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.

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Comment and Controversy
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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 Dermatology*[6] published a large institution registry-based analysis, and *Clinics in Dermatology*[7] 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),[6,9,10] reports agree that local injection site reactions are harmless, transient, and largely resolve within 2 to 5 days.[6,16] 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,[7] 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-

Table 1 Frequently reported cutaneous adverse events after COVID-19 vaccines: study findings

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.[26]	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.[27]	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.[12]	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 (median)	Delayed-type, cell-mediated immunity, likely due to a vaccine excipient, lipid nanoparticle, or mRNA component	Management included topical steroids and oral antihistamines; of 15 patients who developed a reaction to the first dose, 11 developed a second-dose reaction
López-Valle et al.[25]	Poorly defined erythematous and edematous plaque at injection site	Not reported	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.[17]	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[24]	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.[21]	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) *Resolution*: Not reported	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.[16]	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 (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.[13]	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 *Hives*: Immediate immune-mediated allergic reaction	Despite side effects, 97.0% of respondents intended to receive the second dose of the vaccine
Kadali et al.[14]	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 *Hives*: Possible IgE-mediated reaction	Despite side effects, the majority (97.6%) of respondents received the second dose of the vaccine

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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
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	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

Table 2 Frequently reported cutaneous adverse events after COVID-19 vaccines: study methodologies

Study authors	Study design	Study location	Administered vaccine	Number of vaccine recipients	Notable patient history
Delayed large local reactions					
Blumenthal et al.[26]	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.[27]	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.[12]	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.[25]	Case report	Spain	BNT162b2 (Pfizer-BioNTech)	1 F; age: 27	Healthcare worker; no significant personal medical history
Morbilliform eruption					
Ackerman et al.[17]	Case report	France	BNT162b2 (Pfizer-BioNTech)	1 M; age: 55	Healthcare worker; no medical history, no prior allergies
Jedlowski and Jedlowski.[24]	Case report	United States	BNT162b2 (Pfizer-BioNTech)	1 M; age: 30	Healthcare worker; no medical history
Various etiologies					
Bianchi et al.[21]	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.[16]	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.[13]	Randomized, cross-sectional survey	United States	mRNA-1273 (Moderna)	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; primarily (83.8%) non-Hispanic White or Asian (9.5%); medical history was not reported
Kadali et al.[14]	Randomized, cross-sectional survey	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 healthcare workers; medical history was not reported
McMahon et al.[6]	Registry-based study	United States	BNT162b2 (Pfizer-BioNTech) (71 patients) mRNA-1273 (Moderna) (343 patients)	374 F, 40 M; median age: 44	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.[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.[15]	Cross-sectional survey	Czech Republic	BNT162b2 (Pfizer-BioNTech)	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.

ology of allergic-type cutaneous symptoms may be complex, act through non–IgE-mediated mechanisms,[22] and, in some cases, reflect a developing host immune response rather than a specific vaccine allergy.[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.[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.[25-27] They are primarily distinguished from immediate injection site reactions by their later time of onset (eg, days versus hours).[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,[6] another study described these delayed reactions in 2.2% of 4,774 Pfizer vaccine recipients.[27] Two reports separately verified the development of delayed local reactions presenting approximately 1 week after the Moderna vaccine.[12,26] Reports suggest that delayed large local reactions are temporary, resolving 3 to 6 days after onset.[6,12,26] These presentations may also be less frequent after the second dose,[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.[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.[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,[6] herpes zoster,[6,13,14,28,29] erythema multiforme,[6,30,31] reactions to dermatologic fillers,[6,32] pernio or chilblains,[6,33] vasculitis,[6,34] pityriasis rosea,[6,35] and immune thrombocytopenia (ITP).[36-38] There are a small but growing number of these entities listed in the VAERS.[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.[9] After widespread vaccination, reports

Table 3 Rarely reported cutaneous adverse events after COVID-19 vaccines: study findings

Study authors	Cutaneous findings	Pathology findings	Associated systemic symptoms or lab findings	Time course of cutaneous symptoms	Proposed diagnosis and mechanism	Management
Herpes zoster						
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
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	Systemic antiviral treatment (unspecified) led to complete improvement
Delayed reaction to hyaluronic acid fillers						
Munavalli et al.[40]	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
Erythema multiforme						
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	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
Nawiman et al.[30]	Erythematous concentric annular targetoid plaques on the palms and soles of bilateral hands and feet	Biopsy-confirmed but specific findings not reported	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
Immune thrombocytopenia						
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 symptoms	Proposed diagnosis and mechanism	Management
Malayala et al.[37]	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
Tarawneh et al.[38]	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	Dexamethasone for 4 days, platelet transfusion, and intravenous immunoglobulin for 2 days led to improved platelet count and symptoms
Chilblains						
Kha et al.[33]	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						
Cyrenne et al.[35]	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	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

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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						
Lam et al.[34]	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 75 F: Not performed	60 F: None 75 F: None	60 F: *Onset*: 14 days after first dose *Resolution*: Significant improvement 3 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
McMahon et al.[6]	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)	Not reported	Most frequently reported systemic symptoms included fatigue (145 patients), myalgia (138 patients), headache (115 patients)	*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.

Table 4 Rarely reported cutaneous adverse events after COVID-19 vaccines: study methodologies

Study authors	Study design	Study location	Administered vaccine	Number of vaccine recipients	Notable patient history
Herpes zoster					
Furer et al.[29]	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
Eid et al.[28]	Case report	Lebanon	mRNA vaccine (unspecified)	1 M; age: 79	Hypertension, coronary artery disease, antineutrophilic cytoplasmic antibody-related glomerulonephritis
Delayed reaction to hyaluronic acid fillers					
Munavalli et al.[40]	Case series	United States	BNT162b2 (Pfizer-BioNTech) (2 patients) mRNA-1273 (Moderna) (2 patients)	4 F; ages: 31, 36, 43, 76	Patients had previously received hyaluronic acid fillers 1-3 years earlier; no allergic history
Erythema multiforme					
Gambichler et al.[31]	Case report	Germany	BNT162b2 (Pfizer-BioNTech)	1 F; age: 74	Dementia; history otherwise unremarkable
Nawimana et al.[30]	Case report	United Kingdom	BNT162b2 (Prizer-BioNTech)	1 F; age: 58	Rheumatoid arthritis, hypertension, herpes labialis, biopsy-confirmed erythema multiforme three years prior
Immune thrombocytopenia					
Helms et al.[36]	Case report	United States	mRNA-1273 (Moderna)	1 M; age: 74	Hypertension, gout, hyperlipidemia, nonischemic cardiomyopathy
Malayala et al.[37]	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
Tarawneh et al.[38]	Case report	United States	BNT162b2 (Pfizer-BioNTech)	1 M; age: 22	Healthcare worker; no history of bleeding, autoimmune disease, or prior vaccine reactions
Chilblains					
Kha et al.[33]	Case report	United States	mRNA-1273 (Moderna)	1 F; age 70	Healthcare worker; medical history remarkable for pityriasis lichenoides chronica, which was stable
Pityriasis rosea					
Cyrenne et al.[35]	Case series	Canada	BNT162b2 (Pfizer-BioNTech)	1 F; age: 20s 1 M; age: 40s	20 F: Alopecia areata, otherwise unremarkable 40 M: No remarkable medical history
Various etiologies					
Lam et al.[34]	Case series	United Kingdom	BNT162b2 (Pfizer-BioNTech)	2 F; ages: 60, 75	Unremarkable medical history; both patients were non-Hispanic White
McMahon et al.[6]	Registry-based study	United States	BNT162b2 (Pfizer-BioNTech) (71 patients) mRNA–1273 (Moderna) (343 patients)	374 F, 40 M; median age: 44	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.[29] 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.[28] 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.[39] 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.[42,43] 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.[44]

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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