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.

This case reveals a previously undescribed delayed hypersensitivity to the Comirnaty COVID-19 vaccine presenting with pneumonitis and a fixed rash. Although other causes for the patient's presentation were considered, the lack of microbiological findings on bronchial fluid and minimal response to antibiotic therapy supported an inflammatory rather than infective cause, and no evidence of malignancy was subsequently found. Although positive delayed skin testing reactions can indicate a normal cellular immune response to mRNA COVID-19 vaccines,[4] the profound intradermal reaction seen in our patient, in addition to morphologic similarities to the original rash and skin biopsy findings supported vaccine-related hypersensitivity.

Vaccine-related pneumonitis has been reported after influenza vaccination and is thought to occur due to immune-mediated lung injury with demonstrated vaccine dependent in vitro proliferation of lymphocytes.[5] Meanwhile, respiratory complications after other vaccines, including COVID-19 vaccines, are not well described. To date, there has been 1 report of pulmonary nodules after mRNA-1273 vaccination but these were not glucose avid on positron emission tomography and hence likely benign,[6] although a case of acute respiratory distress syndrome has been recently reported.[7]

In contrast, delayed cutaneous local reactions at injection sites, coined "COVID arm," occur in up to 1% of recipients of mRNA COVID-19 vaccines.[8] Distant and generalized cutaneous reactions, including urticaria and morbilliform rashes, have also been described more recently. These typically occur up to 1 week after first dose or 2 to 4 days after the second dose, consistent with our patient's rash.[9]

Although vaccine-specific lymphocyte responses could not be performed in our patient, the intradermal testing and histopathologic features on skin biopsy support a possible T-cell–mediated mechanism. Unlike most of the delayed localized cutaneous reactions, our patient's presentation occurred after the second dose of the vaccine, but this phenomenon is well described in delayed drug hypersensitivity, and it is established that cellular responses are greater after the second vaccine dose.[10] The mechanism by which reactive lymphocytes may be generated remains unclear, but immediate and delayed skin testing to polyethylene glycol (PEG 3350), one of the excipients in the Comirnaty vaccine, was negative at several concentrations. This suggests that the process was possibly driven by other components, including the lipid-based nanoparticle carrier. We therefore recommended that our patient avoid all mRNA COVID-19 vaccines but can receive non–mRNA-based vaccines, when booster doses are required.

In summary, we describe a unique presentation of delayed hypersensitivity to the Comirnaty COVID-19 vaccine. This case adds to the growing evidence for rare delayed reactions to COVID-19 vaccines and highlights the importance of ongoing pharmacovigilance as the vaccine rollout continues.

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Impact of coronavirus disease 2019 pandemic on frequency and severity of asthma exacerbations in an inner-city population

The coronavirus disease 2019 (COVID-19) pandemic profoundly altered the way that society functioned, with resultant shifts in behavior and exposures particularly when the orders for national shelter in place were implemented in mid-March 2020. These changes may have substantially impacted patients with chronic diseases including asthma, which disproportionately affects underserved minority children.[1] In addition to changes in exposures such as viruses and environmental triggers, changes in health care access and utilization impact asthma morbidity.[2–7] Initially, it was unclear whether these changes would have a positive or negative impact on children with asthma.[5] Over the past year, several studies have reported a reduction in emergency department (ED) visits for pediatric asthma throughout the United States.[7–9] The current study sought to evaluate the impact of the COVID-19 pandemic on ED visits and hospitalizations in an inner-city pediatric population with specific comparisons of exacerbation severity.

This study was deemed exempt by our institutional review board. Retrospective data were collected from our urban academic hospital to include children presenting to the ED with a diagnosis of "asthma exacerbation" (International Classification of Diseases Tenth Revision codes J45.901/2, J45.21-25, J45.22-52) as one of the top 2 diagnoses.

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Data included patient demographics and final disposition—discharged from the ED, admitted to the general inpatient unit, or admitted to the pediatric intensive care unit (PICU)—as surrogate markers of illness severity. Data were divided into 12-week quarters with quarter 1 covering January to March, quarter 2 covering April to June, quarter 3 covering July to September, and quarter 4 covering October to December. The onset of COVID-19 was defined as April 1, 2020 (quarter 2). Pre-COVID-19 data were collected from 2016 to 2019 and covered 48 weeks on average for each quarter. During COVID-19, data included were on the average of 12 weeks for each 2020 quarter. Data collection ended December 2020 (quarter 4). Quarter 1 during COVID-19 was from January to March 2021, thus, it was not included in our analysis. The number of ED visits for asthma per week and the percentage of patients with each final disposition (ED, inpatient, or PICU) was averaged for each quarter before and during the COVID-19. Unpaired *t* tests were used to compare the means per week pre- to during COVID-19 for each quarter (2-4).

The overall study population consisted of 4664 unique patients. The overall sample had a mean age of 8.2 years with 56.2% boys and 89.3% African American; the remainder self-identified as either White, multiracial, or other. Age, sex, and race did not significantly differ pre- and during COVID-19; although, during COVID-19, health insurance coverage changed, with 87.3% Medicaid insured pre- and 95.1% during-, 10.7% privately insured pre- and 4.9% during and 2.0% uninsured patients pre- and 0% during COVID-19.

As illustrated in Figure 1, there was a statistically significant decrease in ED presentations for asthma during COVID-19 vs pre–COVID-19 in quarter 2 (decreased 87.2%), quarter 3 (73.5%), and quarter 4 (77.3%), ($P < .001$ for all.) There was a significant increase in the percentage of patients who did not require any admission (discharged from the ED) during COVID-19, compared with pre–COVID-19 in quarters 2 ($P < .001$) and 3 ($P < .05$), but no difference were found in quarter 4. There were no significant differences in the percentage of patients admitted to the general inpatient unit during vs pre-COVID-19 for any quarter. There was a significant reduction in the percentage of patients admitted to the PICU during COVID-19 in quarter 2 ($P < .001$), a reduction in quarter 3 that approached significance ($P = .05$), and no difference in quarter 4.

We found a statistically significant reduction in ED visits for asthma during the pandemic (79.3%), which is higher than other studies (range: 45.2%-75%).[8,9] We initially hypothesized that the significant reduction in pediatric asthma ED visits was because of reluctance to go to the ED because of concerns of contracting COVID-19. If so, we would expect higher exacerbation severity, resulting in increased PICU admissions and decreased ED discharges. However, we found the opposite. To our knowledge, our study is the first to use final disposition (admitted to PICU vs discharged from the ED) as a marker of asthma exacerbation severity, pre and during COVID-19. Decreased ED visits were sustained 9 months after the onset of the pandemic, suggesting that the ongoing COVID-19 precautions such as social distancing, distance learning, and masks may have contributed to this improvement. Though designed to reduce transmission of severe acute respiratory syndrome coronavirus 2, these measures could also reduce transmission of other respiratory viruses that are the primary cause of asthma exacerbations.[7,10] With children and caregivers spending more time at home, other potential contributing factors include changes in indoor allergen exposure from school to home[1] and improved asthma medication adherence.[7]

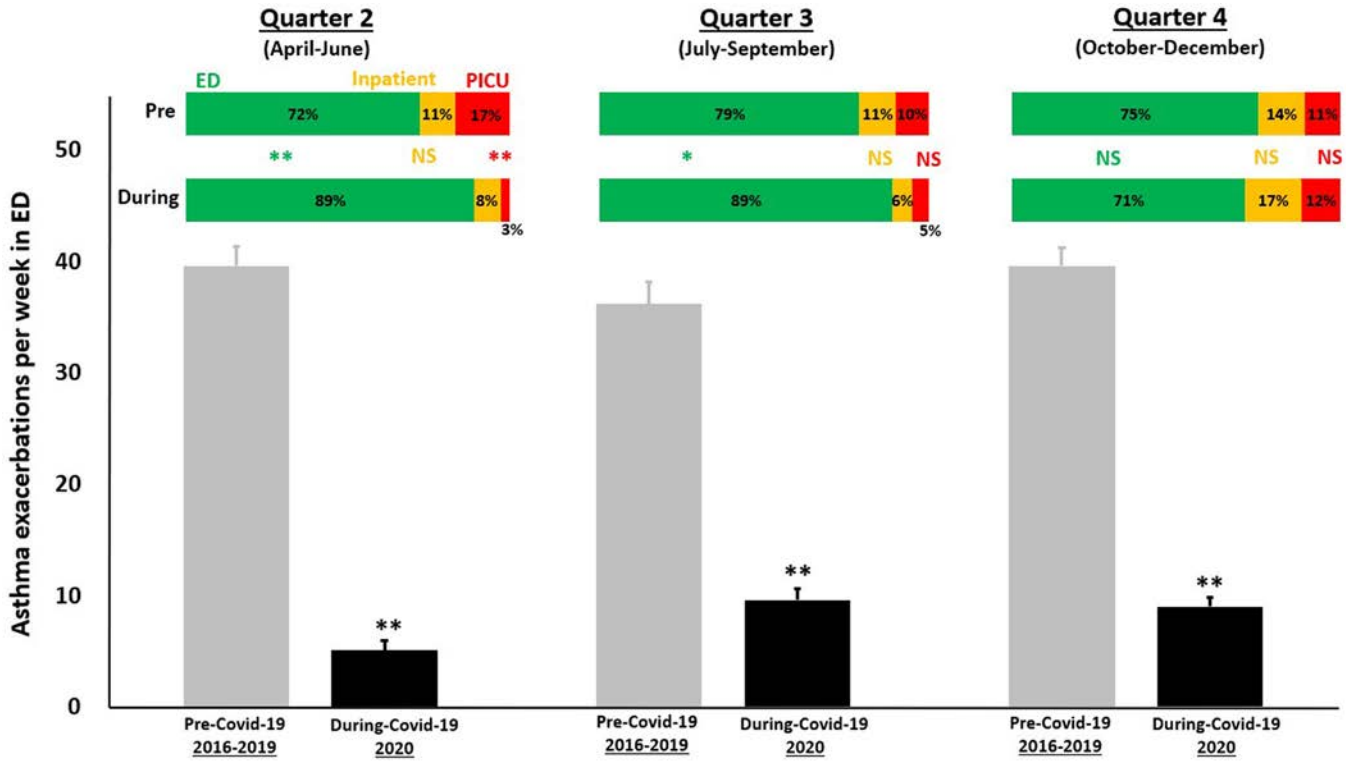

Figure 1. The frequency and severity of pediatric ED visits for asthma before and during COVID-19. The average number of patients per week presenting to the pediatric ED for asthma exacerbations before (gray) vs during (black) COVID-19. The asterisk represents pre–COVID-19 numbers averaged over 2016 to 2019 and during COVID-19 in 2020. Percentage of patients discharged from the ED (green), admitted to the general inpatient unit ("Inpatient", gold), or the PICU (red). COVID-19, coronavirus disease 2019; ED, emergency department; NS, not significant; PICU, pediatric intensive care unit.

The percent reduction in PICU asthma admissions is both striking and novel. We found a significant impact in quarter 2, but not 3 and 4. Although data were unavailable to investigate this, possible explanations include reduced adherence to COVID-19 precautions later in the pandemic and seasonal fluctuations in viral prevalence.

One study limitation is that detailed information, including allergen sensitization, exposure data, receipt of specialty care, and respiratory viral data were unavailable. Unfortunately, fewer respiratory viral panels were obtained during COVID-19, limiting our ability to assess specific pre/during viral triggers. Another factor that could impact our results is a change in the threshold for PICU admissions during COVID-19 because of bed availability. However, we continued to use our standardized asthma pathway admission criteria throughout the pandemic, and there were no PICU bed shortages. Finally, without the availability of comparison data for other diseases, we cannot conclude that COVID-19 measures were specifically only affecting asthma.

In conclusion, we found, in our underserved, minority, inner-city pediatric population, that both the frequency and severity of asthma exacerbations decreased immediately after the onset of the COVID-19 pandemic. Changes in behavior, such as sheltering in place, distance learning, and wearing of masks to reduce the spread of severe acute respiratory syndrome coronavirus 2, had a profound impact on asthma morbidity in our population. These may not be reasonable long-term measures and COVID-19 vaccination of children may change the need for some of them. Further studies may elucidate if any of these measures should be recommended for all or select populations of children to prevent viral illnesses that impact asthma morbidity and mortality.

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Recurrent anaphylaxis owing to chronic cholecystitis

Check for updates

Anaphylaxis is a severe, life-threatening systemic hypersensitivity reaction, triggered by variable allergic and nonallergic exposures.[1] Here, we report a case of recurrent anaphylaxis coinciding with flares of chronic cholecystitis. We hypothesize that in rare cases, inflammatory mediators released during episodes of cholecystitis can trigger anaphylaxis.

A 41-year-old woman with a past medical history of tree nut allergy initially presented for evaluation of idiopathic anaphylaxis occurring on 3 occasions in 3 months. Each episode consisted of urticaria, angioedema, nausea, vomiting, diarrhea, and generalized abdominal cramping. There was no hypotension with these initial episodes. She denied triggers related to temperature, exercise, infection, menstrual cycle, medication, food, or alcohol. The patient was a strict vegetarian and did not have mammalian meat exposure. There were no accidental nut ingestions, and there was no relationship between the time of food ingestion and the onset of anaphylaxis. She was seen in the emergency department (ED) for each encounter and was treated with antihistamines and steroids. She was not given epinephrine. Her laboratory results in the ED were remarkable for elevated transaminase levels: aspartate aminotransferase (AST) of 207 U/L (13-40 U/L) and alanine aminotransferase (ALT) of 66 U/L (5-35 U/L). Levels of alkaline phosphatase, bilirubin, and lipase were within normal limits. No liver imaging was obtained during these initial ED encounters. No tryptase level was also obtained during these episodes. At her initial allergy clinic encounter, a baseline tryptase level was established at 3.3 μg/L (<10.9 μg/L). Repeat laboratory testing revealed a normalization of AST and ALT levels. The patient was started on cetirizine 10 mg twice daily and famotidine 20 mg twice daily. After her initial clinical encounter, she was anaphylaxis free for approximately 1 month, during which time her liver enzyme levels remained normal.

Her next episode of anaphylaxis was the most severe to date. The patient awoke in the night with generalized abdominal pain,

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