Allergies and the COVID Vaccines

What do we know? What don't we know?

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Allergy/Immunology

Disclosures

- I have no disclosures to report

Tuesday, December 8, 2020

- First day the UK is vaccinating for COVID-19, with the Pfizer/BioNTech vaccine
- Two recipients of the vaccine experienced immediate allergic reactions (anaphylaxis)
- They both carried an epinephrine auto-injector for unrelated reasons

Wednesday, December 9, 2020

- "As is common with new vaccines the MHRA (U.K. drug regulator) have advised on a precautionary basis that people with a significant history of allergic reactions do not receive this vaccination after two people with a history of significant allergic reactions responded adversely yesterday,"

- Director of the UK National Health Service (NHS) Stephen Powis

Allergies and Covid Vaccine anaphylaxis?

- These two patients and the subsequent news coverage raised concern about COVID vaccine safety in atopic patients

Anaphylaxis to the Covid Vaccine- what are the numbers?

Summary of v-safe data

	Pfizer-BioNTech	Moderna	All COVID-19 vaccines
People receiving 1 or more doses in the United States*	12,153,536	9,689,497	21,843,033
Registrants completing at least 1 v-safe health check-in†	997,042	1,083,174	2,080,216
Pregnancies reported to v-safe	8,633	6,498	15,131

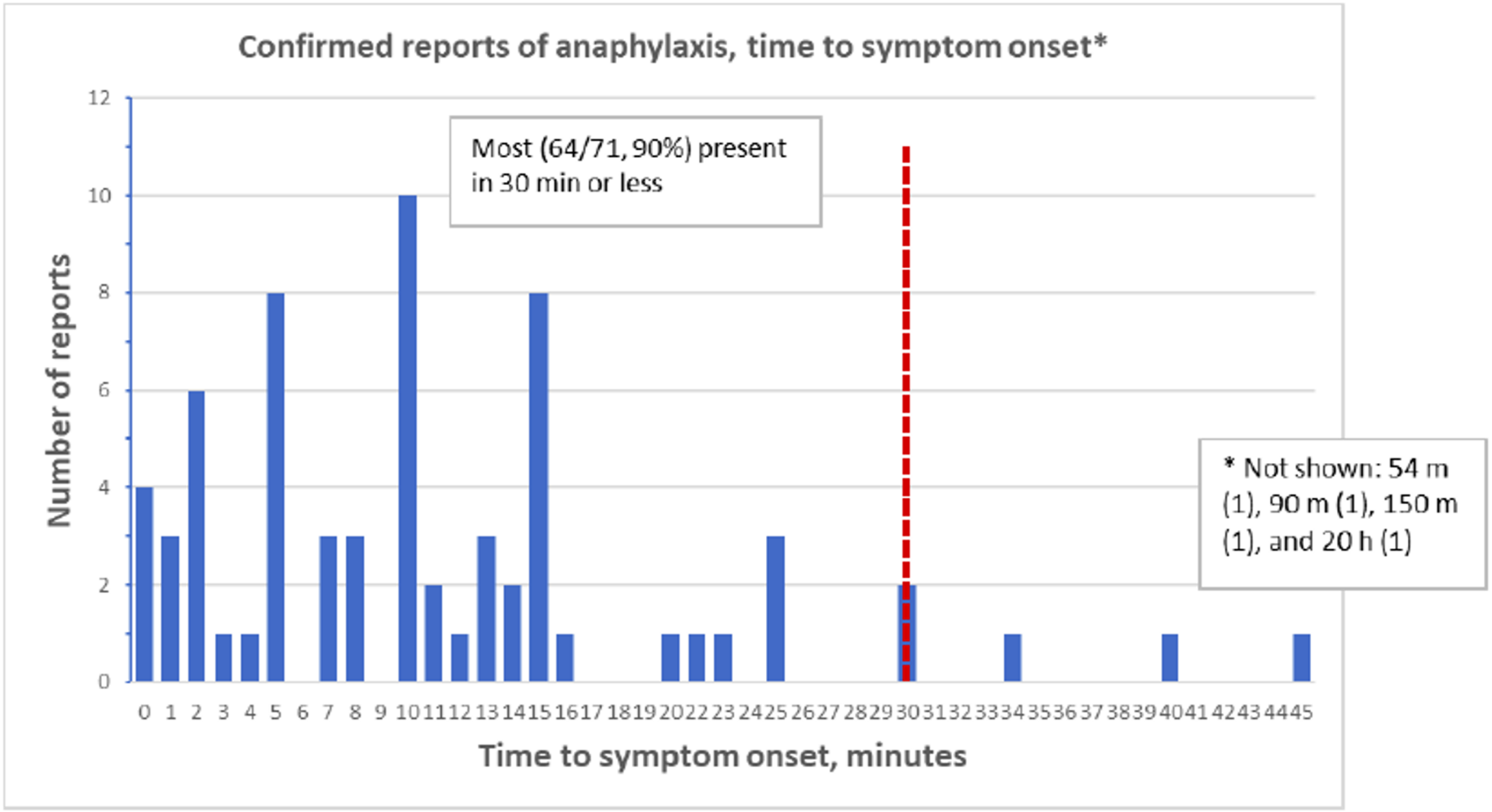
* COVID Data Tracker data as of 1/24/2021
† v-safe data as of 1/20/2021, 5:00 AM ET

Anaphylaxis reports to VAERS following COVID-19 vaccines*

Characteristics	Pfizer-BioNTech (N = 50)	Moderna (N = 21)
Median age, years (range)	38.5 (26–63)	39 (24–63)
Female (%)	47 (94)	21 (100)
Minutes to symptom onset, median (range)	10 (<1–1200 [20 hr])†	10 (<1-45)
Symptom onset ≤15 minutes (%)	37 (74)	18 (86)
Symptom onset ≤30 minutes (%)	45 (90)	19 (90)
Documented h/o of allergies or allergic rxns (%)	40 (80)	18 (86)
Documented h/o of prior anaphylaxis (%)	12 (24)	5 (24)
Dose number (1st, 2nd, unknown)	42, 3, 5	19, 1, 1

- Common allergies and allergic reactions included to drugs and foods
- Anaphylaxis cases occurred following drugs, foods, contrast media, vaccines, insect stings, unspecified

* Reports received through January 18, 2021; Includes case reports that met Brighton Collaboration case definition criteria for anaphylaxis at Levels 1, 2, or 3
†20 hour onset was an outlier, the remaining onset for cases with onset >30 minutes were 34, 54, 90, and 150 minutes



Data through January 18, 2021

Estimated anaphylaxis reporting rates following COVID-19 vaccines based on VAERS reports and reported doses administered*

Reported vaccine doses administered	Anaphylaxis cases	Reporting rate (analytic period Dec 14-Jan 18)
Pfizer-BioNTech: **9,943,247**	50	5.0 per million doses admin.
Moderna: **7,581,429**	21	2.8 per million doses admin.

- Total COVID-19 vaccine doses administered thru Jan 18 by sex: Female 61%, Male 36%, Unk 3%
- Previously reported rate for Pfizer-BioNTech vaccine: 11.1 per million doses admin (Dec 14-Dec 23)
  https://www.cdc.gov/mmwr/volumes/70/wr/mm7002e1.htm
- Previously reported rate for Moderna vaccine: 2.5 per million doses admin (Dec 21-Jan 10)
  https://www.cdc.gov/mmwr/volumes/70/wr/mm7004e1.htm

* Data through January 18, 2021

Appendix B: Triage of persons presenting for mRNA COVID-19 vaccination

	CONTRAINDICATION TO VACCINATION	PRECAUTION TO VACCINATION	MAY PROCEED WITH VACCINATION
ALLERGIES	History of the following are contraindications to receiving either of the mRNA COVID-19 vaccines*: • Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components • Immediate allergic reaction‡ of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components^ (including polyethylene glycol)# • Immediate allergic reaction of any severity to polysorbate^#	Among persons without a contraindication, a history of: • Any immediate allergic reaction‡ to other vaccines or injectable therapies*	Among persons without a contraindication or precaution, a history of: • Allergy to oral medications (including the oral equivalent of an injectable medication) • History of food, pet, insect, venom, environmental, latex, etc., allergies • Family history of allergies
ACTIONS	• Do not vaccinate# • Consider referral to allergist-immunologist	• Risk assessment • 30-minute observation period if vaccinated • Consider deferral of vaccination for further risk assessment and possible referral to allergist-immunologist	• 30-minute observation period: Persons with a history of anaphylaxis (due to any cause) • 15-minute observation period: All other persons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• Softens Stool

Original Article

Immediate Hypersensitivity to Polyethylene Glycols and Polysorbates: More Common Than We Have Recognized

Cosby A. Stone, Jr., MD, MPH[a], Yiwei Liu, PhD[b], Mary V. Relling, PharmD[b], Matthew S. Krantz, MD[c], Amanda L. Pratt, MD[a], Andrew Abreo, MD[a], Jonathan A. Hemler, MD[d], and Elizabeth J. Phillips, MD[e] *Nashville and Memphis, Tenn*

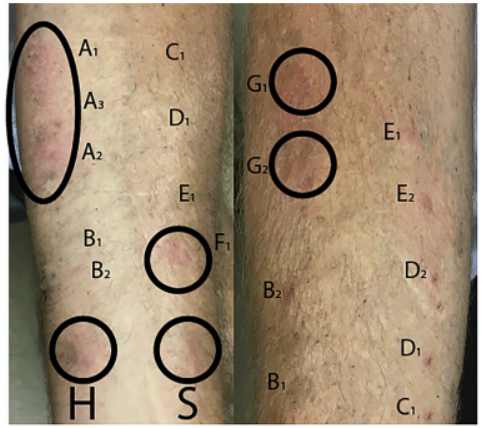


FIGURE 2. Selected skin testing images for patient 1: in the left panel is skin prick testing read at 15 minutes demonstrating positive responses to methylprednisolone acetate (MP acetate), and polyethylene glycol 3350 (PEG 3350). Other tested corticosteroids were negative. In the right panel is intradermal testing read at 15 minutes, which demonstrates a positive response to triamcinolone acetate at 1 and 0.1 mg. Other tested corticosteroids were interpreted as negative (Measurements are recorded in Table I). Key: drug used is indicated by the letter. A = polyethylene glycol 3350 (Miralax), B = methylprednisolone sodium succinate 5 mg/mL, C = budesonide 0.6 mg/mL, D = dexamethason 0.4 mg/mL, E = hydrocortisone 5 mg/mL, F = methylprednisolone acetate 4 mg/mL, G = triamcinolone acetate 1 mg/mL. A subscript 1 = full strength, a subscript 2 = 1:10 dilution, and a subscript 3 = 1:100 dilution.

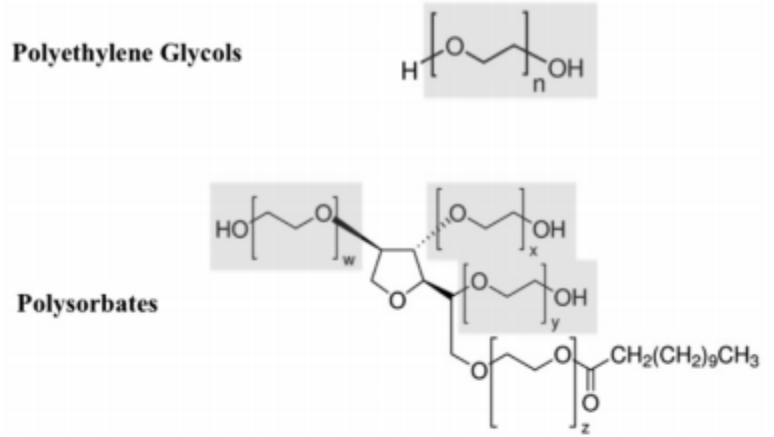


FIGURE 1. Chemical structure of polyethylene glycols and polysorbates. Polysorbate 20 shown. Note the repeating polyether domains contained in both molecules, highlighted in gray.

Pfizer vaccine ingredients

1. The active ingredient is a nucleoside-modified messenger RNA encoding the viral spike (S) glycoprotein of SARS-CoV-2
2. Inactive ingredients:

- Lipids: 4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), [(**polyethylene glycol** [**PEG**])**-2000**]-N,N-ditetradecylacetamide, 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol)
- Electrolytes: potassium chloride, monobasic potassium phosphate, sodiumchloride, dibasic sodium phosphate dihydrate
- Sugar (sucrose)
- The diluent added to the vaccine for administration is saline

Moderna vaccine ingredients

1. The active ingredient is a nucleoside-modified messenger RNA encoding the viral spike (S) glycoprotein of SARS-CoV-2
2. 2.Inactive ingredients:

- Lipids: (SM-102; 1,2-dimyristoyl-rac-glycero-3-methoxy**polyethylene glycol-2000 [PEG2000-DMG]**; cholesterol; and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC])
- Acetic acid
- Sugar (sucrose)
- The diluent added to the vaccine for administration is saline

*several SARS-CoV-2 vaccines in clinical trials also have polysorbate 80 (AstraZeneca, Johnson & Johnson, Novavax, and Sanofi (polysorbate 20)

Note

- No egg as an inactive ingredient in the covid vaccines

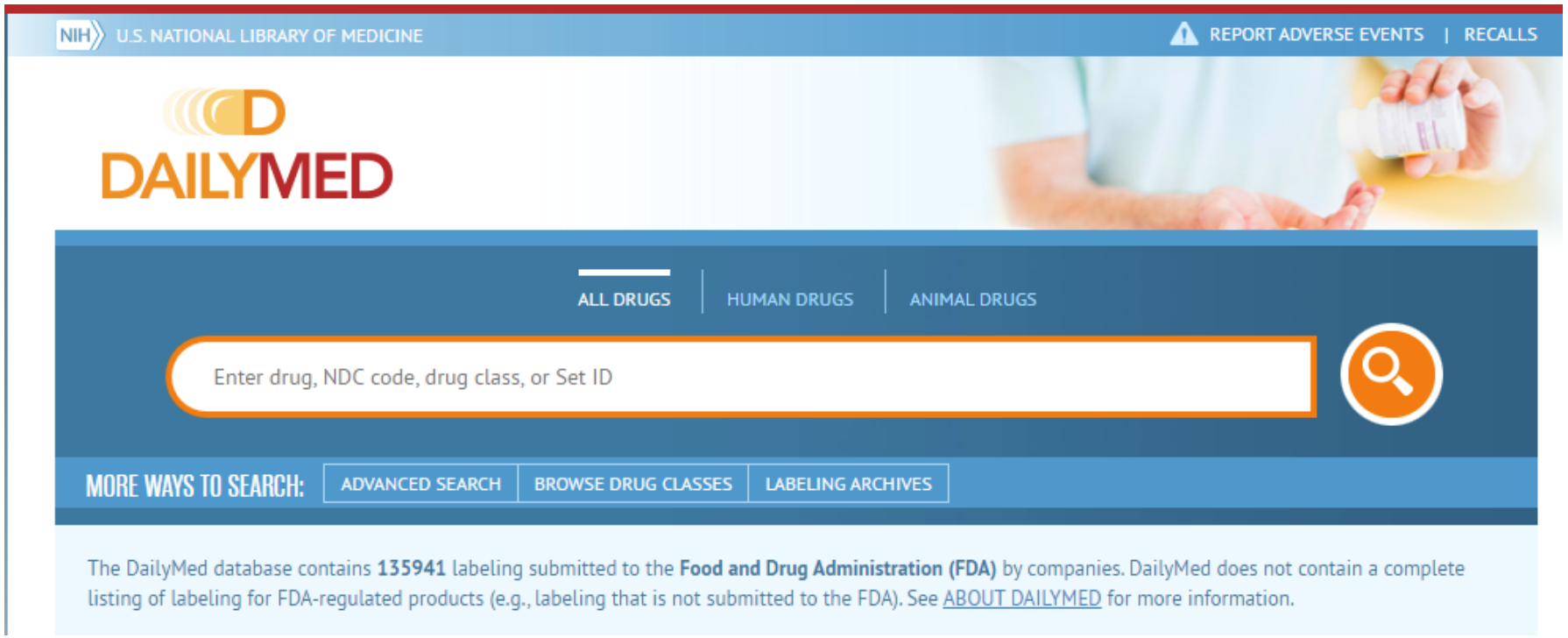
- Pfizer and Moderna both have PEG-2000

Not sure if your patient tolerates/has had issues with PEG or polysorbates?

- Ask them if they have had bowel preps without issue.
- NIH Dailymed

Case 1

- 36yo female with inflammatory bowel disease who one year ago has had hives, wheezing, low blood pressure around the time of receiving adalimumab.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LABEL: HUMIRA- adalimumab kit
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- Medline Plus

NDC Code(s): 0074-0067-02, 0074-0124-01, 0074-0124-02, 0074-0124-03, view more

Packager: AbbVie Inc.

Category: HUMAN PRESCRIPTION DRUG LABEL

DEA Schedule: None

Marketing Status: Biologic Licensing Application

DRUG LABEL INFORMATION

Updated December 17, 2020

If you are a consumer or patient please visit this version.

DOWNLOAD DRUG LABEL INFO: PDF | XML MEDICATION GUIDE: HTML OFFICIAL LABEL (PRINTER FRIENDLY)

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use HUMIRA safely and effectively. See full prescribing information for HUMIRA. HUMIRA® (adalimumab) injection, for subcutaneous ...

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MG/0.2 ML - SINGLE-DOSE PREFILLED SYRINGE - Do not try to inject HUMIRA yourself until you have been ...

INSTRUCTIONS FOR USE

INSTRUCTIONS FOR USE - HUMIRA® (Hu-MARE-ah) (adalimumab) 80 mg/0.8 mL, 40 mg/0.4 mL, 20 mg/0.2 mL and 10 mg/0.1 mL - Single-Dose Prefilled Syringe - Before Injecting: Your ...

PRINCIPAL DISPLAY PANEL

NDC 0074-0124-03 - STARTER PACK FOR - CROHN'S DISEASE, ULCERATIVE COLITIS, OR - HIDRADENITIS SUPPURATIVA - 3 SINGLE-DOSE PREFILLED PENS - HUMIRA® PEN - adalimumab - 80 mg/0.8 mL - FOR SUBCUTANEOUS ...

INGREDIENTS AND APPEARANCE

HUMIRA
adalimumab kit

PRODUCT INFORMATION			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0074-3799

PACKAGING				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0074-3799-02	2 in 1 CARTON	12/31/2002	
1		1 in 1 KIT		
2	NDC:0074-3799-71	2 in 1 CARTON	12/31/2002	11/30/2019
2		1 in 1 KIT		
3	NDC:0074-3799-06	6 in 1 CARTON	12/31/2002	
3		1 in 1 KIT		
4	NDC:0074-3799-03	3 in 1 CARTON	12/31/2002	
4		1 in 1 KIT		

QUANTITY OF PARTS		
Part #	Package Quantity	Total Product Quantity
Part 1	1 SYRINGE	0.8 mL
Part 2	1 PACKET	1 mL

ACTIVE INGREDIENT/ACTIVE MOIETY		
Ingredient Name	Basis of Strength	Strength
ADALIMUMAB (UNII: FYB6T7F842) (ADALIMUMAB - UNII:FYB6T7F842)	ADALIMUMAB	40 mg in 0.8 mL

INACTIVE INGREDIENTS	
Ingredient Name	Strength
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	0.8 mg in 0.8 mL
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	1.22 mg in 0.8 mL
WATER (UNII: 059QF0KO0R)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
MANNITOL (UNII: 3OWL53L36A)	9.6 mg in 0.8 mL
SODIUM PHOSPHATE, MONOBASIC, DIHYDRATE (UNII: 5QW6665956)	0.69 mg in 0.8 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	4.93 mg in 0.8 mL
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	1.04 mg in 0.8 mL
SODIUM CITRATE, UNSPECIFIED FORM (UNII: 1Q73Q2JULR)	0.24 mg in 0.8 mL

Does the patient have a polysorbate 80 issue?

- Unclear, more testing is needed, but it is now on the differential

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* PEG and polysorbate are common excipients in many vaccines, injectable therapies, and other products. Persons with a known (diagnosed) allergy to PEG, another mRNA vaccine component, or polysorbate, have a contraindication to vaccination. Persons with a reaction to a vaccine or injectable therapy that contains multiple components, one of which is PEG, another mRNA vaccine component or polysorbate, but in whom it is unknown which component elicited the immediate allergic reaction have a precaution to vaccination.

‡ Immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms consistent with urticaria, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis that occur within four hours following administration.

Side Effects

Reactogenicity reported to v-safe

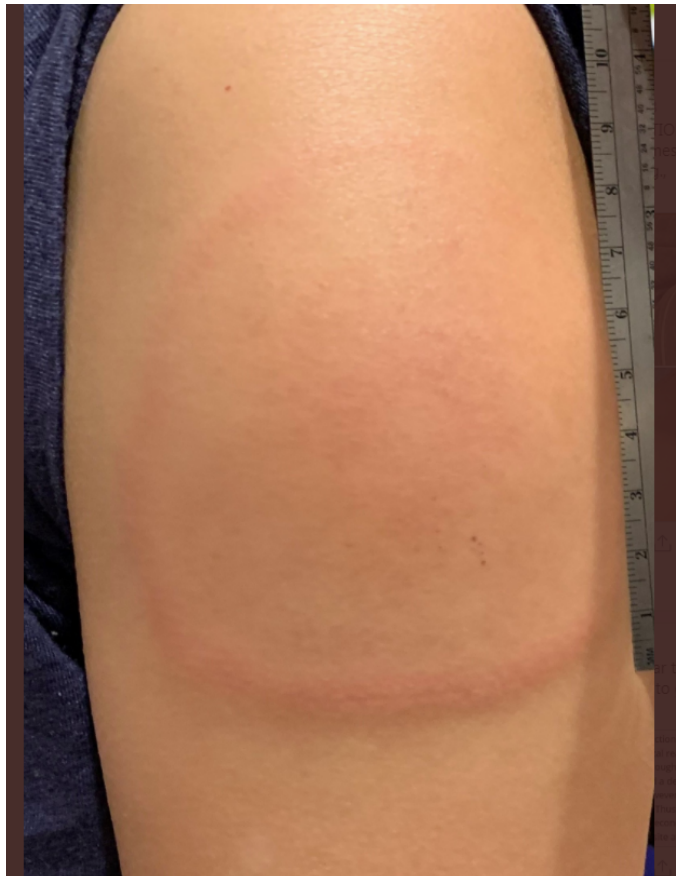
Local and systemic reactions, day 0-7*,†	All vaccines %	Pfizer-BioNTech dose 1 %	Pfizer-BioNTech dose 2 %	Moderna dose 1 %
Pain	70.7	67.7	74.8	70.1
Fatigue	33.4	28.6	50.0	29.7
Headache	29.4	25.6	41.9	26.0
Myalgia	22.8	17.2	41.6	19.6
Chills	11.5	7.0	26.7	9.3
Fever	11.4	7.4	25.2	9.1
Swelling	11.0	6.8	26.7	13.4
Joint pain	10.4	7.1	21.2	8.6
Nausea	8.9	7.0	13.9	7.7

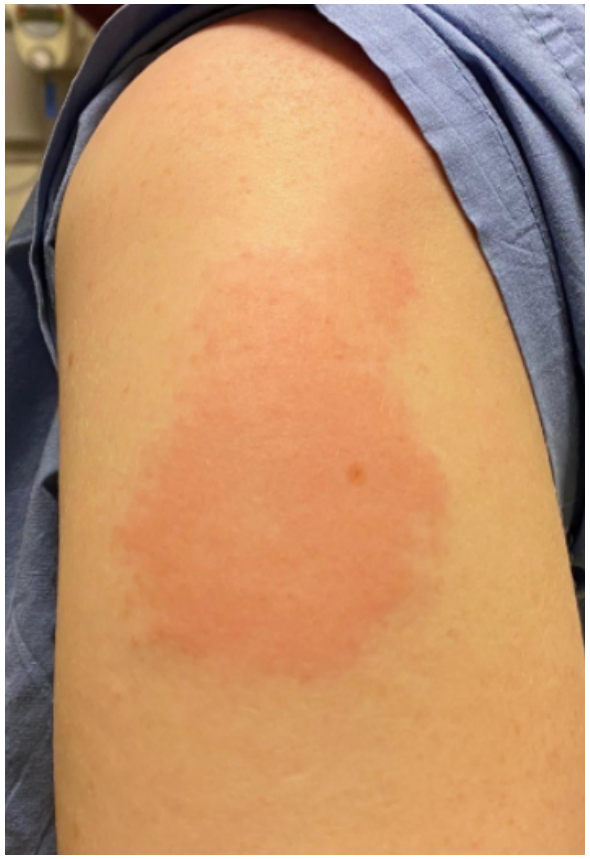
v-safe data lock point 1/14/2021, 5:00 AM ET
Reported on at least one health check-in completed on days 0-7 after receipt of vaccine

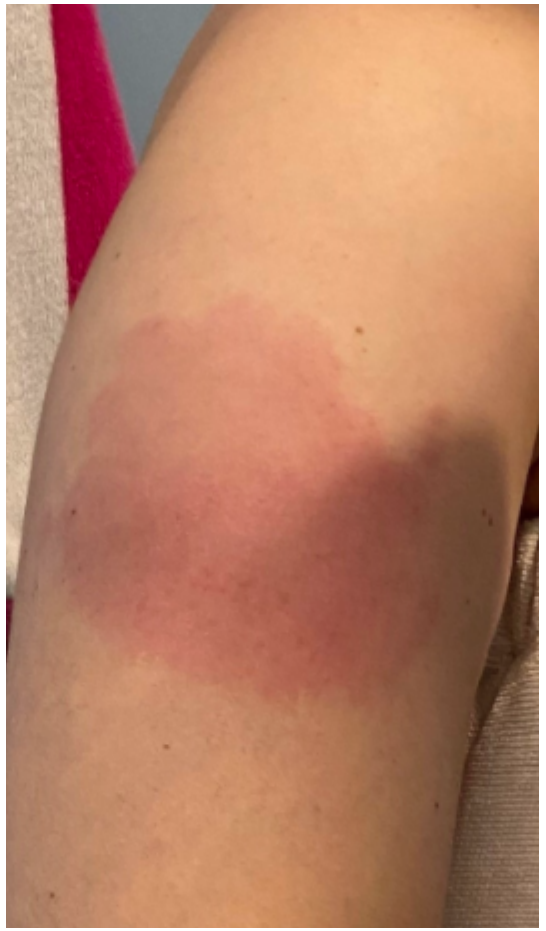
Case 2

- A patient presents to you with concern for allergic reaction to vaccine.

- Received Moderna covid vaccine 1 week ago. Did well in the 15 minutes observation
- Had arm pain and mild headache in the first days, now resolved
- About 1 week into the course developed a red arm







Persons with only a delayed-onset local reaction (e.g., erythema, induration, pruritus) around the injection site area after the first vaccine dose do not have a contraindication or precaution to the second dose. Delayed-onset local reactions have been reported in some individuals, including in Moderna clinical trial participants, beginning a few days through the second week after the first dose, and are sometimes quite large. It is not known whether persons who experienced a delayed-onset injection site reaction after the first dose will experience a similar reaction after the second dose. However, these delayed-onset local reactions are not felt to represent a risk for anaphylaxis upon receipt of the second dose. Thus, individuals with such delayed injection site reactions after the first mRNA COVID-19 vaccine dose should receive the second dose using the same vaccine product as the first dose and at the recommended interval, and preferably in the opposite arm.

QUESTIONS?