker with asthma, the FENO value was not low before and after treatment, but increased after treatment. It is unclear whether FeNO has clinical value in subjects with asthma who smoke.[5]

Also, methacholine provocation testing is considered positive when the PC_{20} FEV_1 is 8 mg/mL or less. Although the test was accepted as positive in the cases of the fourth and sixth patients in the study, the PC_{20} FEV_1 value was above 8 mg/mL.[6]

Furthermore, although it is well-known that asthmatic cough is typically and familiarly a dry cough, unexpectedly all six patients in that study appeared to have sputum.

In one patient in the article, the total IgE level was over 100 IU/mL, which was stated as high. However, it is normal for the total IgE level to be over 100 IU/mL in adulthood. Some sources accept an upper limit of 214 IU/mL.[7]

Finally, the term COVID-19 infection is often used in the article, but the correct term should be SARS-COV-2 infection. If COVID-19 needs to be specified, it should be called a disease.

Clarification of these issues will benefit the reader and lead to a better understanding of the article and its contribution to the literature.

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Reply to "New-onset asthma development in adults after COVID-19 disease"

To the Editor:

We appreciate the opportunity to respond to the concerns raised by Dikici et al[1] regarding our recently published study on the evaluation of new-onset asthma after COVID-19 in adults.[2] Dikici et al raised seven concerns about the diagnostic procedures for cases identified as involving newly developed asthma and the normal values of the tests.

The first concern regards the negative bronchodilator response in all patients. According to the Global Initiative for Asthma (GINA) report,[3] patients suspected as having asthma but who are negative for a bronchodilator response can receive the diagnosis of asthma if they are positive for a provocation test or have documented excessive variability in lung function. All patients met the diagnostic criteria for asthma recommended by the GINA report.

Regarding the second concern about the relatively short duration from SARS-CoV-2 infection to an asthma diagnosis, we suggest that asthma-like symptoms can develop shortly after viral infection. A study showed that a considerable proportion of children developed asthma-like symptoms within two months after human metapneumovirus infection (see Figure 1, *A* in the publication by Coverstone et al).[4]

The third and fourth concerns were about the normal range of FeNO and methacholine concentration (provocation concentration), respectively, causing a 20% decrease in FEV_1 (PC_{20}). In our institution, we define a low FeNO level as that less than 20 ppb based on the GINA recommendation that FeNO of 20 ppb or greater is indicative of type 2 inflammation. We also noted the absence of a decrease in FeNO level after treatment in two cases (numbers 4 and 5). However, FeNO may not change in some patients, as shown in a study by Haldar et al.[5] The authors also questioned the clinical value of FeNO in patients with asthma who smoke, by referring to an article.[6] However, that article mentioned that "FeNO may be useful in detecting eosinophilic airway inflammation and in diagnosing asthma in smoking subjects." This suggests FeNO has a clinical role in subjects with asthma who smoke. Regarding the positive PC_{20} value, the European Respiratory Society guideline categorized airway response to methacholine as normal (>16 mg/mL), borderline airway hyperresponsiveness (4-16), and mild to marked airway hyperresponsiveness (<4).[7] Thus, the two

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patients in our study (numbers 4 and 6) can be considered to be positive for provocation.

The fifth concern was about the nature of cough in asthma. Although the authors insisted that cough in asthma is typically dry, a considerable proportion of patients with asthma can have sputum production, especially when the disease is severe.[8] Also, sputum production in chronic cough may suggest asthma.[9]

The sixth concern was about the normal range of total IgE levels. Classically, a serum IgE value above 100 IU/mL has been used to indicate positive results.[10] Accordingly, we used 100 IU/mL as the cutoff for the total IgE level.

Finally, Dikici et al kindly mentioned that COVID-19 infection is not a correct term. We agree with them that it should be described as COVID-19 instead of COVID-19 infection. We appreciate their comments.

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