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Attention all anti-vaccinators: The cutaneous adverse events from the mRNA COVID-19 vaccines are not an excuse to avoid them!

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Abstract Despite the growing availability of coronavirus disease 2019 (COVID-19) vaccines in the general population, a significant proportion of individuals demonstrate vaccine hesitancy. We sought to consolidate and update current evidence on cutaneous adverse events from COVID-19 vaccines to aid in the education and counseling of patients concerned about potential cutaneous side effects. We conducted a literature review of PubMed in May 2021 to identify reports of cutaneous events after vaccination with the Pfizer-BioNTech and Moderna vaccines (postauthorization clinical reports pertaining to the Johnson & Johnson and AstraZeneca vaccines were limited). Event reports in the Vaccine Adverse Event Reporting System were reviewed. Localized cutaneous reactions were common after the mRNA vaccines, consistent with clinical trial findings. Reported urticarial and morbilliform eruptions may reflect immediate hypersensitivity but have rarely been associated with anaphylaxis. There are infrequent reports of herpes zoster, dermatologic filler reactions, and immune thrombocytopenia, mainly occurring in high-risk patient groups. Ultimately, the identified cutaneous reactions are largely self-limited and should not discourage vaccination. Existing reports should reassure patients of the overall compelling safety profiles of the mRNA COVID-19 vaccines and benignity of skin reactions after vaccination.

Emergency authorizations for several severe acute respiratory syndrome coronavirus 2 vaccines have critically improved our ability to combat the spread of the virus. Despite growing availability of these vaccines, a notable portion of the population has demonstrated vaccine opposition. Survey data in the United States indicate that approximately 27% of individuals are reluctant to receive a coronavirus disease 2019 (COVID-19) vaccine, with a majority citing concern surrounding potential adverse effects.1

Misrepresentation or exaggeration of potential cutaneous adverse events may be contributing to these concerns—reports and photos of “Covid-arm” frequently appear on social and public media despite the overall benign and transient nature of this presentation. Additionally, the media coverage of dermal filler reactions after the vaccine sparked alarm amongst those patients who had undergone filler injections.2,3 Similarly, reports of vaccine-associated anaphylaxis may increase vaccine hesitancy for individuals with a history of allergic reactions, despite the overall rarity of this event.4 The Wall Street Journal ran with a headline: “Covid-19 Vaccines Have Triggered Severe Allergic Reactions in 29 People in US to Date; Rate of reactions to Covid-19 vaccines

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is higher than it is for flu shot, but the Centers for Disease Control (CDC) says it is rare and encourages inoculation,” causing anti-vaccinators to eschew vaccination centers.⁵

Peer-reviewed and highly cited journals like the Journal of the American Academy of Dermatology⁶ published a large institution registry-based analysis, and Clinics in Dermatology⁷ published a contribution that reviewed some of the adenovirus and mRNA vaccines cutaneous side effects; both of these contributions should have provided reassurance regarding the safety of these vaccines vis-à-vis the skin. Clinical trials for the COVID-19 vaccines have provided baseline understanding of the most common cutaneous side effects, including erythema or swelling at the injection site (Pfizer-BioNTech: 9.5%-10.5% of patients; Moderna: 10.0%-14.7%; Johnson & Johnson: 5.3%-7.3%)⁸-¹⁰ and delayed injection site reactions (Moderna: 0.2%-0.8%).⁹ Given that postauthorization clinical reports have further characterized cutaneous side effects, we sought to consolidate and discuss these findings to aid in patient education and help alleviate hesitancy surrounding COVID-19 vaccination.

We reviewed currently available literature on PubMed in May 2021 to identify reports describing cutaneous adverse effects from currently authorized COVID-19 vaccines. Abstracts and titles of identified contributions published in 2020 and 2021 were reviewed for relevance. Assessment of these contributions’ references yielded several additional studies. We primarily focused this assessment on the Pfizer-BioNTech and Moderna mRNA vaccines because reports of cutaneous events from adenovirus vaccines (beyond clinical trials) were limited. We supplemented our analysis with data from the CDC’s Vaccine Adverse Event Reporting System (CDC-VAERS).¹¹ We first present a discussion of frequently reported cutaneous adverse events, followed by a consideration of more rarely reported entities.

This study used publicly available online reports and did not qualify as human subject research; therefore, institutional review board approval was not required at the University of Connecticut Health Center.

Frequently reported cutaneous adverse events

Postauthorization reports substantiate Pfizer and Moderna clinical trial data that localized reactions are the most prevalent cutaneous adverse events.⁹,¹⁰ Presently, injection site swelling, erythema, dermatitis, and urticaria account for 3.9% of all VAERS-reported adverse effects for both vaccines, with 92.2% of these reports occurring in female patients.¹¹ The largest registry-based study to date reported cutaneous reactions in 414 unique patients receiving the Pfizer and Moderna vaccines, primarily noting injection site reactions (52.4% of cutaneous adverse events), delayed large local reactions (49.2%), and urticaria (9.0%).⁶ These common symptoms have typically been reported with lower reported frequency after the second vaccine dose.⁶,¹² which may help to assuage patient concerns surrounding these effects. Tables 1 and 2 summarize the most commonly reported cutaneous adverse events.

Local injection site reactions

Local injection site reactions occur soon after vaccine administration and may take the form of swelling, redness or erythema, and pain.⁶,⁹,¹₀,¹₃-¹₆ Overall, the incidence rate of injection site reactions after mRNA vaccines from cross-sectional analyses has varied from 5.5% to 23.7%,¹₃-¹₅ which is comparable or slightly higher than that identified in clinical studies.⁹,¹₀ There are rare reports of generalized or diffuse eruptions that begin as localized injection site erythema.¹⁷ Despite some variation in the timeline used to distinguish these events from delayed large local reactions (eg, 3 days versus 7 days).⁶,⁹,¹₈ reports agree that local injection site reactions are harmless, transient, and largely resolve within 2 to 5 days.⁵,¹₆ These reactions are nonetheless important to distinguish from immediate hypersensitivity reactions, which may warrant closer monitoring.⁶

Urticaria, angioedema, and morbilliform eruption

The CDC classifies immediate hypersensitivity or allergic reactions as urticaria, angioedema, respiratory distress, or anaphylaxis that occur within 4 hours of vaccine administration.¹⁸ Given that anaphylaxis has been rarely reported for the Pfizer and Moderna vaccines (rates ranging from 2.5-11.1 per 1 million).⁴,¹⁹,²⁰ potentially associated cutaneous findings are important to recognize.

There are several reports of allergic-type cutaneous reactions occurring shortly after administration of the mRNA vaccines. A study identified flushing, generalized acute urticaria, and mucocutaneous angioedema in 0.1% of 5,574 healthcare workers within 4 hours of receiving the Pfizer vaccine.²¹ One study reported localized urticaria, erythema, and pruritus in 0.1% of 3,170 health care workers within a similar timeframe.¹⁶ Another study described 5 patients with a confirmed polyethylene glycol allergy who displayed allergic cutaneous manifestations within 4 hours of receiving either the Pfizer or Moderna vaccines.²² Generally, immediate hypersensitivity reactions to vaccines are caused by inactive ingredients rather than specific vaccine antigens,² but few reports have confirmed sensitization to specific mRNA vaccine excipients (eg, polyethylene glycol).²¹,²²,²³

Several reports note allergic-type cutaneous manifestations that begin after the 4-hour mark from COVID-19 vaccine administration and therefore do not signify immediate hypersensitivity. One study noted that urticarial eruptions predominately occurred >24 hours after vaccination.⁶ Nonlocalized erythema and morbilliform eruptions have likewise been reported days after vaccination.²⁴ The eti-
| Study authors | Cutaneous findings | Pathology findings | Associated systemic symptoms or lab findings | Time course of cutaneous symptoms | Proposed diagnosis and mechanism | Management |
|---------------|-------------------|-------------------|---------------------------------------------|----------------------------------|---------------------------------|-----------|
| **Delayed large local reactions** | | | | | | |
| Blumenthal et al. | 5-19 cm erythematous plaques with associated pruritus near or at the injection site | Superficial perivascular and perifollicular lymphocytic infiltrates with rare eosinophils | Fatigue, headache, chills | Onset: 8 days after first dose (median) Resolution: 6 days after onset (median) | Delayed-type or T-cell mediated hypersensitivity | Occasional glucocorticoid therapy; patients were advised to receive second dose, to which only 50% developed similar effects |
| Fernandez-Nieto et al. | Erythematous and slightly indurated patches at the injection site, urticaria (2 patients) | Superficial and deep perivascular lymphocytic infiltrate with dilated vessels (2 patients) | Not reported | Onset: “Delayed” (unspecified) Resolution: Typically within 72 hours of onset | Delayed injection-site reaction, likely due to hypersensitivity to the COVID-19 spike protein or other vaccine components | Patients with urticaria received oral antihistamines; all patients encouraged to receive second vaccine dose |
| Johnston et al. | Pruritic and variably painful erythematous reactions near the injection site | Mild predominantly perivascular and focal interstitial mixed infiltrate with lymphocytes and eosinophils consistent with a dermal hypersensitivity reaction | Most frequent other symptoms and signs included fevers, chills, and sore arm | Onset: 7 days after first dose (median); 2 days after second dose (median) Resolution: 3-5 days after onset | Delayed-type, cell-mediated immunity, likely due to a vaccine excipient, lipid nanoparticle, or mRNA component | Management included topical steroids and oral antihistamines; 15 patients who developed a reaction to the first dose, 11 developed a second-dose reaction |
| López-Valle et al. | Poorly defined erythematous and edematous plaque at injection site | Not performed | Fever | Onset: 7 days after first dose Resolution: 2 days after symptom onset | Delayed injection-site reaction, possibly due to hypersensitivity to vaccine components or nonspecific inflammation | Paracetamol, prednisone, and dexchlorpheniramine; more mild symptoms recurred after second dose |
| **Morbilliform eruption** | | | | | | |
| Ackerman et al. | Erythematous, pruritic injection site eruption which spread to the face, trunk, and extremities | Slight lymphocytic perivascular infiltrate | Injection site soreness; liver enzymes were elevated to 2 × normal limit | Onset: 3 hours after first dose Resolution: Improvement 1 month after onset | Persistent morbilliform drug eruption, likely secondary to vaccine | Due to persistence of drug eruption, second dose of vaccine was not provided |
| Jedlowski and Jedlowski | Erythematous macular morbilliform eruption over the lower back | Not performed | Subjective fever, headache, and injection site soreness | Onset: 48 hours after first dose Resolution: 24 hours after onset | Morbilliform drug eruption, likely secondary to vaccine-induced immune activation | None; patient developed a similar but more widespread eruption after receiving the second vaccine dose |

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### Table 1 (continued)

| Study authors | Cutaneous findings | Pathology findings | Associated systemic symptoms or lab findings | Time course of cutaneous symptoms | Proposed diagnosis and mechanism | Management |
|---------------|--------------------|--------------------|---------------------------------------------|----------------------------------|----------------------------------|------------|
| **Various etiologies** |                   |                    |                                             |                                  |                                  |            |
| Bianchi et al. | Flushing of the face (2 patients), generalized urticaria (2 patients), angioedema of tongue and lips (2 patients) | Not reported | Not reported | Onset: 5 minutes to 24 hours after first dose; within 4 hours (5 patients) | Possible hypersensitivity to vaccine components; however, patients demonstrated negative skin prick test to vaccine residues; desired immune protection considered | No treatment (5 patients), betamethasone (1 patient); patients did not demonstrate similar adverse events after second vaccine dose |
| Corbeddu et al. | Localized pruritus, erythema, or urticaria at injection site (3 patients); erythematous eruption of trunk, foot, face, legs, or chest (8 patients) | Not reported | Laryngospasm, periorbital edema, and angioedema of tongue and lips (4 patients) | Onset: 1 hour to 8 days after first dose; within 4 hours (3 patients) Resolution: 2-3 days after onset (except for 1 patient) | Injection site reaction and diffuse morbilliform drug eruption, both likely secondary to vaccination | 1 patient received oral steroids for flare of atopic dermatitis; other patients were not treated and advised to receive second dose |
| Kadali et al. | Localized eruption (58 patients), hives (unspecified location) (7 patients) | Not reported | Most frequently reported other symptoms included injection site soreness (94.2%), generalized weakness (65.7%) | Onset: Not reported Resolution: Not reported | Localized eruption: No hypothesis outlined | Despite side effects, 97.0% of respondents intended to receive the second dose of the vaccine |
| Kadali et al. | Localized eruption (20 patients), hives (unspecified location) (5 patients) | Not reported | Most frequently reported other symptoms included injection site soreness (88.0%), generalized weakness (58.9%) | Onset: Not reported Resolution: Not reported | Localized eruption: No hypothesis outlined | Despite side effects, the majority (97.6%) of respondents received the second dose of the vaccine |

*Note: The table continues on the next page.*
| Study authors         | Cutaneous findings                                                                 | Pathology findings                  | Associated systemic symptoms or lab findings | Time course of cutaneous symptoms | Proposed diagnosis and mechanism                                                                                                                                                                                                 | Management                                                                                                                                 |
|-----------------------|------------------------------------------------------------------------------------|-------------------------------------|---------------------------------------------|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| McMahon et al.⁶       | Local injection site reaction (Moderna: 214/Pfizer: 18 patients); Delayed large local reaction (206/12 patients); Nonlocalized urticaria (23/17 patients); Morbilliform eruption (18/9 patients) | Not reported                         | Most frequently reported systemic symptoms included fatigue (145 patients), myalgia (138 patients), headache (115 patients) | Local site reaction: Onset: 1 day (median) after first dose Resolution: 5 days (median) after first dose *Delayed large local reaction: Onset: 7 days (median) Resolution: 11 days (median) *Urticaria: Onset: 3 days (median) Resolution: 8 days (median) *Morbilliform: Onset: 3 days (median) Resolution: 7 days (median) *Shorter onset after second doses | Urticaria and morbilliform: Possible allergy to vaccine components but more likely related to host immune response Delayed large local reaction: Likely hypersensitivity to polyethylene glycol in vaccine | Patients typically received topical corticosteroids, oral antihistamines, and pain-relieving medications |
| Pitlick et al.²²      | Urticaria (unspecified site) (3 patients), angioedema (2 patients), and facial flushing (1 patient) | Not performed                        | Tachycardia, throat tightness                | Onset: 20 minutes to 8 hours after first dose; within 4 hours (5 patients) Resolution: 6-24 hours after onset | Given negative skin prick testing to polyethylene glycol, possible immediate hypersensitivity to other vaccine components or non–IgE-mediated allergy Hypotheses for specific etiologies not specified; however, positive association between allergic history and injection site redness established | All patients had negative polyethylene glycol skin prick testing and received second vaccine dose |
| Riad et al.¹⁵         | Injection site erythema (187 patients), eruption, unspecified (28 patients), urticaria (10 patients) | Not performed                        | Most frequently reported systemic symptoms included fatigue (232 patients), headache (160 patients), muscle pain (132 patients) | Onset: Not specified Resolution: >90% of all side effects resolved within 1 week of onset | Hypotheses for specific etiologies not specified; however, positive association between allergic history and injection site redness established | Management approaches not reported |

The table summarizes the findings from studies and reports that identified common cutaneous adverse events after the Pfizer-BioNTech or Moderna vaccines. COVID-19, coronavirus disease 2019
COVID-19 vaccine and cutaneous adverse events

| Study authors           | Study design                        | Study location       | Administered vaccine         | Number of vaccine recipients | Notable patient history                                                                 |
|------------------------|-------------------------------------|----------------------|------------------------------|------------------------------|-----------------------------------------------------------------------------------------|
| **Delayed large local reactions** |                                     |                      |                              |                              |                                                                                          |
| Blumenthal et al.      | Case series                         | United States        | mRNA-1273 (Moderna)          | 10 F, 2 M; age range: 31-61   | Mainly non-Hispanic White patients; 6 patients had prior documented allergies            |
| Fernandez-Nieto et al. | Retrospective review                | Spain                | BNT162b2 (Pfizer-BioNTech)   | 91 F, 12 M (representing 2.2% of 4,774 reviewed cases); age range: 20-64 | Patients were healthcare workers; medical history was not reported                        |
| Johnston et al.        | Case series                         | United States        | mRNA-1273 (Moderna)          | 16 patients; age range: 25-89  | The majority of patients were healthcare workers; 50% demonstrated prior seasonal or medication allergy |
| López-Valle et al.     | Case report                          | Spain                | BNT162b2 (Pfizer-BioNTech)   | 1 F; age: 27                  | Healthcare worker; no significant personal medical history                                |
| Ackerman et al.        | Case report                          | France               | BNT162b2 (Pfizer-BioNTech)   | 1 M; age: 55                  | Healthcare worker; no medical history, no prior allergies                                 |
| Jedlowski and Jedlowski | Case report                         | United States        | BNT162b2 (Pfizer-BioNTech)   | 1 M; age: 30                  | Healthcare worker; no medical history                                                    |
| Bianchi et al.         | Case series                          | Italy                | BNT162b2 (Pfizer-BioNTech)   | 5 F, 1 M (representing 0.11% of 5,574 reviewed cases); age range: 24-58 | Patients were healthcare workers with a history of allergic rhinitis; no prior history of drug or polyethylene glycol hypersensitivity |
| Corbeddu et al.        | Retrospective review                 | Italy                | BNT162b2 (Pfizer-BioNTech)   | 7 F, 4 M (representing 0.3% of 3,170 reviewed cases); age range: 29-67 | 8 patients endorsed prior allergic history                                                |
| Kadali et al.          | Randomized, cross-sectional survey   | United States        | mRNA-1273 (Moderna)          |                              | Patients were healthcare workers; primarily (83.8%) non-Hispanic White or Asian (9.5%); medical history was not reported |
| Kadali et al.          | Randomized, cross-sectional survey   | United States        | BNT162b2 (Pfizer-BioNTech)   | Injection site eruption: 58 patients (representing 13.4% of 432 survey respondents); Hives: 7 patients (1.6%); Among respondents, 64.6% were age 31-50; 89.4% were F | Patients were healthcare workers; medical history was not reported                         |
| McMahon et al.         | Registry-based study                 | United States        | BNT162b2 (Pfizer-BioNTech)   | Injection site eruption: 20 patients (representing 2.5% of 803 survey respondents); Hives: 5 patients (0.1%); Among respondents, 68.4% were age 31-50; 86.5% were F | Patients were mainly non-Hispanic White (78%); followed by Asian (11%); and Hispanic (7.5%); prior injection site reactions noted in 3.1%; most patients had no comorbidities (62%); although most common was hypertension (15%) |

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Table 2 (continued)

| Study authors | Study design | Study location | Administered vaccine | Number of vaccine recipients | Notable patient history |
|---------------|--------------|----------------|----------------------|------------------------------|-------------------------|
| Pitlick et al.\textsuperscript{22} | Case series | United States | BNT162b2 (Pfizer-BioNTech) (3 patients) mRNA-1273 (Moderna) (2 patients) | 4 F, 1 M; age range: 20-45 | All patients had prior documented polyethylene glycol or polysorbate allergy |
| Riad et al.\textsuperscript{15} | Cross-sectional survey | Czech Republic | Injection site redness: 187 patients (representing 20.2% of 922 survey respondents) Eruption, unspecified: 28 patients (representing 3.0%) Urticaria: 10 patients (representing 1.1%) | Patients were healthcare workers, most common comorbidities included hypertension, diabetes mellitus, asthma, and thyroid disease |

The table summarizes the methodologies of studies and reports that identified common cutaneous adverse events after the Pfizer-BioNTech or Moderna vaccines. COVID-19, coronavirus disease 2019; F, Female; M, Male.

Theology of allergic-type cutaneous symptoms may be complex, act through non–IgE-mediated mechanisms,\textsuperscript{22} and, in some cases, reflect a developing host immune response rather than a specific vaccine allergy.\textsuperscript{6,21,24} Existing studies should nonetheless provide reassurance to patients and providers because the outlined allergic cutaneous symptoms are transient and rarely associated with anaphylaxis.\textsuperscript{6,16,22}

**Delayed large local reactions**

The improved characterization of delayed large local reactions in postauthorization studies is important because these events were not specifically described in Pfizer’s clinical trial. These eruptions may vary morphologically but are typically characterized by erythema with mild induration at or near the initial injection site.\textsuperscript{25-27} They are primarily distinguished from immediate injection site reactions by their later time of onset (eg, days versus hours).\textsuperscript{6,9}

Further study is needed to delineate the precise prevalence of these reactions after the Pfizer vaccine. Although one study identified these events less frequently after the Pfizer (versus Moderna) vaccine,\textsuperscript{6} another study described these delayed reactions in 2.2% of 4,774 Pfizer vaccine recipients.\textsuperscript{27}

Two reports separately verified the development of delayed local reactions presenting approximately 1 week after the Moderna vaccine.\textsuperscript{12,26} Reports suggest that delayed large local reactions are temporary, resolving 3 to 6 days after onset.\textsuperscript{6,12,26} These presentations may also be less frequent after the second dose,\textsuperscript{6,12,26} a finding that is important to communicate to concerned patients.

Previous studies concur that these delayed cutaneous findings likely represent T-cell–mediated hypersensitivity, which is supported by skin pathology readings demonstrating perivascular and perifollicular lymphocytic infiltrates.\textsuperscript{6,12,25-27} Although the specific hypersensitivity trigger remains unclear, prior studies affirm that these manifestations likely do not lessen vaccine safety. Recognition of delayed reactions is nonetheless important to guide patient expectations and avoid unnecessary medical therapies (eg, antibiotics), because these eruptions are not infectious in nature.\textsuperscript{26}

**Rarely reported cutaneous adverse events**

Previous studies have less frequently noted cases of more unusual cutaneous reactions to the COVID-19 vaccines, including erythromelalgia,\textsuperscript{6} herpes zoster,\textsuperscript{5,13,14,28,29} erythema multiforme,\textsuperscript{6,30,31} reactions to dermatologic fillers,\textsuperscript{6,32} pemino or chilblains,\textsuperscript{6,33} vasculitis,\textsuperscript{6,34} pityriasis rosea,\textsuperscript{6,35} and immune thrombocytopenia (ITP).\textsuperscript{36-38} There are a small but growing number of these entities listed in the VAERS.\textsuperscript{11} Postauthorization studies have been essential in describing these clinical findings; however, reports are limited in their ability to identify overall incidence rates, making it difficult to define a direct association to mRNA vaccinations. Etiologies with significant clinical reports are discussed in this review, and all studies are outlined in Tables 3 and 4.

**Herpes zoster**

Moderna’s clinical trial described the presence of vesicular eruptions in three patients, although a specific diagnosis was not provided.\textsuperscript{5} After widespread vaccination, reports
| Study authors | Cutaneous findings | Pathology findings | Associated systemic symptoms or lab findings | Time course of cutaneous symptoms | Proposed diagnosis and mechanism | Management |
|---------------|--------------------|--------------------|---------------------------------------------|----------------------------------|---------------------------------|------------|
| Furer et al.29 | Vesicular, pruritic, painful skin eruptions of the V1, T4, T6, T10, T12, and L5 dermatomes (varied by patient) | Not reported | Headache and malaise (2 patients), none (4 patients) | Onset: 2 days to 2 weeks after first dose Resolution: Improvement in pain and cutaneous symptoms in 10 days to 6 weeks after onset | Herpes zoster reactivation, likely secondary to vaccine-induced immune modulation, although use of immunosuppressants (eg, JAK inhibitors) also considered | Acyclovir for 1 week (3 patients), valacyclovir for 1 week (2 patients), no treatment (1 patient); 4 patients received the second dose without side effects, Systemic antiviral treatment (unspecified) led to complete improvement |
| Eid et al.28 | Confluence of vesicles on an erythematous base on the right thigh in a dermatomal distribution | Not reported | No additional systemic symptoms | Onset: 5 days after receiving the first dose Resolution: Complete improvement, unspecified timing | Herpes zoster reactivation, secondary to immune modulation from the COVID-19 vaccine | |
| Munavalli edema and swelling et al.30 | Infraorbital and perioral edema and swelling | Not reported | Generalized myalgias, fever, mild injection site pain | Onset: 12 hours to 10 days after first or second dose Resolution: 3-7 days after onset | Delayed inflammatory reaction to hyaluronic acid fillers triggered by exposure to the COVID-19 spike protein | All patients responded to therapy with low dose oral lisinopril, which authors proposed decreased the inflammatory reaction |
| Gambichler et al.31 | Erythematous and slightly violaceous coalescing macules and papules on the trunk and extremities | Vacuolar interface dermatitis with lymphocytic infiltrates; dyskeratoses of basal keratinocytes | Biopsy-confirmed but specific findings not reported | Onset: 1 day after first dose Resolution: Timeline not reported | Erythema multiforme, likely due to vaccine or vaccine components (eg, PEG) acting as an antigen to initiate a cytotoxic T-cell response | Systemic prednisolone with gradual improvement in skin eruption |
| Nawimani et al.30 | Erythematous concentric targetoid plaques on the palms and soles of bilateral hands and feet | Not reported | | Onset: 12 hours after first dose Resolution: Timeline not reported | Erythema multiforme, potentially due to expression of viral antigens on keratinocyte DNA and subsequent activation of immune response | Topical clobetasol, which led to clinical improvement |
| Helms et al.36 | Diffuse cutaneous purpura and severe epistaxis | Not reported | Weakness, back pain, urinary retention, and encephalopathy (acute inflammatory demyelinating polyneuropathy suspected); low platelets of 10,000/μL | Onset: Within 12 hours of first dose Resolution: Marked improvement in platelet count 22 days after symptom onset | ITP, refractory to standard management, likely induced by vaccination | Dexamethasone, methylprednisolone, platelet transfusion, intravenous immunoglobulin, rituximab, eltrombopag, romiplostim, plasma exchange |

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## Table 3 (continued)

| Study authors | Cutaneous findings | Pathology findings | Associated systemic symptoms or lab findings | Time course of cutaneous findings | Proposed diagnosis and mechanism | Management |
|---------------|--------------------|--------------------|--------------------------------------------|----------------------------------|---------------------------------|------------|
| Malayala et al. | Brown to red-colored, purpuric, nonblanching generalized eruption across the entire body | Not reported | Low-grade fever, chills, nausea; patient also had elevated liver enzymes, heavy hepatitis C viral load, and decreased platelets of 84,000/μL | Onset: Within 24 hours of first dose; Resolution: >3 days after onset | ITP induced by the COVID-19 vaccine, possibly through molecular mimicry | Patient received further inflammatory and autoimmune work-up, further management was limited because patient left against medical advice | Dexamethasone for 4 days, platelet transfusion, and intravenous immunoglobulin for 2 days led to improved platelet count and symptoms |
| Tarawneh et al. | Widespread petechiae and gum bleeding | Not reported | Platelets of 2,000/μL, mildly elevated liver enzymes, Sjogren Syndrome A antibody elevated with otherwise normal autoimmune labs | Onset: 3 days after vaccination; Resolution: Significant improvement 6 days after onset | ITP, likely due to vaccination, although underlying autoimmune conditions or idiopathic conditions possible | | |
| **Chilblains** | | | | | | |
| Kha et al. | Pruritic papular eruption on the digits of the right hand | Dense and predominantly perivascular lymphocytic (CD3+ T-cells) infiltrate within the superficial-to-deep reticular dermis | Pain, erythema, and swelling of the right proximal interphalangeal joint; normal lab findings | Onset: Within 2 days of first dose; Resolution: Complete improvement 2 weeks after onset | Chilblains, possibly due to potent type I interferon reaction from the vaccine | Clobetasol ointment for 2 weeks; similar eruption appeared on the same hand after second dose |
| **Pityriasis rosea** | | Interface changes, with parakeratosis and scattered dyskeratotic keratinocytes | No systemic symptoms | Onset: 2 days to 3 weeks after first or second vaccine dose; Resolution: 2-3 weeks after treatment | Pityriasis rosea or pityriasis rosea-like eruptions, possibly secondary to vaccine reactivation of HHV-6/7 or T-cell-mediated response triggered by molecular mimicry from a viral epitope | Topical corticosteroids or combination doxycycline and bilastine led to complete improvement |
| Cyrenne et al. | 20 F: Oval pink-to-tan colored thin plaques with peripheral scale on the trunk and extremities 40 M: classic herald patch on his left lateral axilla, as well as many symmetrically distributed smaller plaques with peripheral scale on the trunk and proximal extremities 40 M: Herald patch on left axilla, symmetrically distributed smaller plaques with peripheral scale on trunk and extremities | | | | | |

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Table 3 (continued)

| Study authors | Cutaneous findings | Pathology findings | Associated systemic symptoms or lab findings | Time course of cutaneous symptoms | Proposed diagnosis and mechanism | Management |
|---------------|-------------------|--------------------|---------------------------------------------|---------------------------------|---------------------------------|------------|
| Various etiologies | 60 F: Widespread symmetric erythematous and purpuric eruption of the lower limbs; 75 F: symmetric, purpuric eruption over the lower limbs | 60 F: Superficial perivascular lymphohistiocytic infiltrate and scattered eosinophils without blood vessel necrosis | 60 F: None; 75 F: None | 60 F: Onset: 14 days after first dose; Resolution: 21 days after onset; 75 F: Onset: 2 days after first dose; Resolution: 10 days after onset | Unclear etiology, possibly vaccine-induced small-vessel vasculitis | 60 F: Oral prednisone and topical treatments led to resolution of eruption; 75 F: Oral prednisolone for 7 days led to resolution of the eruption |
| Lam et al. | 60 F: Erythromelalgia: (Moderna: 11 patients/Pfizer: 3 patients); Zoster (5/5 patients); Erythema multiforme (3/0 patients); Filler reaction (8/1 patients); Pernio/chilblains (3/5 patients); Vasculitis (2/1 patients); Pityriasis rosea (1/3 patients) | Most frequently reported systemic symptoms included fatigue (145 patients), myalgia (138 patients), headache (115 patients) | Not reported | *Zoster: Onset: 15 days (median) after first dose; Resolution: 21 days (median) after first dose; Filler reaction: Onset: 1 day (median) Resolution: 3 days (median) *Shorter onset after second doses | Filler reaction: Delayed hypersensitivity to filler after immunologic vaccine trigger; Pernio or chilblains, pityriasis rosea, erythromelalgia: Related to host immune response stimulated by vaccine, reflective of that seen against actual virus; Zoster: Reactivation of varicella virus | Patients typically received topical corticosteroids, oral antihistamines, and pain-relieving medications |

The table summarizes the findings from studies and reports that identified infrequent cutaneous adverse events after the Pfizer-BioNTech or Moderna vaccines. COVID-19, coronavirus disease 2019; F, Female; ITP, immune thrombocytopenia; JAK, Janus kinase; M, Male; PEG, polyethylene glycol.
| Study authors       | Study design | Study location | Administered vaccine | Number of vaccine recipients | Notable patient history                                                                                                                                 |
|--------------------|--------------|----------------|----------------------|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| **Herpes zoster**  | Case series  | Israel         | BNT162b2 (Pfizer-BioNTech) | 6 F (representing 1.0% of 590 reviewed cases); age range: 36-61 | Of all patients, 491 (83.2%) had a history of autoimmune inflammatory rheumatic disease; all patients had a history of varicella and 1 was vaccinated against herpes zoster with a live-attenuated vaccine. Hypertension, coronary artery disease, antineutrophilic cytoplasmic antibody-related glomerulonephritis. |
| Furer et al.²⁹     | Case report  | Lebanon        | mRNA vaccine (unspecified) | 1 M; age: 79 | Hypertension, coronary artery disease, antineutrophilic cytoplasmic antibody-related glomerulonephritis. Patients had previously received hyaluronic acid fillers 1-3 years earlier; no allergic history. |
| **Delayed reaction to hyaluronic acid fillers** | Case series  | United States  | BNT162b2 (Pfizer-BioNTech) | 4 F; ages: 31, 36, 43, 76 | Patients had previously received hyaluronic acid fillers 1-3 years earlier; no allergic history. |
| Munavalli et al.³⁰ | Case series  | United States  | mRNA-1273 (Moderna) (2 patients) | 1 F; age: 74 | Dementia; history otherwise unremarkable. Rheumatoid arthritis, hypertension, herpes labialis, biopsy-confirmed erythema multiforme three years prior. |
| **Erythema multiforme** | Case report  | Germany        | BNT162b2 (Pfizer-BioNTech) | 1 F; age: 74 | Unremarkable. Rheumatoid arthritis, hypertension, herpes labialis, biopsy-confirmed erythema multiforme three years prior. |
| Gambichler et al.³¹ | Case report  | United Kingdom | mRNA-1273 (Moderna) (2 patients) | 1 F; age: 60 | African-American; history of tobacco use, liver cirrhosis, chronic kidney disease, congestive heart failure. Healthcare worker; no history of bleeding, autoimmune disease, or prior vaccine reactions. |
| **Immune thrombocytopenia** | Case report  | United States  | mRNA-1273 (Moderna) | 1 M; age: 74 | Hypertension, goit, hyperlipidemia, nonischemic cardiomyopathy. |
| Helms et al.³²     | Case report  | United States  | mRNA-1273 (Moderna) | 1 M; age: 60 | African-American; history of tobacco use, liver cirrhosis, chronic kidney disease, congestive heart failure. Healthcare worker; no history of bleeding, autoimmune disease, or prior vaccine reactions. |
| Malayala et al.³³  | Case report  | United States  | mRNA-1273 (Moderna) | 1 M; age: 22 | Healthcare worker; medical history remarkable for pityriasis lichenoides chronica, which was stable. |
| Tarawneh et al.³⁴  | Case report  | United States  | BNT162b2 (Pfizer-BioNTech) | 1 F; age: 70 | Unremarkable medical history; both patients were non-Hispanic White. Patients were mainly non-Hispanic White (78%), followed by Asian (11%), and Hispanic (7.5%); prior injection site reactions noted in 3.1%; most patients had no comorbidities (62%), although most common was hypertension (15%). |
| **Chilblains**     | Case report  | United States  | mRNA-1273 (Moderna) | 1 F; age: 20s 1 M; age: 40s | 20 F: Alopecia areata, otherwise unremarkable 40 M: No remarkable medical history. |
| Kha et al.³⁵       | Case report  | United States  | BNT162b2 (Pfizer-BioNTech) | 1 F; age: 70 | Unremarkable medical history; both patients were non-Hispanic White. Patients were mainly non-Hispanic White (78%), followed by Asian (11%), and Hispanic (7.5%); prior injection site reactions noted in 3.1%; most patients had no comorbidities (62%), although most common was hypertension (15%). |
| **Pityriasis rosea** | Case series  | Canada         | BNT162b2 (Pfizer-BioNTech) | 2 F; ages: 60, 75 | Unremarkable medical history; both patients were non-Hispanic White. Patients were mainly non-Hispanic White (78%), followed by Asian (11%), and Hispanic (7.5%); prior injection site reactions noted in 3.1%; most patients had no comorbidities (62%), although most common was hypertension (15%). |
| Cyrenne et al.³⁶   | Case series  | United States  | BNT162b2 (Pfizer-BioNTech) | 374 F, 40 M; median age: 44 | Unremarkable medical history; both patients were non-Hispanic White. Patients were mainly non-Hispanic White (78%), followed by Asian (11%), and Hispanic (7.5%); prior injection site reactions noted in 3.1%; most patients had no comorbidities (62%), although most common was hypertension (15%). |

The table summarizes the methodologies of studies and reports that identified infrequent cutaneous adverse events after the Pfizer-BioNTech or Moderna vaccines. COVID-19, coronavirus disease 2019; F, Female; ITP, immune thrombocytopenia; M, Male.
have noted several patients with crusted, vesicular, painful skin lesions, consistent with herpes zoster reactivation, after both the Pfizer and Moderna vaccines. Two studies reported on a total of 13 patients with zoster-like symptoms, although specific patient factors were not elucidated.⁶,¹³,¹⁴ Another study described 6 patients with autoimmune inflammatory disease who developed herpes zoster reactivation within 2 weeks of receiving the Pfizer vaccine, including in one patient who had previously been vaccinated against herpes zoster. ¹⁷ Most cases were mild and resolved within 6 weeks of antiviral treatment. One study also described a case of zoster reactivation in an older patient. ¹⁸ Currently, there are 1,046 reports of herpes zoster after the Pfizer or Moderna vaccines listed in the VAERS, with nearly 50% of these cases occurring in patients aged >65 years.¹¹ Authors have postulated that immunomodulatory effects of the COVID-19 vaccines may have promoted zoster reactivation,²⁸,²⁹ as has been demonstrated with prior vaccines. ³⁰ Although this temporal association proposes a causal relationship, the concomitant use of immunosuppressive therapies and coexisting comorbidities in select patients confounds this assessment. Further studies that enable incidence measurements may more clearly delineate a mechanism for these findings. In the meantime, heightened monitoring for patients with risk factors for herpes zoster reactivation is warranted.

**Inflammatory reactions to dermal fillers**

Cases of facial swelling in two vaccine recipients with a history of dermatological fillers were noted in Moderna’s clinical trial.⁹ Another study additionally reported on four women with a history of hyaluronic acid dermal filler injections who developed infraorbital and/or perioral edema hours to days after receiving the Pfizer and Moderna vaccines.⁴⁰ These patients ultimately responded to treatment with low-dose oral lisinopril. The authors also noted similar symptoms in patients with confirmed COVID-19 infection, leading them to hypothesize that the inflammatory reaction was potentially triggered by the COVID-19 spike protein. Cases of inflammatory reactions to dermal fillers have also been reported, predominately after the Moderna vaccine.⁶ Despite the apparent rarity of these events, they are important to recognize amidst the expansion of vaccines to the general population and the growing popularity of dermal fillers.⁴¹

**Immune thrombocytopenia**

The VAERS currently lists 260 reports of thrombocytopenia or ITP after the Pfizer or Moderna vaccines.¹¹ Case reports of ITP after these vaccines suggests that it may have a heterogeneous presentation and occur in varying patient populations. A case of thrombocytopenia with markedly decreased platelets to 2,000/µL was described in an otherwise healthy 22-year-old patient after receiving the Pfizer vaccine. ³⁸ Whereas this patient demonstrated notable improvement shortly after treatment with dexamethasone and intravenous immunoglobulin, other patients with additional comorbidities have exhibited a more refractory course. A study reported on a 60-year-old man with liver cirrhosis and chronic kidney disease who developed a generalized purpuric eruption and decreased platelets to 84,000/µL, within a day of receiving the Moderna vaccine.³⁷ There is also a report of severe post-vaccination thrombocytopenia refractory to all standard therapies in a 72-year-old man with several comorbidities.³⁶ The temporal associations in these studies may suggest immune-mediated platelet destruction after the COVID-19 vaccine,³⁶⁻³⁸ as has previously been shown after rubella and influenza vaccines. ³²,³³ Given the overall rarity, authors have also considered that underlying autoimmune conditions or idiopathic causes may play a role. ³⁸ The optimal treatment of suspected ITP after the COVID-19 vaccine also merits further study given that aggressive immunosuppression may dampen the desired immune response. ³⁴

**Final recommendations**

This analysis is limited by variations in the diagnostic criteria for certain eruptions (eg, local injection site reaction versus delayed large local reaction), potentially leading to inconsistent classifications of these events. Additionally, the majority of the referenced studies and the VAERS do not provide case incidence rates among all vaccinated individuals, making it difficult to estimate the specific frequency of each entity. Finally, many initial studies reported findings in health care workers, potentially limiting external validity in the broader population.

Despite these shortcomings, we propose several reassuring clinical considerations for those who are hesitant to be vaccinated. First, the reported reactions are largely self-limited, with the most frequent presentations (eg, local injection site reactions) echoing those from clinical trials. Studies widely concur that these local findings should not discourage vaccination. Allergic-type cutaneous symptoms, including urticaria and angioedema, have been transient and rarely associated with anaphylaxis. The development of uncommon entities such as herpes zoster, dermal filler reactions, and ITP were seldom serious in nature but justify clinical monitoring among certain groups. Although further studies are needed to elucidate specific reaction mechanisms and identify optimal management approaches, these existing reports should reassure patients of the overall compelling safety profiles and benignity of skin reactions that may occur after mRNA COVID-19 vaccination.

**Conflict of interest**

The authors declare no conflict of interest.
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