

Evaluation and Management of Reactions to Vaccines Including COVID-19

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Disclosures

- None relevant to the talk

Objectives

- Upon completion of this learning activity, participants should be able to discuss CDC guidance on allergy history and COVID-19 vaccination
- Upon completion of this learning activity, participants should be able to advise patients with high-risk allergy histories on COVID-19 vaccination
- Upon completion of this learning activity, participants should be able to integrate an algorithmic approach into evaluation of first dose COVID-19 vaccine reactions

Severe Allergic Reactions to Vaccines are Rare

Table 1. Serious Adverse Reactions to Vaccines

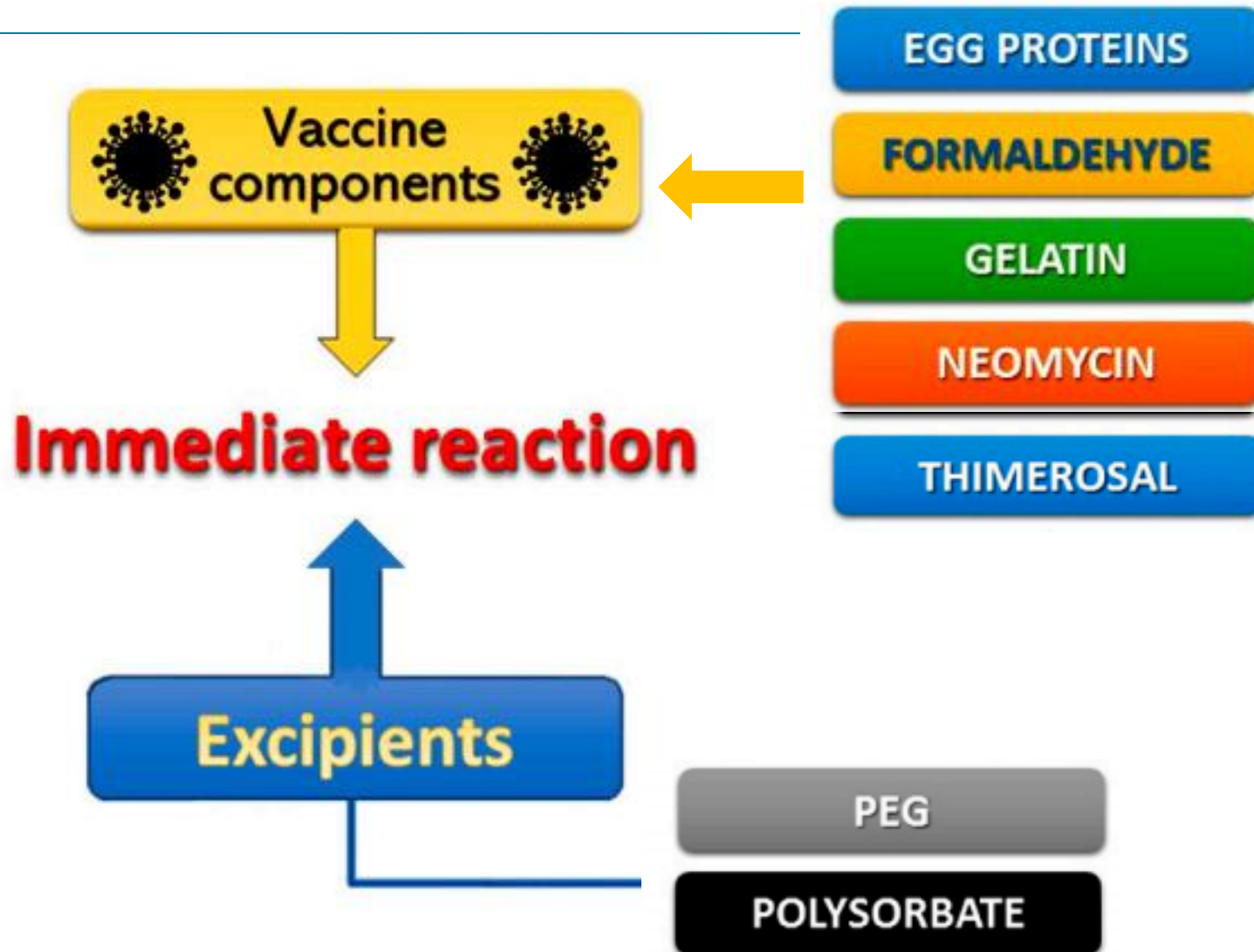
Vaccine	Documented reaction	Approximate rate	Potential allergen
Diphtheria and tetanus toxoids and acellular pertussis (DTaP)	Serious allergic reaction ¹²⁻¹⁴	1 per 1,000,000 doses ¹³	Infanrix syringe contains latex ¹¹
Measles, mumps, and rubella	Immune thrombocytopenic purpura ¹⁴⁻¹⁸ Serious allergic reaction ^{14-19,21}	1 per 20,000 doses ^{19,20} < 1 per 1,000,000 doses ^{19,22,23}	Contains neomycin and gelatin ⁸
Measles, mumps, rubella, and varicella	Febrile seizure ^{14,15,17-21,24}	8.5 per 10,000 doses ²⁰	Contains neomycin and gelatin ⁸
Meningococcal	Serious allergic reaction ^{14,25}	Rare ²⁵	Menomune and Bexsero contain latex ¹¹
Rotavirus	Intussusception ^{12,26}	1 per 20,000 to 100,000 doses ²⁶	Rotarix contains latex in oral applicator of diluents ¹¹

Information from references 8, and 11 through 26.

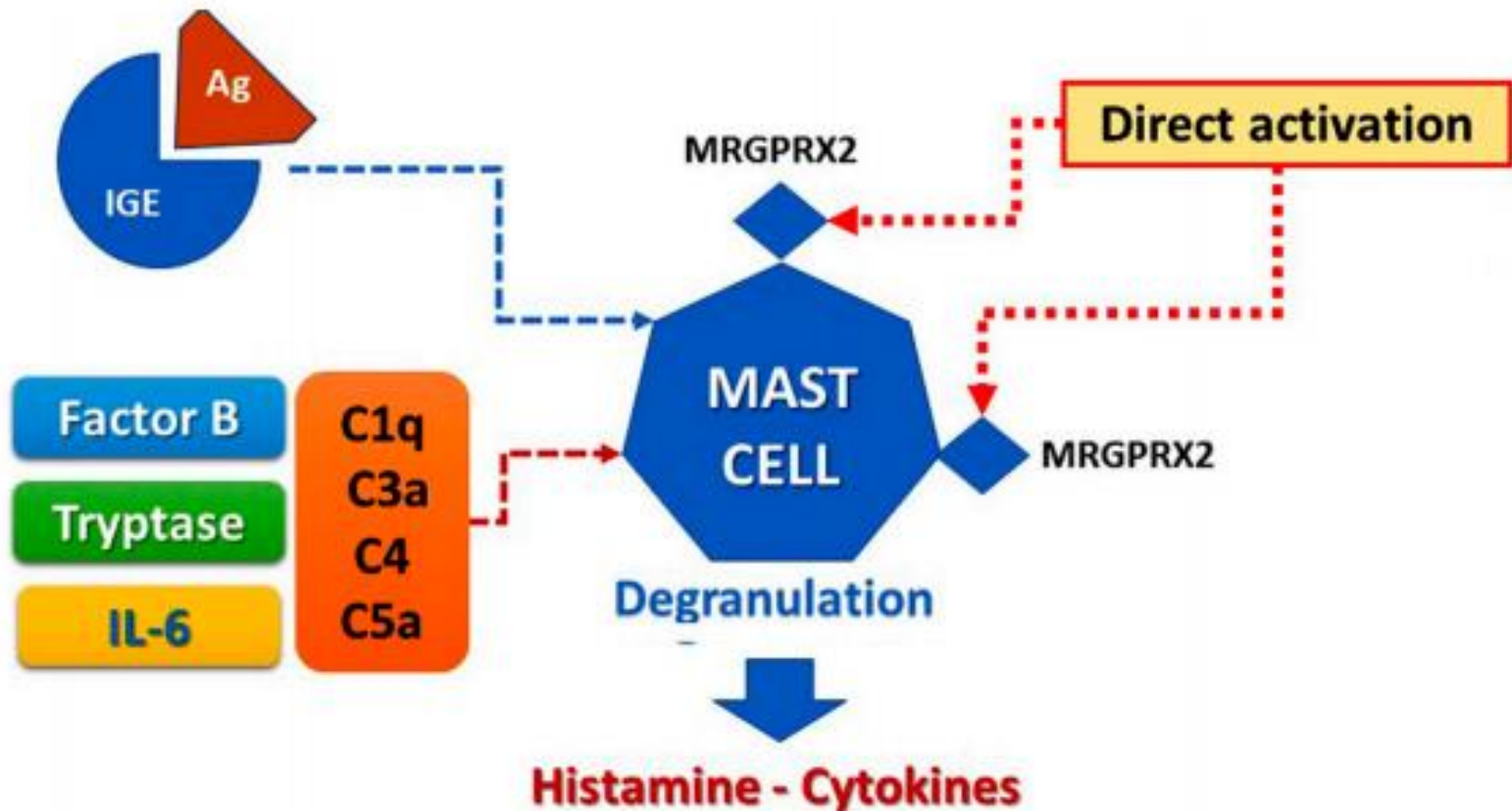
- 33 anaphylaxis cases after administration of 25,173,965 vaccinations
- 1.31 (95% CI, 0.90-1.84) cases per million vaccine doses
- 100% recovered with no deaths
- Attributed to different components or excipients in vaccines



Vaccine Components and Excipients as the Cause of Reactions



Pathophysiology of Vaccine Induced Reactions



What do we know about the Pfizer-BioNTech and Moderna COVID vaccines?

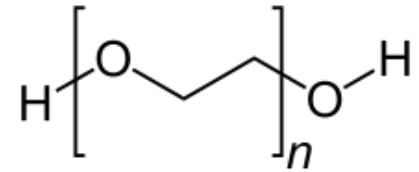
Desc	Pfizer-BioNTech COVID-19 Vaccine	Moderna COVID-19 Vaccine
mRNA	Nucleoside-modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2	Nucleoside-modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2
Lipids	2[(polyethylene glycol)-2000]-N,N- ditetradecylacetamide	1 monomethoxypolyethyleneglycol-2-3-dimyristylglycerol with polyethylene glycol of average molecular weight 2000 (PEG2000-DMG)
	1,2-distearoyl-sn-glycero-3-phosphocholine	1,2-distearoyl-an-glycero-3-phosphocholine
	Cholesterol	Cholesterol
	(4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)	SM-102 (proprietary to Moderna)
Salts & Sugars	Potassium chloride	Tris buffer containing sucrose and sodium acetate
	Monobasic potassium phosphate	
	Sodium chloride	
	Dibasic sodium phosphate dihydrate	
	Sucrose	



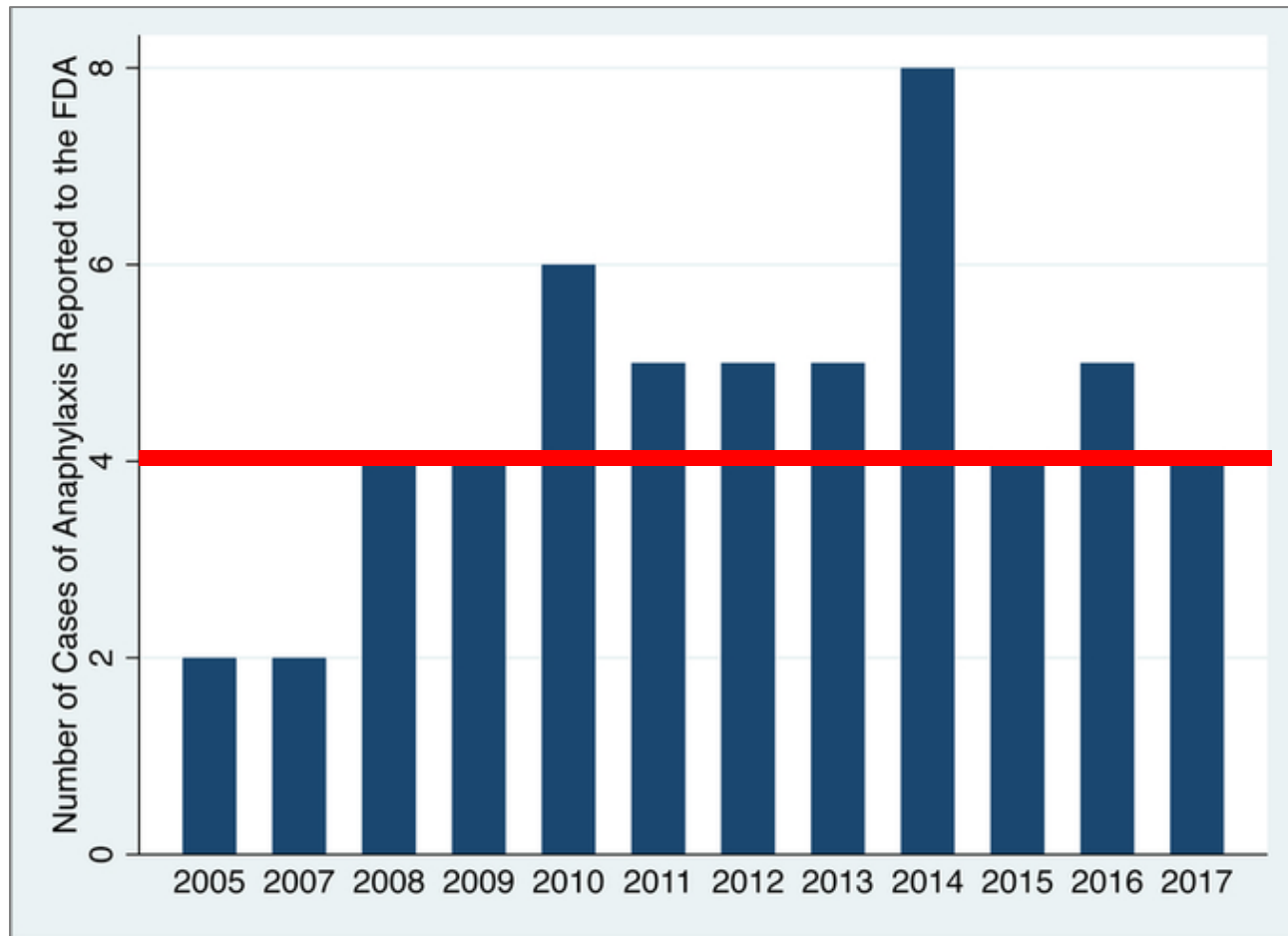
What is Polyethene Glycol (PEG)?

Common, water-soluble ingredient in many products

- Used as a laxative
- Excipient in many pharmaceutical products
- Fused to protein medication to slow clearance from blood

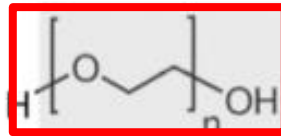


Anaphylaxis to PEG is Rare

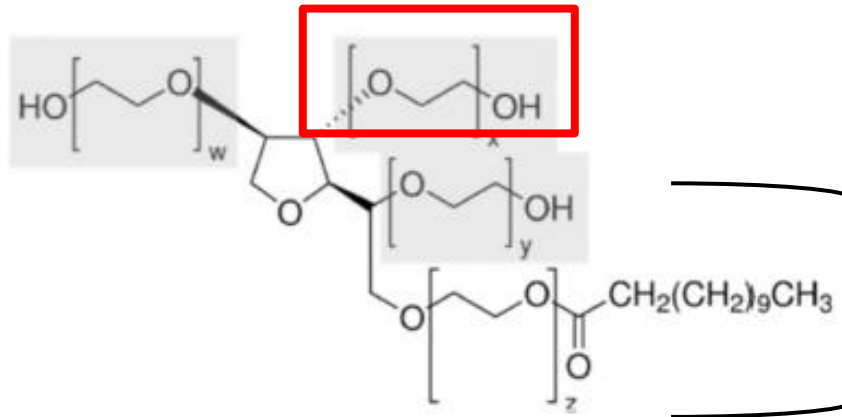


Are Polysorbates Important?

Polyethylene Glycols



Polysorbates



Tdap, Influenza, HPV,
Hepatitis, DTaP + IPV,
Rotavirus,
Zoster, Meningococcal
group B

COVID-19 Vaccine Development Timeline



Five Allergic Reactions (December 17, 2020)

United Kingdom

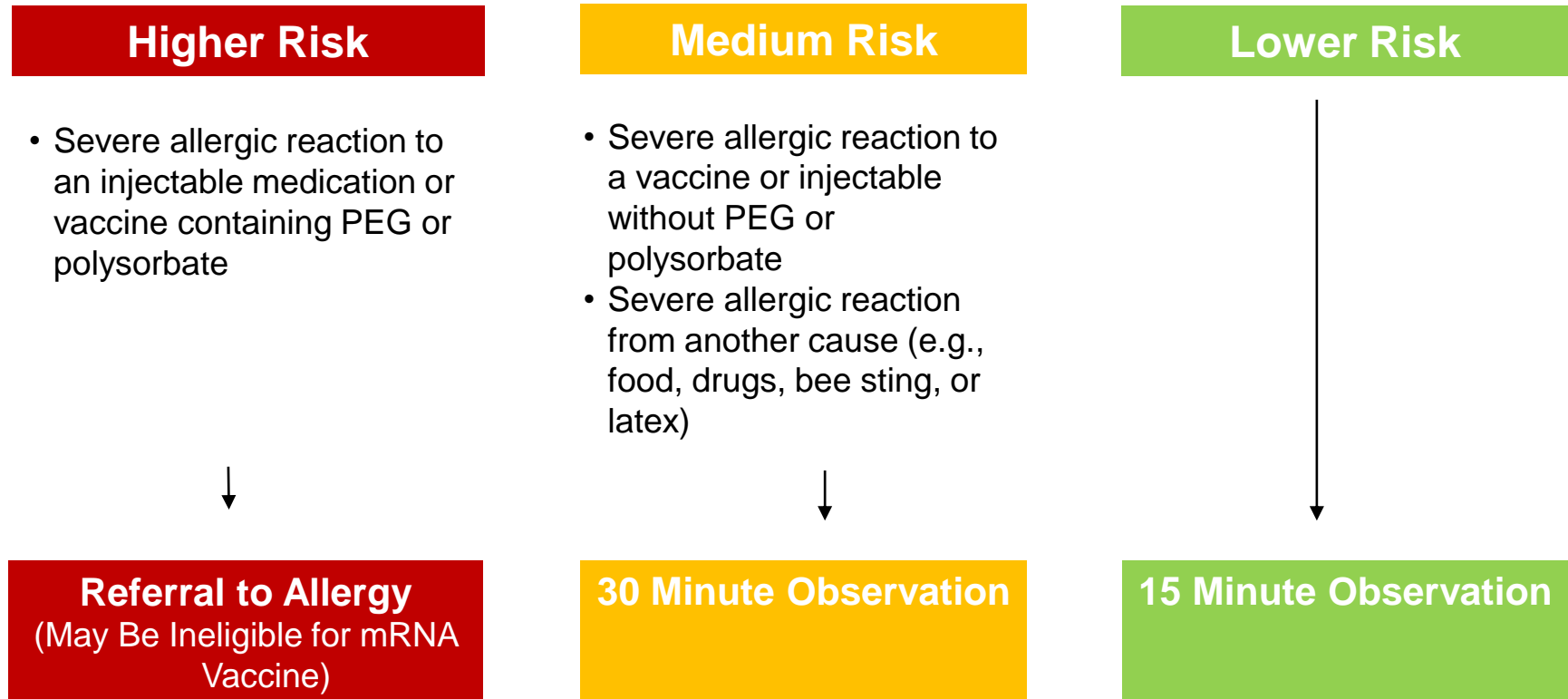
- Three patients with allergic reactions, two potentially anaphylactic
- Patients had a prior history of food or medication allergy
- All fully recovered
- **135,000 vaccinations (as of 12/16/20) but no patients with severe allergies being vaccinated**

United States

- Two patients with presumed anaphylactic reactions (Alaska)
- Case #1: No prior allergic history, flushing and shortness of breath at 10 min, required two doses of epi followed by drip
- Case #2: Eye puffiness, light headedness, and scratchy throat at 10 min, treated with epi
- **Symptoms were during the 15-minute observation period recommended by the CDC**



CDC Guidance: Risk Stratification (Dec 2020)



Role of the Allergist: Pre-Vaccine

Patient Directed Questions

1. Do you have a history of a *severe* allergic reaction to an injectable medication (intravenous, intramuscular, or subcutaneous)? *
2. Do you have a history of a *severe* allergic reaction to a prior vaccine?*
3. Do you have a history of a *severe* allergic reaction to another allergen (e.g., food, venom, or latex)?
4. Do you have a history of a *severe* allergic reaction to polyethylene glycol (PEG), a polysorbate or polyoxyl 35 castor oil (e.g. paclitaxel) containing injectable or vaccine?

Answer "yes" to question 4

Answer "yes" to questions 1, 2 or 3

Answer "no" to all 4 questions

Allergist Risk Assessment and First Vaccine Dose Recommendation

Higher Risk

- History of potential anaphylaxis to an injectable medication or vaccine containing PEG, PEG derivatives, or polysorbate with lack of proven tolerance since incident reaction
- History of potential anaphylaxis to oral PEG (eg, Miralax)

**Clinical Phenotyping
Expanded Skin Testing[§]**
(May Be Ineligible for mRNA Vaccine)

Medium Risk

- History of potential anaphylaxis to a vaccine or injectable medication without PEG or polysorbate
- History of potential anaphylaxis to food, drugs, venom, or latex[¶]
- History of idiopathic anaphylaxis

**Routine Vaccination with
30 Minute Observation**

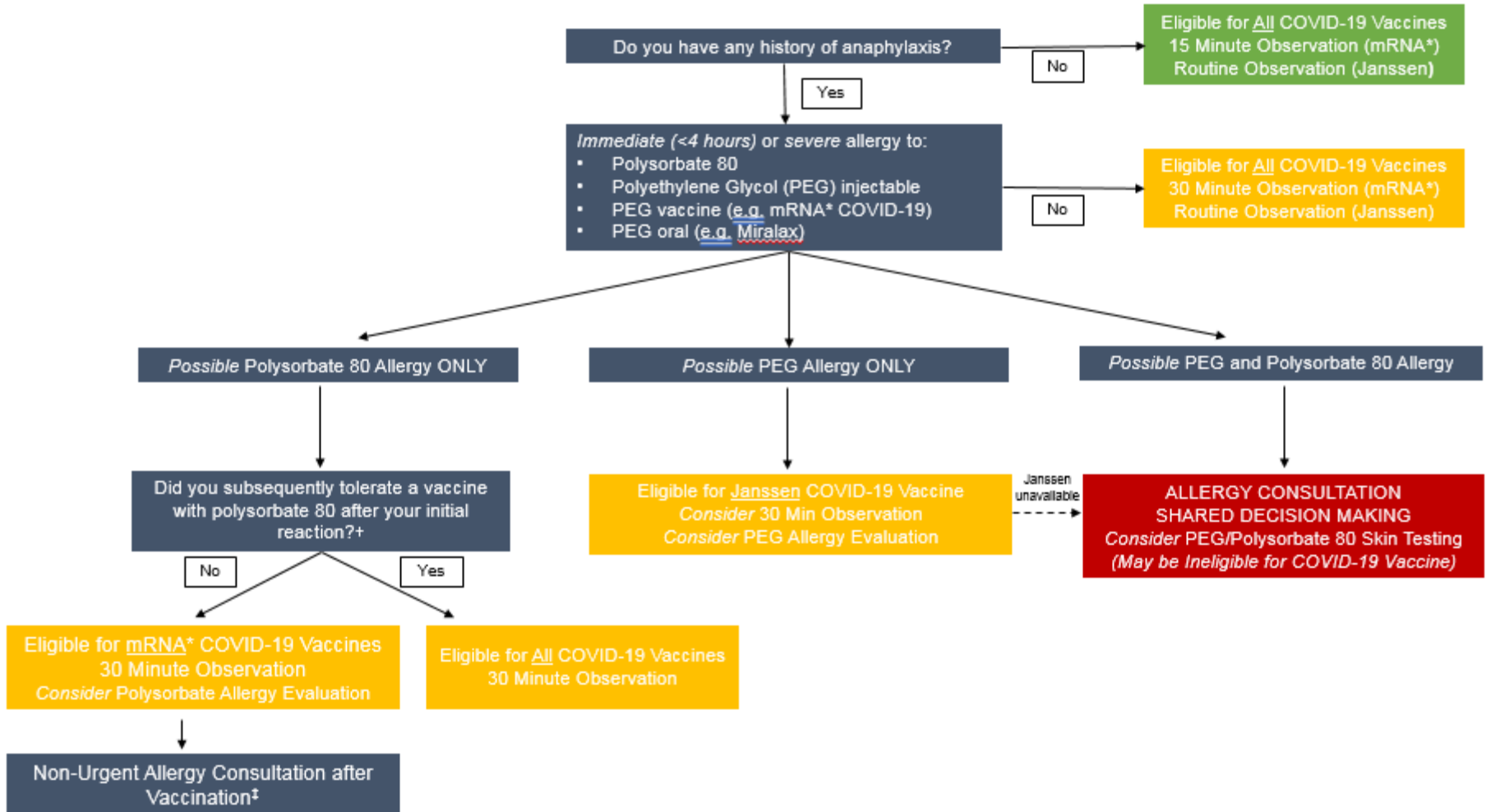
Lower Risk

- History of food, drug(s), venom, or latex allergy except anaphylaxis
- Any prior reaction to vaccines except anaphylaxis
- Mastocytosis/mast cell activation
- Allergic rhinitis and asthma

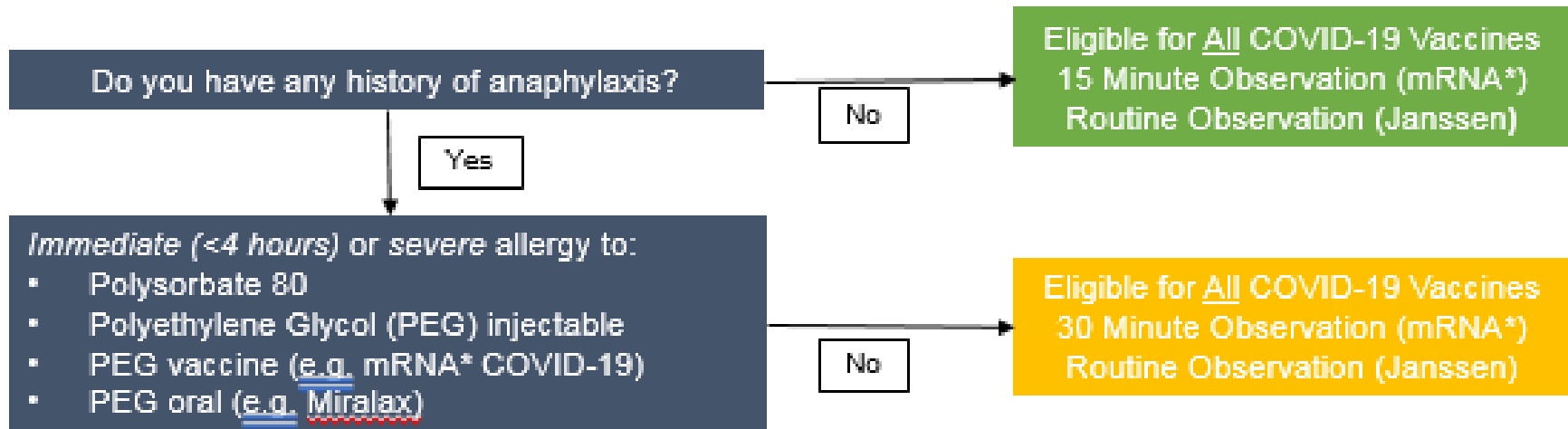
**Routine Vaccination with
15 Minute Observation**



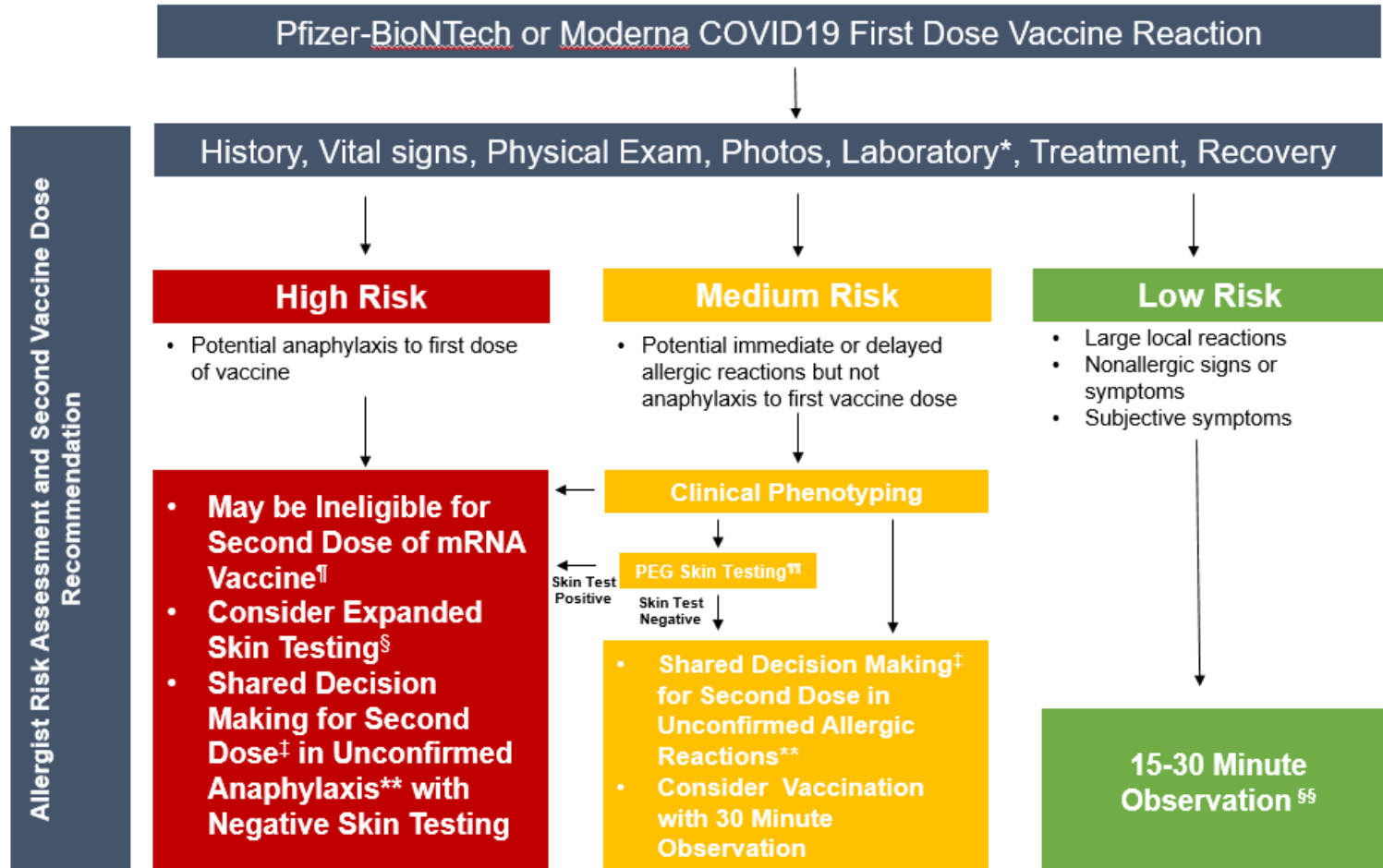
Updated Algorithm: Pre-Vaccination



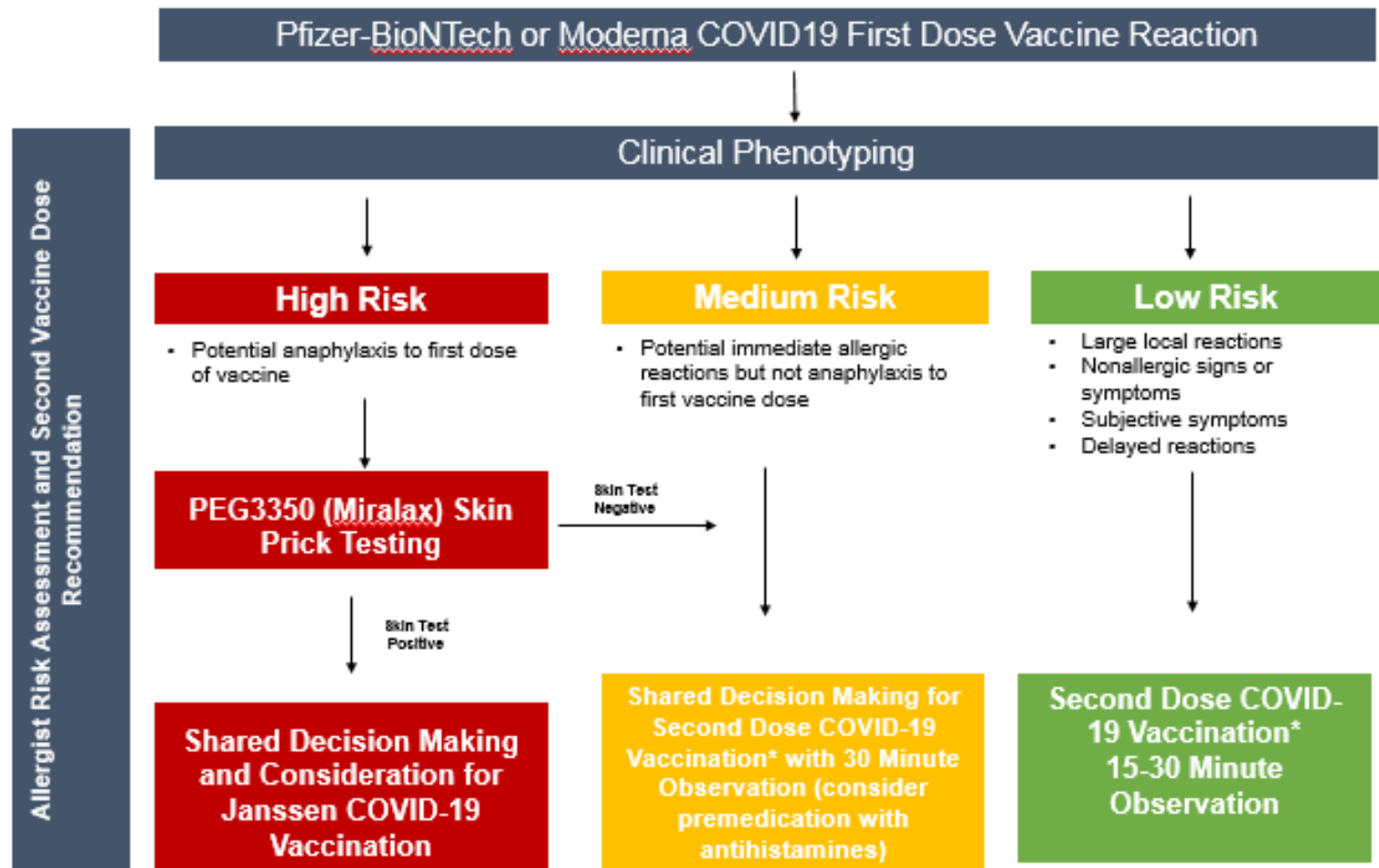
Updated Algorithm: Pre-Vaccination



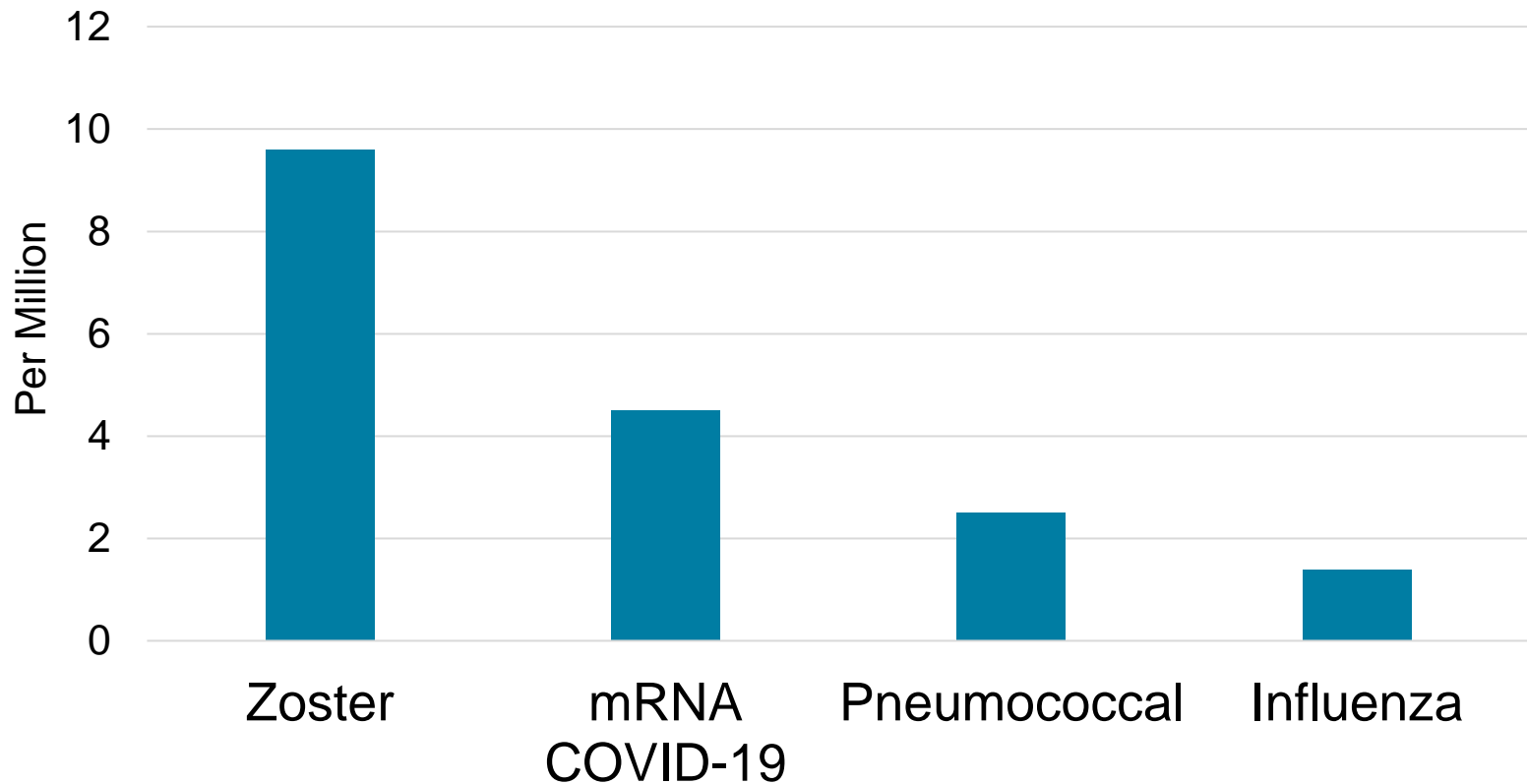
Role of the Allergist: First Dose Reaction



Updated Algorithm: After First Dose mRNA Vaccine Reaction



Vaccine Anaphylaxis Rates: United States



J&J COVID-19 Vaccine and Allergic Reactions

- One hypersensitivity reaction likely related to the vaccine, not classified as anaphylaxis, was reported
 - urticaria two days after vaccination and angioedema of the lips without respiratory distress four days after vaccination
- One case of anaphylaxis among 110,000 in an ongoing open-label study in South Africa has been reported

Case 1

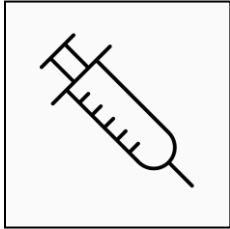
23-year-old female with history of tree nut anaphylaxis, hives after sulfa antibiotics and ulcerative colitis.

No history of vaccine or injectable medication allergic reactions.

No known allergy to polyethylene glycol.

Case 1: COVID-19 Vaccine Dose 1

Moderna



Cetirizine 10 mg

Diphenhydramine 50 mg

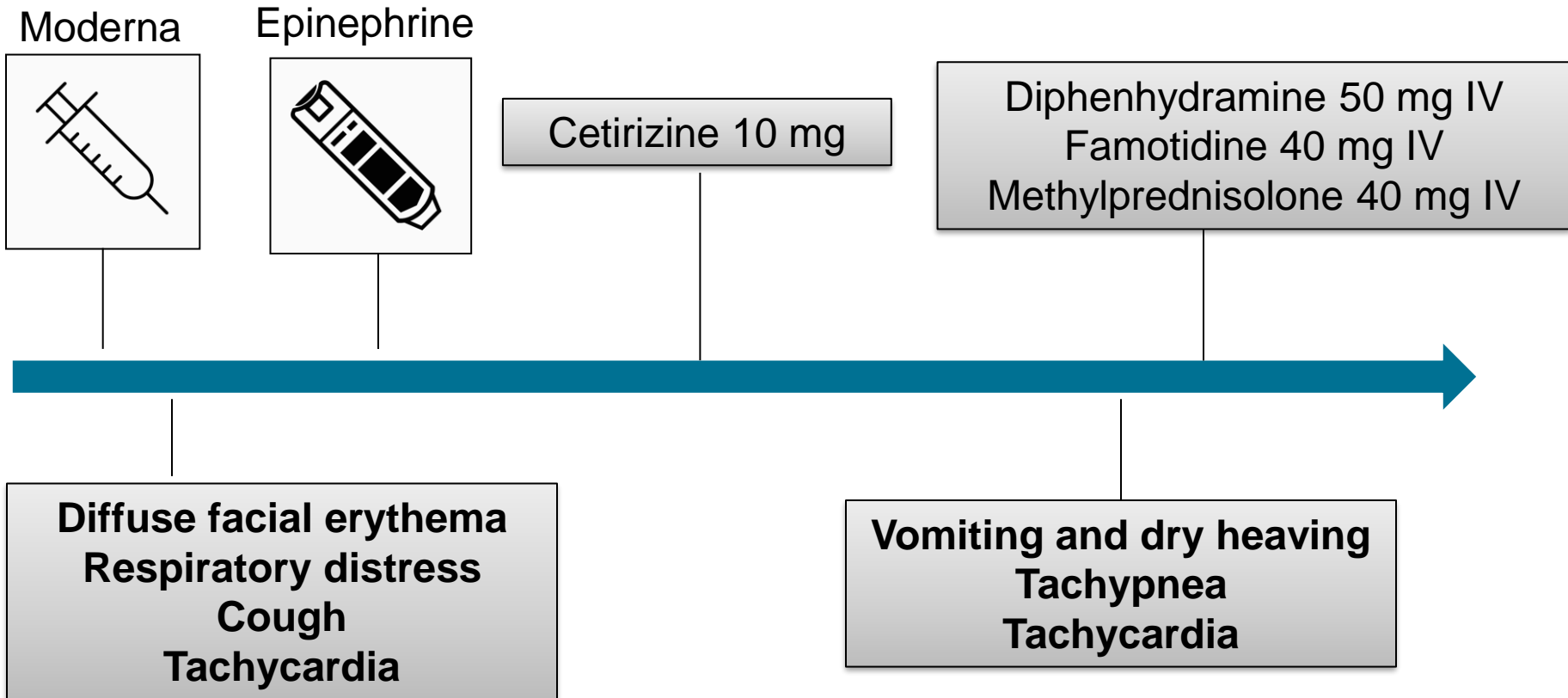


10 mins

Pruritus of mouth and throat
Eye angioedema
Nasal congestion
Nausea

Diffuse hives
Vomiting

Case 1: COVID-19 Vaccine Dose 2



Case 1: COVID-19 Vaccine Allergy Diagnostics

Tryptase

Acute 3.7 ng/mL

Baseline 3.6 ng/mL

ELEVATED TRYPTASE

>11.5 ng/mL

1.2 x baseline +2 ng/mL

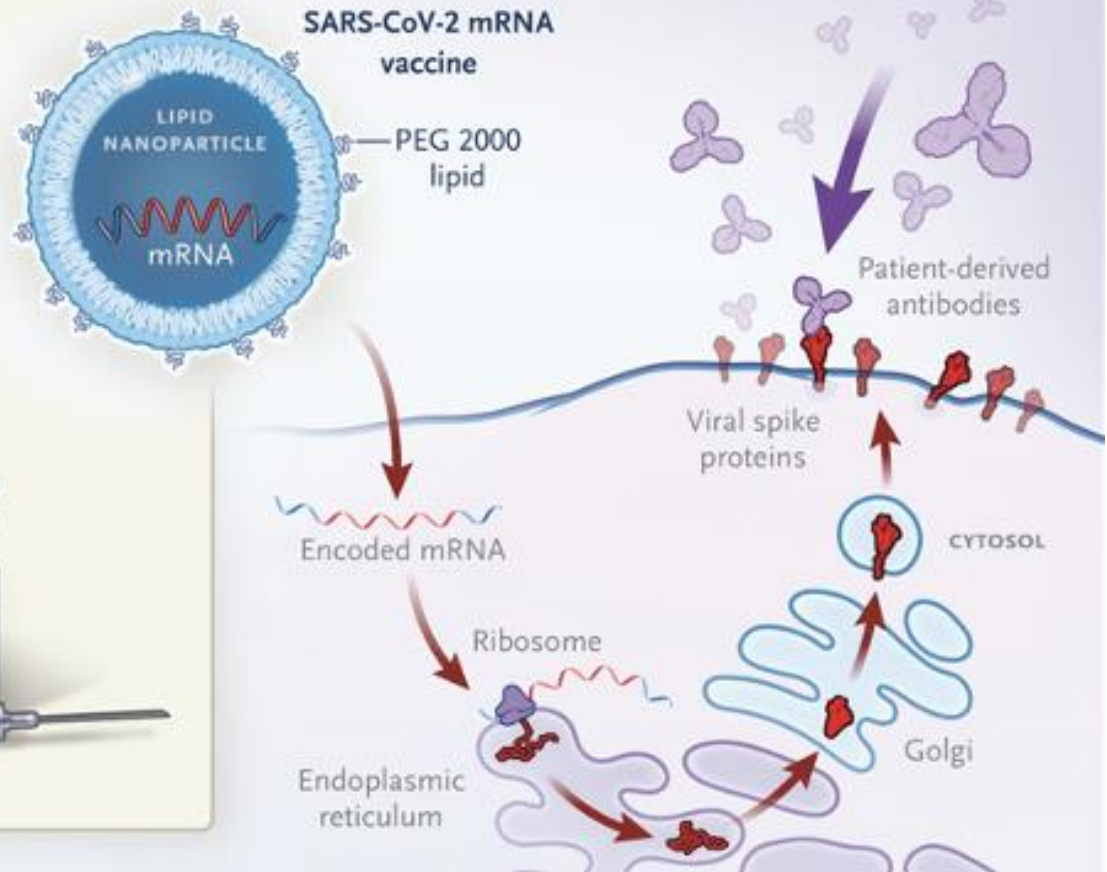
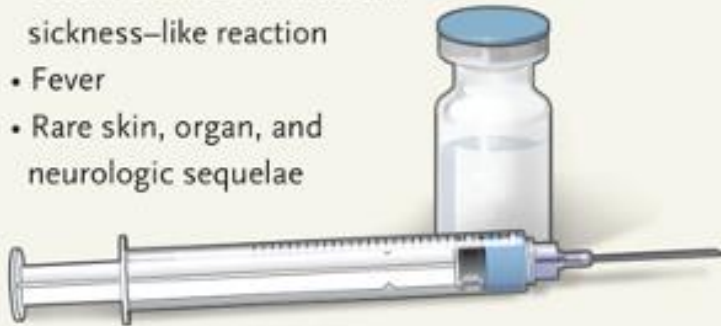
Tryptase level 1-2 hours post reaction



mRNA COVID-19 Vaccine Anaphylaxis

Vaccine Reactions

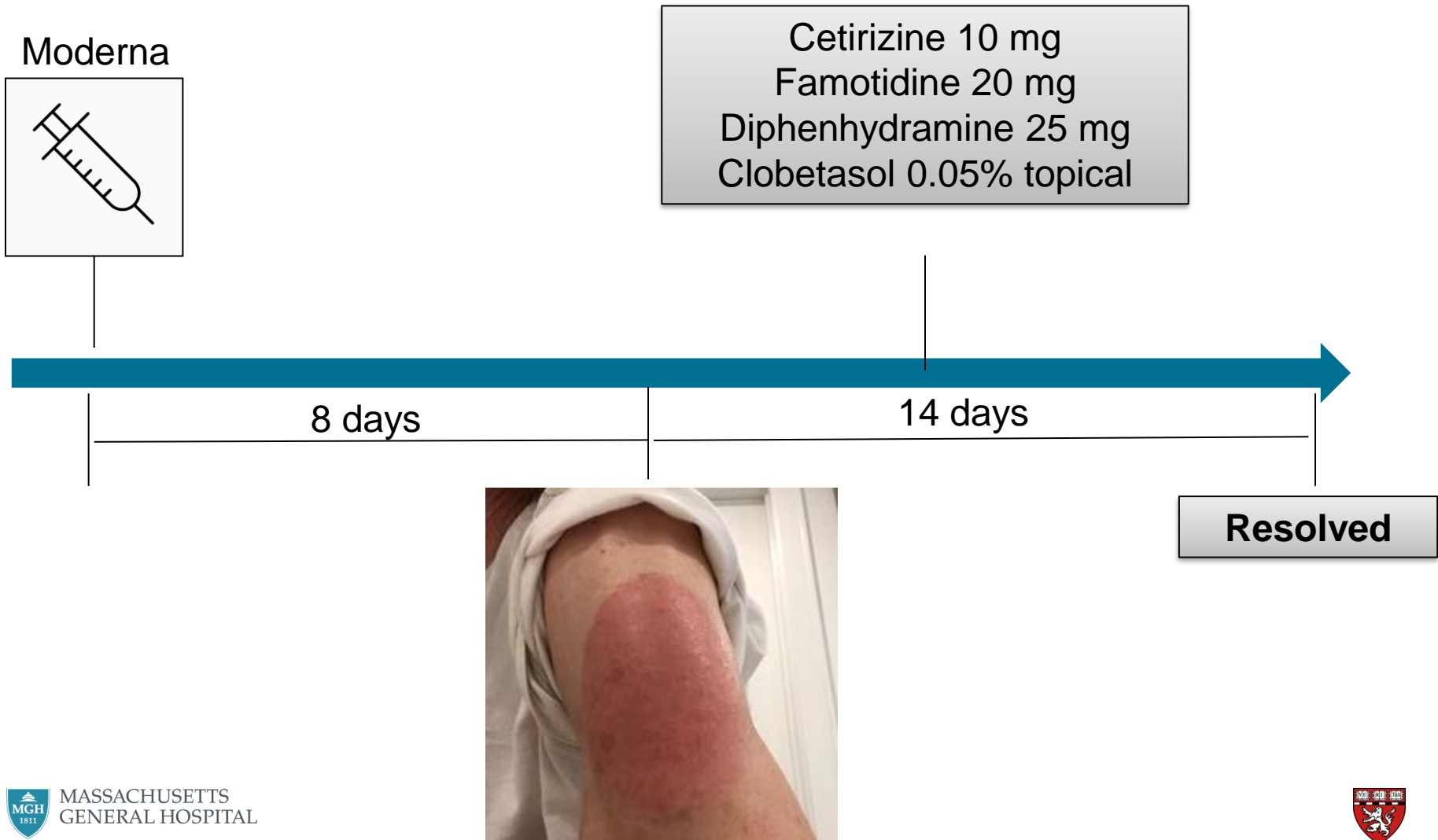
- Immediate
 - IgE
 - Non-IgE
 - Nonimmune (vasovagal syncope)
- Delayed
 - Site reactions
 - Urticaria or benign exanthem
 - Serum sickness and serum sickness–like reaction
 - Fever
 - Rare skin, organ, and neurologic sequelae



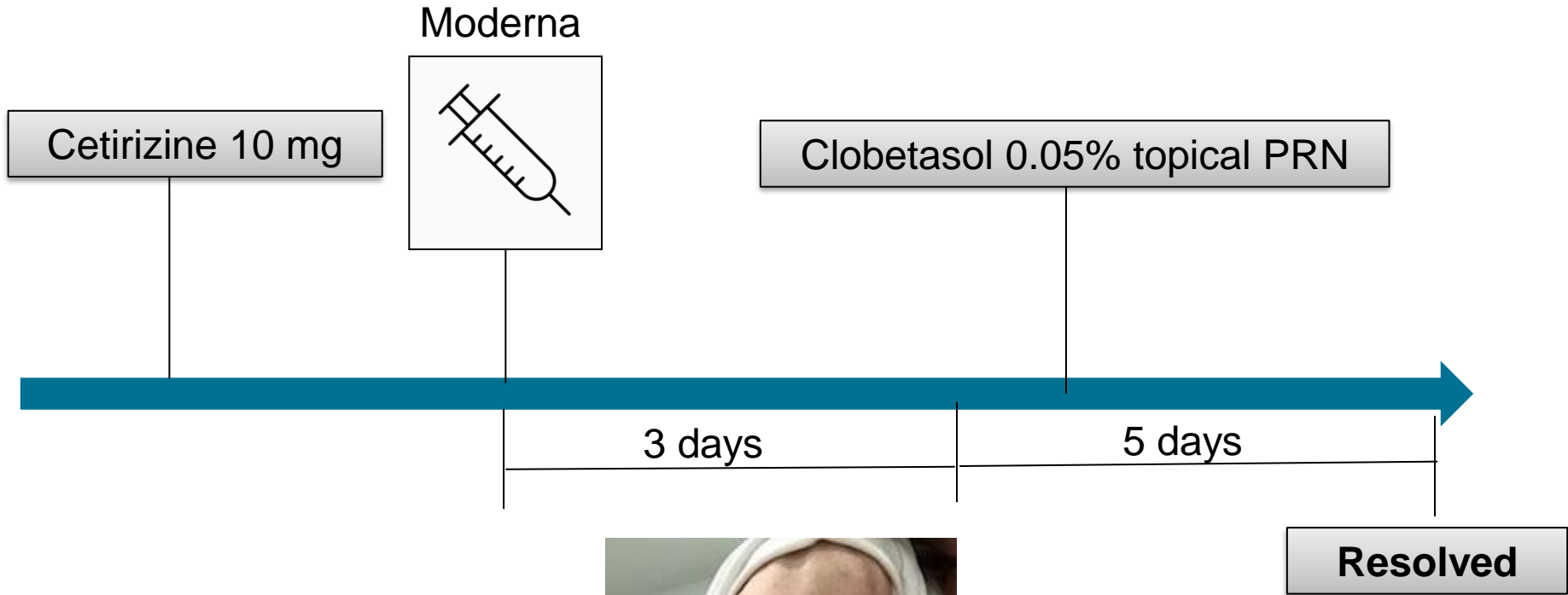
Case 2

61-year-old female with history of hives to iodinated contrast media.

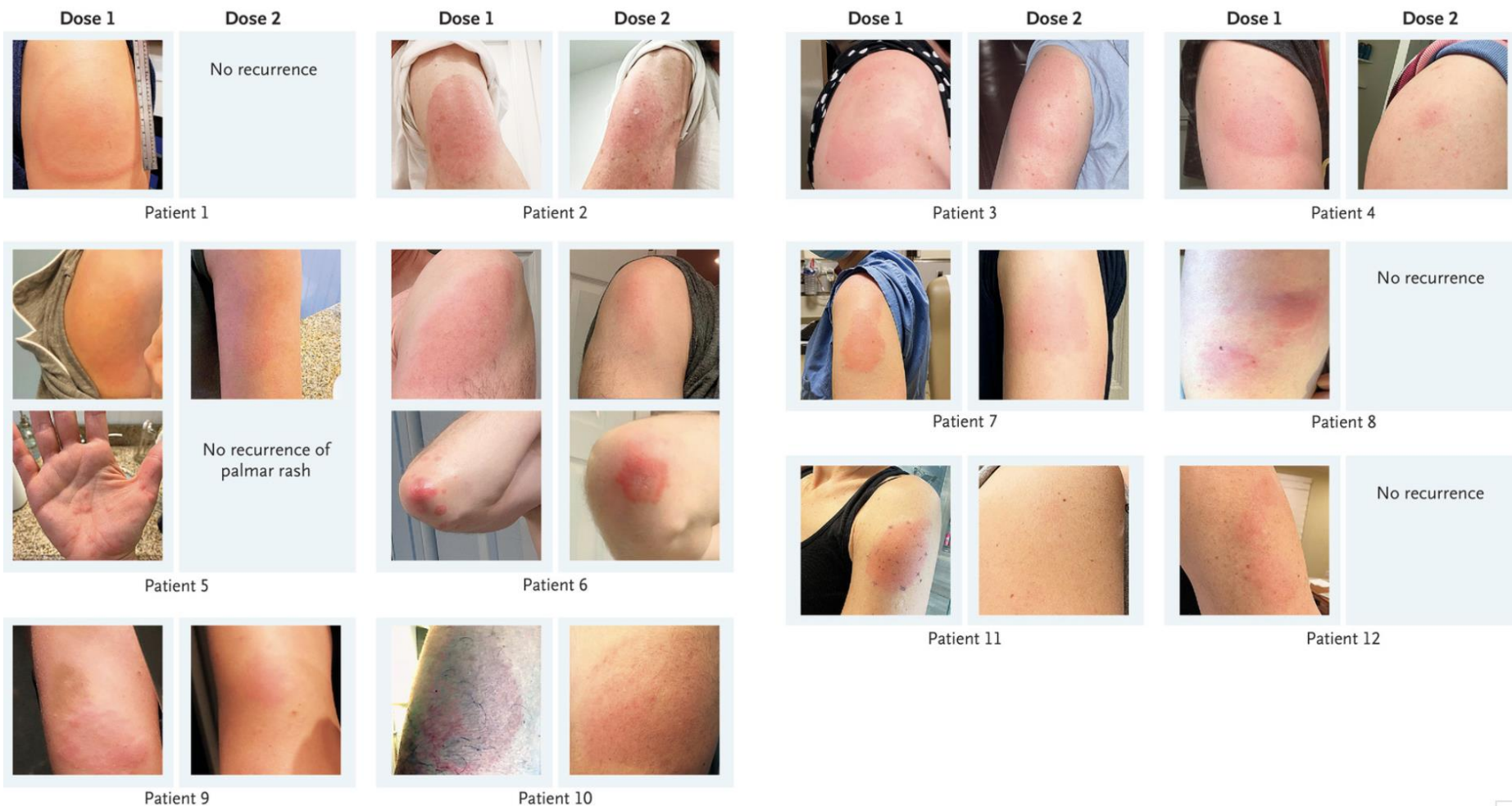
Case 2: COVID-19 Vaccine Dose 1



Case 2: COVID-19 Vaccine Dose 2



Case Series of 12 Patients with Delayed Large Local Reactions after Moderna Vaccination



COVID-19 Vaccine Large Local Reactions

Injection site reactions are **not** a contraindication to subsequent vaccination.

Treatment

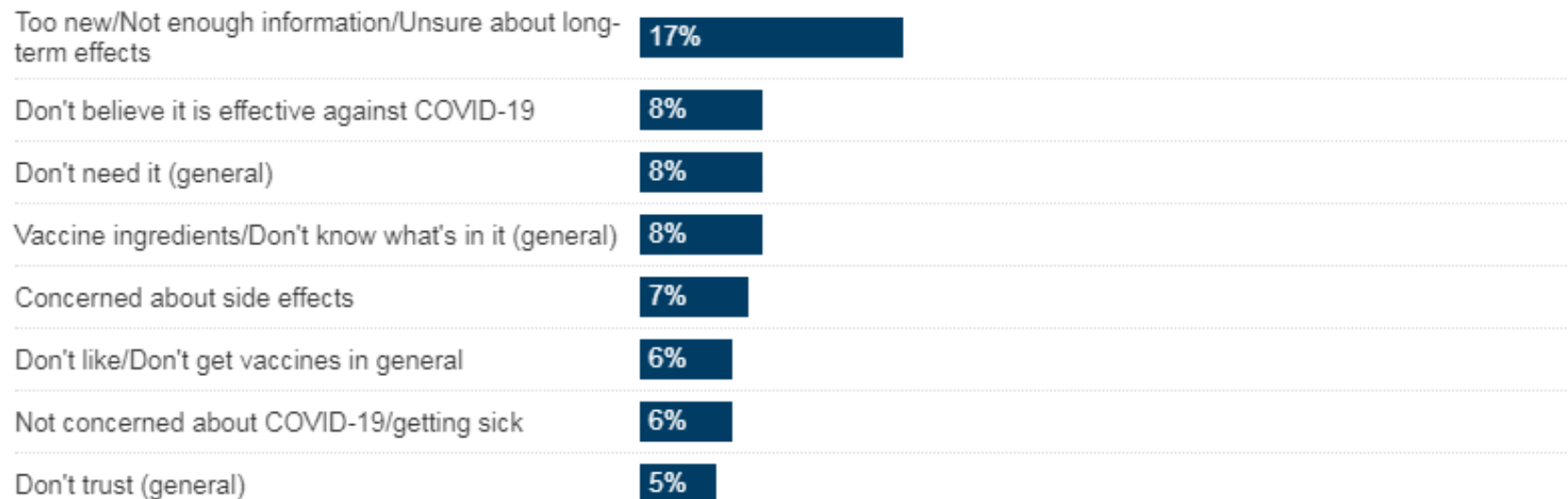
- Ice
- Antihistamines
- Topical corticosteroids



Vaccine Hesitancy

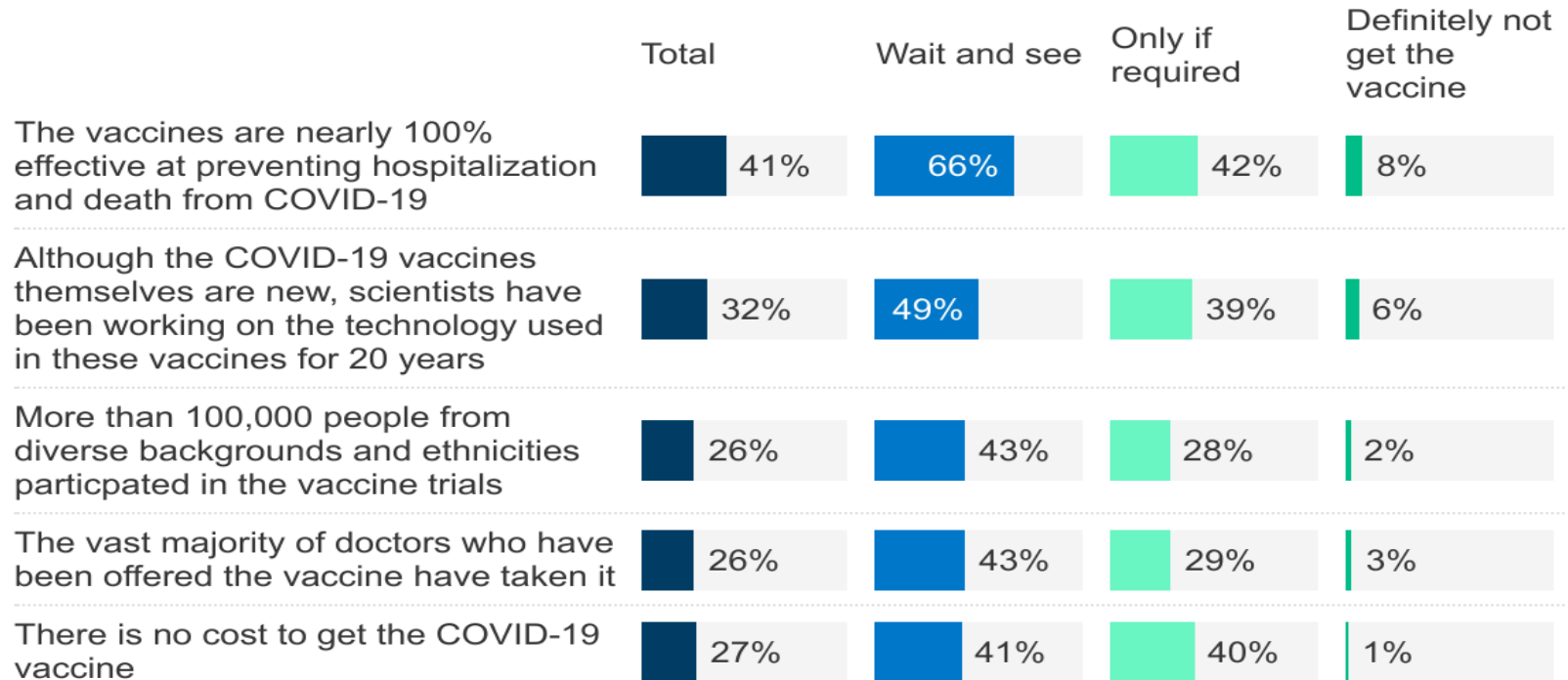
Those Who Say They Will "Definitely Not" Get Vaccinated Cite A Range Of Reasons, Led By Lack Of Long-Term Information

What is the **main** reason you don't want to get the COVID-19 vaccine? (*Open-ended responses*)



Vaccine Hesitancy: What are the Most Effective Messages?

Percent who say they are more likely to get the COVID-19 vaccine if they heard each of the following:



KFF COVID-19
Vaccine Monitor

family
allergy & asthma
care

Credit: Mary Hudelson, M.D.
Managing Partner, Family Allergy & Asthma CARE

Kaiser Family Foundation March Monitor (<https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-march-2021/>)

COVID-19 Vaccine Allergy Learning Points

- Delayed reactions are not a contraindication to second dose mRNA vaccination
- Severe immediate reactions (<4h) should be referred to allergy for further evaluation
- Skin testing to PEG may be helpful in individuals with a history of severe allergic reaction to oral PEG containing medications (e.g. Miralax or Golytely)
- Prior tolerance of a vaccine containing the excipient polysorbate 80 suggests J&J vaccine is an option (*if available*)