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Allergic reactions including anaphylaxis after receipt of the first dose of Moderna COVID-19 vaccine — United States, December 21, 2020–January 10, 2021

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As of January 20, 2021, a total of 24 135 690 cases of coronavirus disease 2019 (COVID-19) and 400 306 associated deaths had been reported in the United States (https://covid.cdc.gov/covid-data-tracker/#cases_cases per100klast7days). On December 18, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for Moderna COVID-19 vaccine administered as 2 doses, 1 month apart to prevent COVID-19. On December 19, 2020, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of Moderna COVID-19 vaccine.¹ As of January 10, 2021, a reported 4 041 396 first doses of Moderna COVID-19 vaccine had been administered in the United States, and reports of 1266 (0.03%) adverse events after receipt of Moderna COVID-19 vaccine were submitted to the Vaccine Adverse Event Reporting System (VAERS). Among these, 108 case reports were identified for further review as possible cases of severe allergic reaction, including anaphylaxis. Anaphylaxis is a life-threatening allergic reaction that occurs rarely after vaccination, with onset typically within minutes to hours.² Among these case reports, 10 cases were determined to be anaphylaxis (a rate of 2.5 anaphylaxis cases per million Moderna COVID-19 vaccine doses administered), including nine in persons with a documented history of allergies or allergic reactions, five of whom had a previous history of anaphylaxis. The median interval from vaccine receipt to symptom onset was 7.5 min (range = 1–45 min). Among eight persons with follow-up information available, all had recovered or been discharged home. Among the remaining case reports that were determined not to be anaphylaxis, 47 were assessed to be nonanaphylaxis allergic reactions, and 47 were considered nonallergic adverse events. For four case reports, investigators have been unable to obtain sufficient information to assess the likelihood of anaphylaxis. This report summarizes the clinical and epidemiologic characteristics of case reports of allergic reactions, including anaphylaxis and nonanaphylaxis allergic reactions, after receipt of the first dose of Moderna COVID-19 vaccine during December 21, 2020–January 10, 2021, in the United States. CDC has issued updated interim clinical considerations for use of mRNA COVID-19 vaccines currently authorized in the United States³ and interim considerations for preparing for the potential management of anaphylaxis.⁴ Using methods previously described,⁵ CDC and FDA identified reports of suspected anaphylaxis in VAERS, the national passive surveillance (i.e., spontaneous reporting) system for monitoring adverse events after immunization.⁶ CDC physicians screened VAERS reports describing suspected severe allergic reactions and anaphylaxis and applied Brighton Collaboration case definition criteria for anaphylaxis*.⁷ After initial screening, reports with sufficient evidence to suggest anaphylaxis were followed up by collecting information from medical records and through direct outreach to health care facilities and treating health care providers, and, in some cases, vaccine recipients. Physician reviewers classified all initially identified case reports as anaphylaxis or not anaphylaxis and used clinical judgment to further categorize reports that were considered not anaphylaxis as nonanaphylaxis allergic reactions or nonallergic adverse events. Nonallergic adverse events, mostly vasovagal (e.g., fainting or the sensation of fainting) or suspected anxiety-related, were excluded from the final analyses. Anaphylaxis and nonanaphylaxis allergic reaction cases with symptom onset occurring later than the day after vaccination (i.e., outside the 0–1-day risk window) were also excluded because of the difficulty in clearly attributing allergic reactions with onset later than this to vaccination.¹

During December 21, 2020–January 10, 2021, the administration of 4 041 396 first doses of Moderna COVID-19 vaccine (2 465 411
Early safety monitoring of Moderna COVID-19 vaccine detected 10 cases of anaphylaxis after reported administration of 4041396 first doses of Moderna COVID-19 vaccine (2.5 cases per million Moderna COVID-19 vaccine doses administered) as well as cases of less severe nonanaphylaxis allergic reactions, based on U.S. data for December 21, 2020–January 10, 2021. Anaphylaxis is potentially life-threatening and requires immediate treatment. Based on this early monitoring, anaphylaxis after receipt of Moderna COVID-19 vaccine appears to be a rare event; however, comparisons of anaphylaxis risk with that associated with non–COVID-19 vaccines are constrained at this time by the limited data available this early in the COVID-19 vaccination program. A previous analysis of the Pfizer-BioNTech COVID-19 vaccine, also an mRNA vaccine, estimated an initial rate of 11.1 cases per million doses administered after receipt of the first dose of the Pfizer-BioNTech vaccine. CDC and FDA will continue enhanced monitoring for anaphylaxis among recipients of COVID-19 vaccines and will review case reports to VAERS.

In nine of 10 cases of anaphylaxis after receipt of Moderna COVID-19 vaccine, patients had symptom onset within 30 min of vaccination, and nine anaphylaxis patients also had a history of allergies or allergic reactions, including some with previous anaphylaxis events; up to 30% of persons in the general population might have some type of allergy or history of allergic reactions. All 10 anaphylaxis cases reported after receipt of Moderna COVID-19 vaccine occurred in women. Whereas a previous review of anaphylaxis reports to VAERS found that 80% of cases reported in adults involved females, the current finding could be affected by the observation that more women than men had received a first dose of Moderna COVID-19 vaccine during the analytic period (61% of doses administered versus 36%, respectively). In a previous analysis of the Pfizer-BioNTech COVID-19 vaccine, two thirds
| Age, years | Sex | Past history | Previous anaphylaxis episode | Onset after receipt (min) | Signs and symptoms | Treatment setting | Epi received | Brighton level | Outcome or disposition |
|------------|-----|--------------|-----------------------------|--------------------------|-------------------|-----------------|--------------|---------------|---------------------|
| 37         | F   | Penicillin, phenytoin, ibuprofen | No                          | 1                        | Respiratory failure, vomiting | Inpatient        | Yes          | 2              | Discharged home     |
| 39         | F   | Penicillin, aloes | Yes, penicillin             | 2                        | Decreased peripheral perfusion, persistent dry cough, nausea | Inpatient        | Yes          | 3              | Discharged home     |
| 63         | F   | Acetaminophen, azithromycin | No                          | 4                        | Periorbital edema, nausea | ED              | Yes          | 2              | Not specified       |
| 55         | F   | Multiple unspecified environmental and food allergies | Yes, unspecified           | 5                        | Hypotension, wheezing | Inpatient        | Yes          | 2              | Not specified       |
| 31         | F   | No            | No                          | 5                        | Diffuse erythematous rash, throat swelling | ED              | Yes          | 1              | Discharged home     |
| 49         | F   | Gadolinium, iodine | Yes, gadolinium, iodine | 10                       | Diffuse erythematous rash, tongue swelling, wheezing | ED              | Yes          | 1              | Recovered at time of report |
| 37         | F   | Unspecified intravenous contrast dye, penicillin | Yes, intravenous contrast dye | 11                       | Generalized urticarial rash, tongue swelling | Inpatient        | Yes          | 1              | Discharged home     |
| 50         | F   | Unspecified allergies or allergic reactions | Yes, unspecified           | 12                       | Diffuse erythematous rash, wheezing | Inpatient        | Yes          | 1              | Discharged home     |
| 57         | F   | Multiple drugs including penicillin and sulfa | No                          | 13                       | Periorbital edema, tongue swelling | ED              | Yes          | 1              | Recovered at time of report |
| 44         | F   | Morphine, codeine | No                          | 45                       | Diffuse erythematous rash, marked tongue swelling | Inpatient        | Yes          | 1              | Discharged home     |

Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department; Epi, epinephrine; F, female.

*As documented in the VAERS report or medical records, or through confirmation with the treating health care provider or the patients themselves.
†Inpatient hospitalization.
§The Brighton Collaboration case definition uses combinations of symptoms to define levels of diagnostic certainty. Brighton level 1 represents the highest level of diagnostic certainty that a reported case is indeed a case of anaphylaxis; levels 2 and 3 are successively lower levels of diagnostic certainty. Level 4 is a case reported as anaphylaxis but that does not meet the Brighton Collaboration case definition. Level 5 is a case that was neither reported as anaphylaxis nor meets the case definition (https://doi.org/10.1016/j.vaccine.2007.02.064).
¶As documented in the description of the adverse event in the VAERS report in Box 18 or as documented in recovery status in Box 20.
of first doses were administered in women.\textsuperscript{5} The clinical and epidemiologic characteristics of anaphylaxis case reports after receipt of Moderna COVID-19 vaccine are similar to those reported after receipt of the Pfizer-BioNTech COVID-19 vaccine.\textsuperscript{5} For both vaccines, symptom onset after vaccination occurred quickly, usually within minutes. A strong female predominance of anaphylaxis case reports exists for both vaccines. Finally, many persons experiencing anaphylaxis after receiving either vaccine had a history of allergies or allergic reactions, with several having experienced an anaphylaxis episode in the past. Similar patient characteristics in case reports of nonanaphylaxis allergic reactions were observed among the two vaccines.

The findings in this report are subject to at least two limitations. First, analyses of passive surveillance data include reporting biases, both underreporting because of lack of awareness or compliance with reporting requirements and reporting guidance, as well as stimulated reporting related to increased awareness from media or other public information sources. Second, incomplete information in reports and potential data lags because of processing times might result in an undercount of cases, and lags in reporting for vaccine doses administered might underestimate denominator data. However, reporting efficiency to VAERS for clinically severe adverse events is believed to be high.\textsuperscript{9} It is reasonable to expect that diagnosis and reporting of an acute and clinically severe condition

![](https://example.com/figure1.png)

FIGURE 1 Minutes from vaccine receipt to onset of anaphylaxis (A)* and nonanaphylaxis allergic reactions (B)† after receipt of the first dose of Moderna COVID-19 vaccine — Vaccine Adverse Events Reporting System (VAERS), United States, December 21, 2020–January 10, 2021. Abbreviation: COVID-19, coronavirus disease 2019. *The interval from vaccine receipt to symptom onset was >30 min for one anaphylaxis case (45 min). †The interval from vaccine receipt to symptom onset was ≥60 min for three nonanaphylaxis patients who had a documented history of allergies or allergic reactions at 60, 90, and 98 min and for four who did not have a documented history of allergies or allergic reactions (60 min, 10, 20, and 24 h). The interval from vaccine receipt to symptom onset was missing in two case reports, both of which documented a history of allergies or allergic reactions. Four cases of nonanaphylaxis allergic reactions with symptom onset occurring later than the day after vaccination (i.e., outside of the 0–1-day risk window) were excluded from the final analysis.
such as anaphylaxis occurs relatively quickly, and VAERS is likely sensitive at capturing anaphylaxis cases occurring after COVID-19 vaccination.

Mortality from COVID-19 in populations at increased risk for severe illness is substantial, and treatment options are limited. Widespread vaccination against COVID-19 with highly effective vaccines represents a critical tool in efforts to control the pandemic and save lives. CDC and FDA will continue to monitor for adverse events, including anaphylaxis, after administration of COVID-19 vaccines and will regularly assess the benefits and risks of vaccination in the context of the evolving epidemiology of the pandemic. Continued monitoring in VAERS and additional monitoring in population-based surveillance systems, such as the CDC’s Vaccine Safety Datalink (https://www.cdc.gov/vaccinesafety/ensuringafety/monitoring/vsd/index.html), will help to further characterize the risk for anaphylaxis after administration of COVID-19 vaccines.

CDC guidance on use of mRNA COVID-19 vaccines and management of anaphylaxis is available. Persons with an immediate allergic reaction to the first dose of an mRNA COVID-19 vaccine should not receive additional doses of either of the mRNA COVID-19 vaccines. In addition to screening for contraindications and precautions before administering COVID-19 vaccines, vaccine locations should have the necessary supplies and trained staff members available to manage anaphylaxis, implement postvaccination observation periods, immediately treat persons experiencing anaphylaxis signs and symptoms with intramuscular injection of epinephrine, and transport patients to facilities where they can receive advanced medical care. In addition, all patients should be instructed to seek immediate medical care if they develop signs or symptoms of an allergic reaction after their observation period ends and they have left the vaccination location. Health care providers can play an important role in vaccine safety monitoring by being vigilant in recognizing and reporting adverse events after immunization to VAERS at https://vaers.hhs.gov/reportevent.html.

**TABLE 2** Characteristics of patients with reported anaphylaxis and nonanaphylaxis allergic reactions after receipt of the first dose of Moderna COVID-19 vaccine — Vaccine Adverse Events Reporting System (VAERS), United States, December 21, 2020–January 10, 2021

| Characteristic | Type of reported reaction, no. (%) |
|---------------|-----------------------------------|
|               | Anaphylaxis (n = 10) | Nonanaphylaxis allergic reactions (n = 43) |
| Median age, years (range) | 47 (31–63) | 43 (22–96) |
| Female | 10 (100) | 39 (91) |
| Minutes to symptom onset, median (range) | 7.5 (1–45) | 15 (<1–1440 [24 h]) |
| Symptom onset ≤15 min | 9 (90) | 21 (51)† |
| Symptom onset ≤30 min | 9 (90) | 30 (73)† |
| Documented history of allergies or allergic reactions | 9 (90)§ | 26 (60) |

Abbreviation: COVID-19, coronavirus disease 2019.

*Four of the initial 47 nonanaphylaxis allergic reaction reports were excluded from the final analysis because symptom onset occurred later than the day after vaccination (i.e., outside the 0–1-day risk window).

†Two nonanaphylaxis allergic reaction reports were missing information on time of symptom onset; percentage calculated among 41 case reports with onset documented.

§Five anaphylaxis reports included a patient history of a previous anaphylaxis episode.

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**ENDNOTES**

1. Brighton level 1 represents the highest level of diagnostic certainty that a reported case is indeed a case of anaphylaxis; levels 2 and 3 represent successively lower levels of diagnostic certainty. Level 4 is a case reported as “anaphylaxis” but that does not meet the Brighton Collaboration case definition. Level 5 is a case that was neither reported as anaphylaxis nor meets the case definition.

†Anaphylaxis and nonanaphylaxis allergic reaction cases with symptom onset occurring later than the day after vaccination (i.e., outside of the 0–1-day risk window) were excluded because of the difficulty in clearly attributing allergic reactions with onset outside this risk window to vaccination.

§Four of the initial 47 nonanaphylaxis allergic reactions were excluded from the final analysis. Based on the Code of Federal Regulations, a serious adverse event is defined if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly, or birth defect. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/cfsearch.cfm?fr=312.32

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