Asthma in the Time of COVID-19

During the last 15 months, all human activity has been profoundly affected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. The great urgency to tackle the enormous scientific challenges created by the pandemic has been reflected in the large number of manuscripts on the epidemiology, pathogenesis, and treatment of coronavirus disease (COVID-19) that the *Journal* has published during those months. The Editors are keenly aware, however, that the threat to the health and well-being of the population from other major illnesses has not disappeared and requires the continued attention of the scientific community. On the basis of that understanding, we called for submissions for this special asthma issue, and we received a large number of meritorious papers. We selected eight original contributions and two perspectives that span the whole gamut of asthma research today worldwide, from basic molecular mechanisms to applied clinical investigations, demonstrating the high quality of the research still being done despite all the barriers erected by COVID-19's devastating effects on public health.

We still could not ignore the pandemic and its sequelae. It is well established by now that the presence of chronic comorbidities such as chronic obstructive pulmonary disease, obesity, and hypertension increase the risk of developing severe COVID-19, but its relation with asthma remains controversial. In this special issue, we publish a large meta-analysis assessing this association (1), which is reviewed in more detail in a separate editorial. The most important conclusion from that study is that the course of COVID-19 is less severe in patients with asthma as compared with patients without asthma even after adjusting for known potential confounders. Similar results had been reported before (2), and the consistency of the evidence suggests that we are in the face of a surprising paradox: how is it possible that a disease that is known to be associated with increased susceptibility to a wide variety of viruses (including coronaviruses) (3) may decrease the severity of one of the most lethal respiratory viruses ever encountered by humanity? It is certainly possible that type 2 inflammation may interfere with the receptor system for SARS-CoV-2 (4) and that therapy with inhaled corticosteroids may decrease susceptibility to COVID-19 (5), but the issue is far from settled. Nevertheless, people with mild asthma have already been excluded from early vaccination against COVID-19 in the United Kingdom, and this has created anxiety and controversy (6).

The paradox of a potential decreased susceptibility to severe COVID-19 in asthma is made even more evident by the concomitant observation of a remarkable reduction in asthma exacerbations requiring emergency department (ED) visits among children and young adults. At the Children's Hospital of Philadelphia, the mean number of daily ED visits for asthma between January 1 and March 18, 2020, was 24.3. After local authorities implemented a city-wide stay at home order on March 19, the daily mean during the subsequent month dropped to 5.8, 76% lower than the pre–COVID-19 period and to that observed during the same week the previous year (7). Similarly, at Boston Children's Hospital, an 82% decrease in ED visits for asthma was observed between March and May 2020 as compared with the same period during the previous 2 years (8). These changes took place while concomitantly there was a sharp decline in influenza circulation, which occurred within 2 weeks of the COVID-19 emergency declaration on March 1, 2020, and widespread implementation of community mitigation measures in the United States (9). It is plausible to surmise that these measures, aimed at decreasing the transmission of SARS-CoV2, also dramatically decreased infection rates for all other respiratory viruses, which are a known major cause of asthma exacerbations in children. Similar drops in exacerbation rates have been reported for cystic fibrosis (10) and for chronic obstructive pulmonary disease and adult asthma (11), although in the latter two cases, reductions (approximately one-third fewer hospital admissions/wk) were less striking than those for childhood asthma. It is likely that many factors contributed to these changes, including safety concerns refraining patients from seeking health care, but the fact that they occurred concurrently with dramatic decreases in circulation of respiratory viruses gives credence to a causal relation between these two trends. A potential silver lining related to this pandemic could thus be the prospect that mitigation strategies, such as the use of well-fitted facemasks, could be tested in the future to prevent exacerbations in patients with severe asthma.

Still, the pandemic is hitting patients with asthma in other, more subtle ways. Apart from the fact that they (or their loved ones) may have had to suffer the effects of a threatening infection, with consequent increased stress and anxiety, emerging evidence suggests that the pandemic has decreased the opportunity for patients to exercise and socialize (12). It is likely that enhanced sedentariness will generate weight gain, with the consequent aggravation of asthma symptoms. In the case of young children, contact with their peers in daycares and other settings increase exposure to environmental microbes that have been shown to decrease asthma risk (13). Home confinement may thus have had positive short-term effects, but in the long run, living in face communication with others is the best way to foster mental and respiratory health.

In summary, the SARS-CoV-2 pandemic has greatly tested healthcare systems and the scientific community. This issue of the *Journal* proves that, those challenges notwithstanding, asthma research continues to provide innovative insights into the pathogenesis and treatment of this complex disease. ■

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A, B, and C Rhinoviruses: New Knowledge from an Impressive Consortium

A Step Forward for Rhinovirus Vaccine Efforts or a Step Back?

Rhinovirus (RV) infections cause asymptomatic infections, wheezing, and nonwheezing lower respiratory tract infections in young children (1) and the majority of acute attacks of asthma (2) and chronic obstructive pulmonary disease (3), resulting in substantial morbidity and deaths. There are 157 numbered RVs, which are divided into A, B, and C species based on sequence homology (4). One hundred RV-As and RV-Bs have been serotyped, and most do not crossneutralize (5). Studies with RV-Cs have been prevented by difficulties growing these viruses, but given the sequence divergence between A/B and C strains, it is unlikely the 51 numbered C strains will crossneutralize. The need for >150 strains in RV vaccines has hampered vaccine development. However, if certain RVs were more common causes of severe disease, could vaccine efforts be focused on these RVs to help move vaccine development forward?

RV-Bs are less likely to cause severe illness in children than RV-A or RV-C (1). However, data on RV-A/Cs and severe respiratory illnesses are not consistent, as studies in children have reported more RV-Cs than RV-As (6), whereas studies in adults reported more RV-As than RV-Cs (7).

In this issue of the *Journal*, Choi and colleagues (pp. 822–830) have made significant progress in understanding the importance of different RV species and strains in respiratory illnesses in children (8). They analyzed nasal and plasma samples from birth to age 18 in the COAST (Childhood Origins of ASThma) study, which studied 289 children from Madison, Wisconsin, at birth, 210 of whom were followed to age 18. They partially sequenced >8,000 RV-positive samples from asymptomatic and illness visits to compare RV-A and RV-C frequencies at ages 0–3, 4–8, 9–13, and 14–18 and found that RV-A and RV-C were similarly common at ages 0–3, but thereafter, RV-A was approximately twice as

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