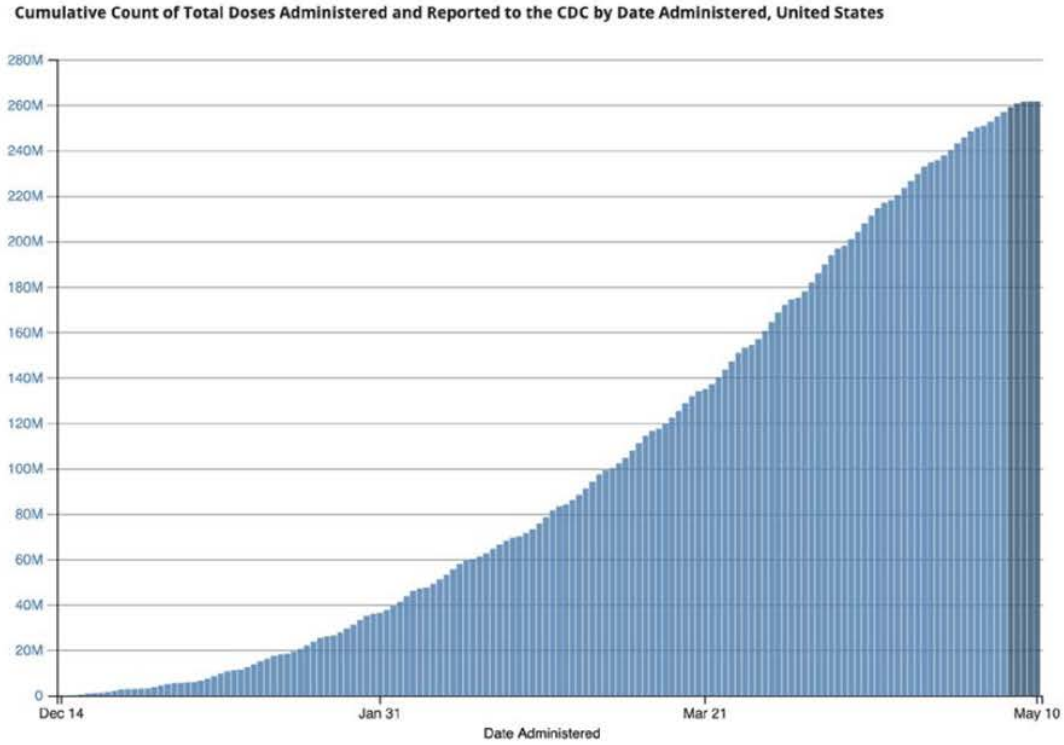
COVID Vaccine Hesitancy And other Vaccine updates

June 7, 2021

U.S. Vaccination Program

- As of May 10
  - 262 million doses administered in the U.S.
    - 140 million Pfizer-BioNTech
    - 113 million Moderna
    - 9 million Janssen
  - 153 million individuals who received ≥1 dose



Vaccine hesitancy is real

- COVID-19 has been a long haul of not having full information
- CDC and WHO have had to back-track on guidelines and recommendations
- 25-30% of Americans in a poll in said they wouldn’t get a COVID-19 vaccine
- The anti-vaccine rhetoric was already very organized with a strong online presence
- Experts not relatable to tackle the misinformation

Basic Vaccine Fact Sheets- United States

The Pfizer-BioNTech COVID-19 vaccine EUA Fact Sheet for Recipients and Caregivers is available here: www.fda.gov/media/144414/download.
The Moderna COVID-19 vaccine EUA Fact Sheet for Recipients and Caregivers is available here: www.modernatx.com/covid19vaccine-eua/eua-fact-sheet-recipients.pdf.

Both are mRNA vaccines- 91% reduction in the risk of symptomatic COVID-19

The Janssen COVID-19 vaccine EUA Fact Sheet for Recipients and Caregivers is available here: www.fda.gov/media/146305/download.

Janssen COVID-19 vaccine is a recombinant, replication-incompetent (unable to reproduce) adenovirus serotype 26 (Ad26) vector vaccine, encoding the stabilized prefusion spike glycoprotein of SARS-CoV-2.

- 66% reduction in the risk of symptomatic COVID-19

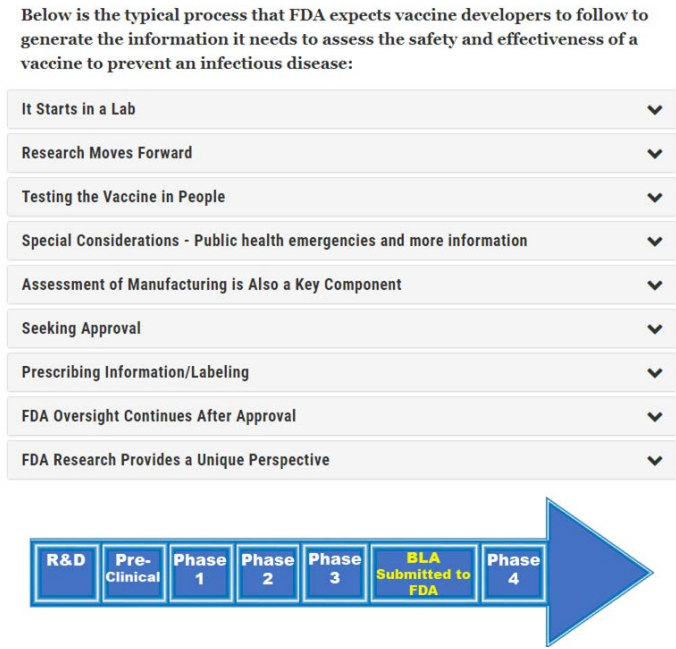
Vaccines were developed too fast?

Operation Warp Speed

- Vaccine Trials, Review, Approval, and Manufacturing are usually sequential
- OWS took several of the steps and instead did them at the same time.
  - As interim data was available during the clinical trial, it would be reviewed
  - They began manufacturing the vaccine while they were running the Phase 3 trials
- The prelicensure safety was thorough and reviewed
- Now there is extensive post licensure safety being reviewed weekly
- Line for patients: “The slow bureaucracy was removed from the process.”

Still seems too fast?

- Govt $$$$$ prioritized COVID-19 vaccines
- Vaccine trials usually take a long time to enroll- not with COVID-19
- Efficacy can be difficult to assess with low prevalence disease- not with COVID-19
- Both the mRNA and adenovirus technologies behind the COVID-19 vaccines were built on decades of research and experience
- Line: “All the money and all the people were focused on this goal.”



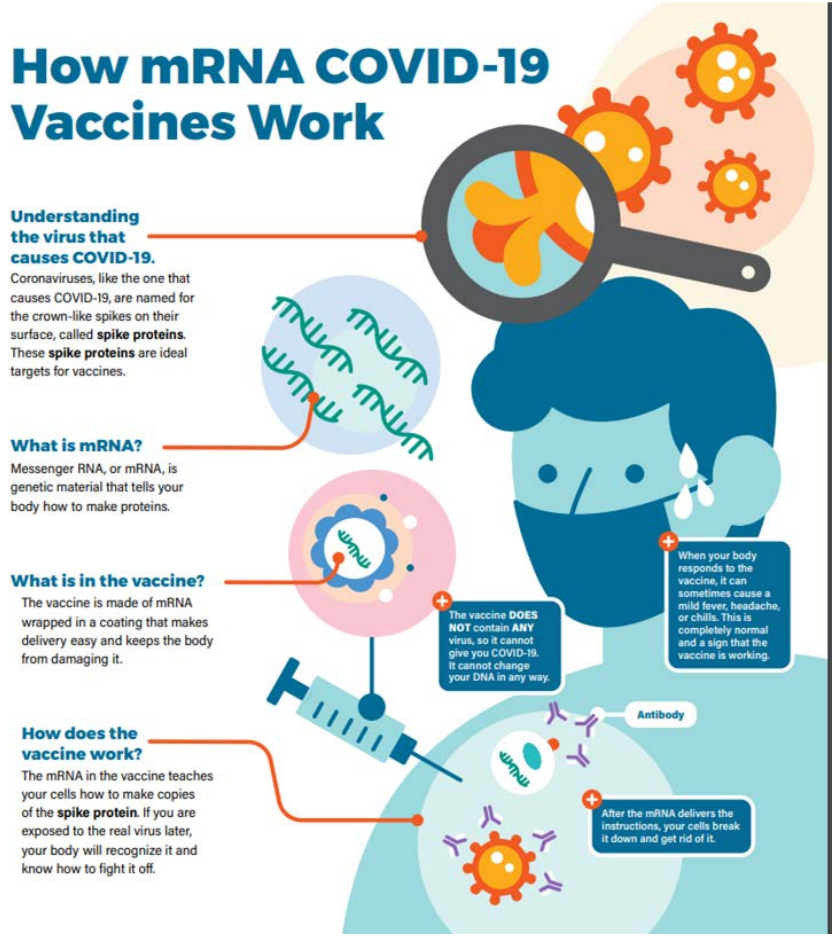
Brand new technology?

Interest has grown in these vaccines because they can be developed in a laboratory using readily available materials.

This means the process can be standardized and scaled up, making vaccine development faster than traditional methods of making vaccines.

Line for patients: "The mRNA technology in vaccines has been around for 15+ years"

mRNA vaccines have been studied before for flu, Zika, rabies, RSV, EBV, and cytomegalovirus (CMV)



Who knows what is in it?

NOT in the COVID-19 mRNA vaccines:

- Animal Products
- Antibiotics
- Blood products
- DNA
- Egg Proteins
- Fetal material
- Gluten
- Microchips
- Pork products
- Preservatives, like thimerosal
- Soy

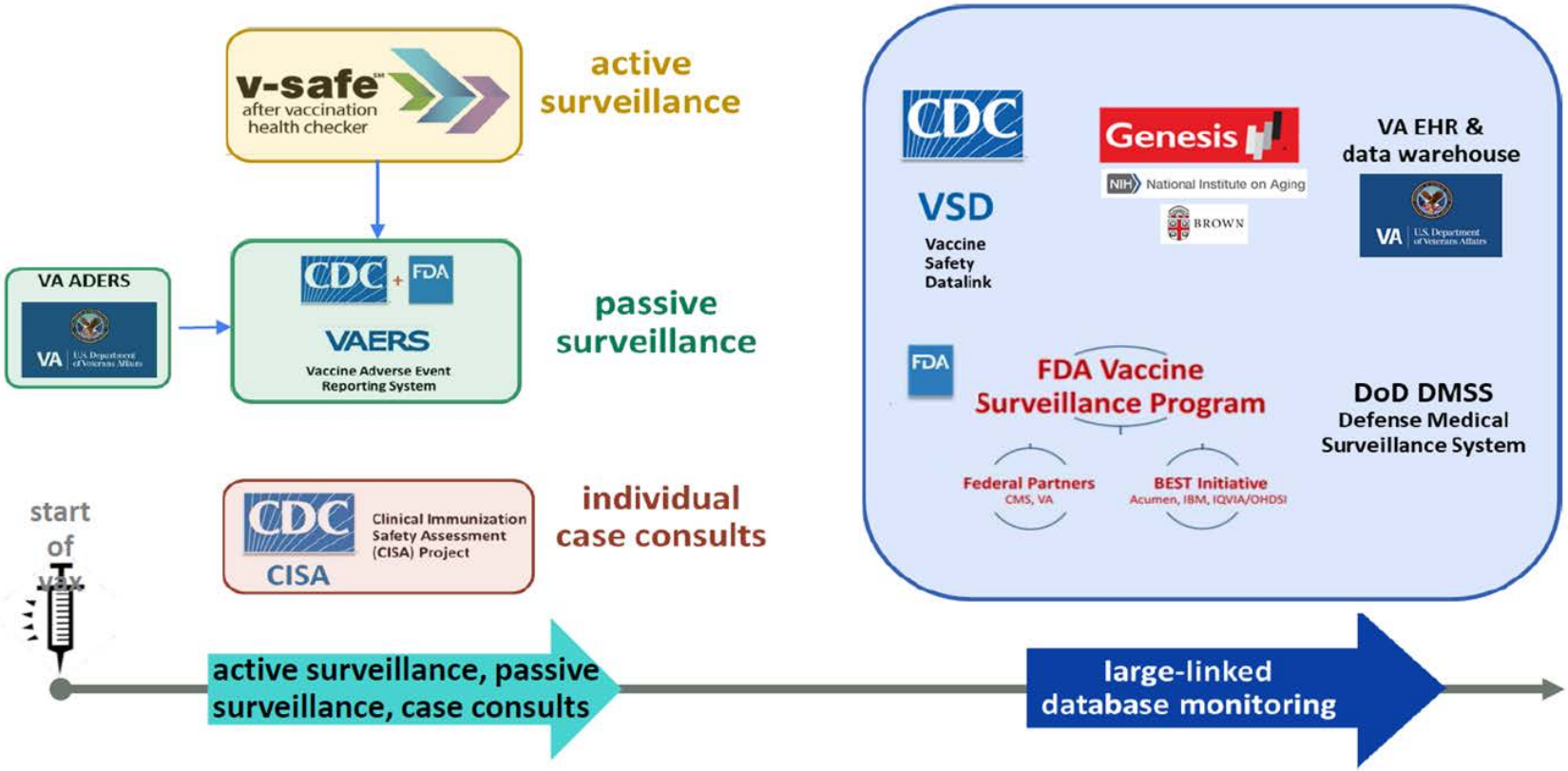
1. mRNA
2. Lipids
3. Salt and Amines
4. Sugars

https://www.aruplab.com/news/12-21-2020/video-resource-how-first-sars-cov-2-vaccines-work

What are the side effects?

Shots hurt.

Vaccine Safety Monitoring Timeline

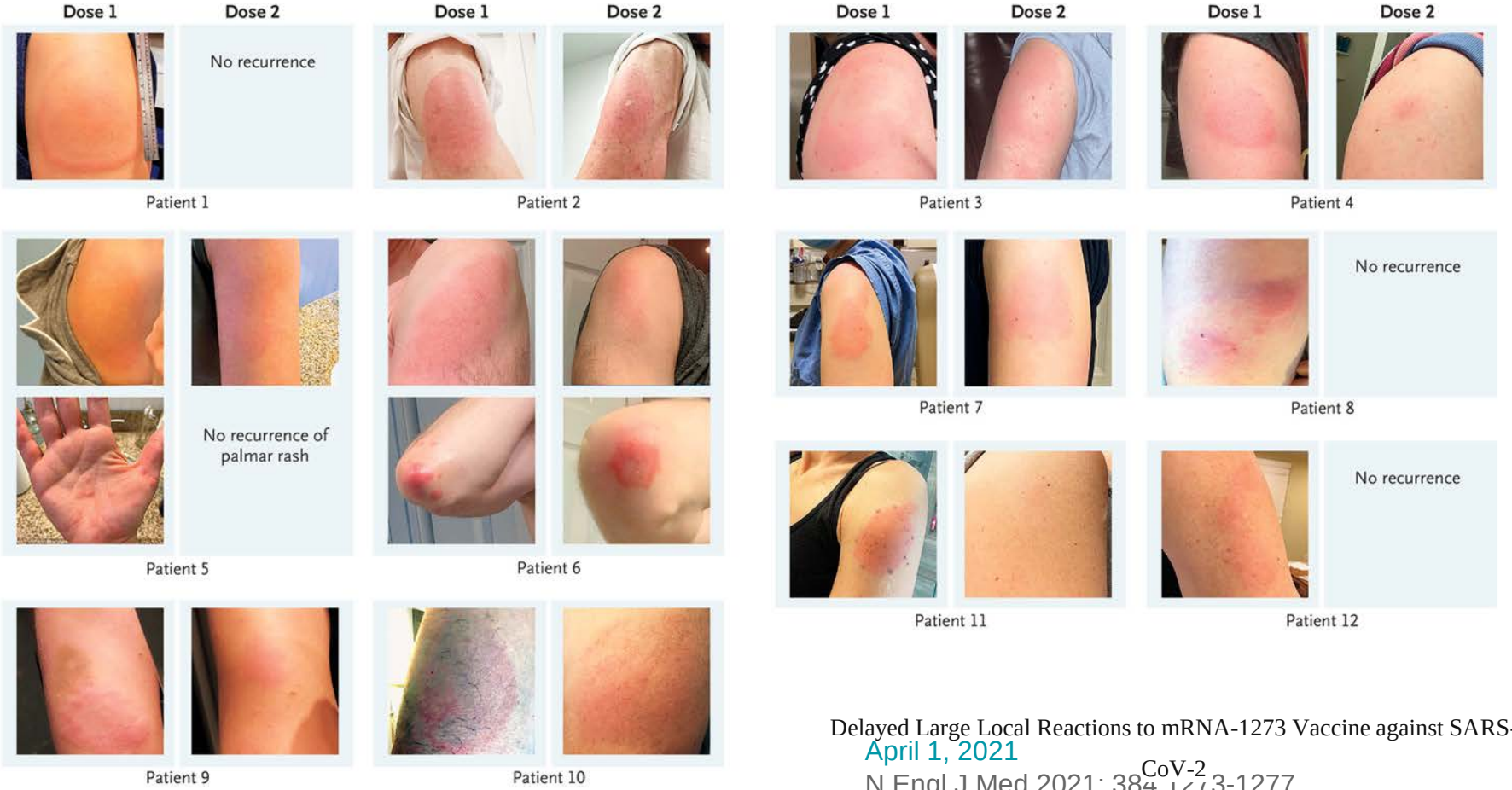


v-safe℠ after vaccination health checker

icited Local and Systemic Reactions[a] to mRNA-Based COVID-19 Vaccines Reported 0 to 7 Days After Vaccination—Centers for Disease nd Prevention V-safe Surveillance System, December 14, 2020, to February 28, 2021

Reaction	No. (%)					
	Dose 1			Dose 2		
	Both vaccines (N = 3 643 918)	Pfizer-BioNTech (n = 1 659 724)	Moderna (n = 1 984 194)	Both vaccines (N = 1 920 872)	Pfizer-BioNTech (n = 971 375)	Moderna (n = 949 497)
Any injection site reaction	2 550 710 (70.0)	1 085 242 (65.4)	1 465 468 (73.9)	1 443 899 (75.2)	666 635 (68.6)	777 264 (81.9)
Pain	2 472 373 (67.8)	1 055 604 (63.6)	1 416 769 (71.4)	1 389 629 (72.3)	645 917 (66.5)	743 712 (78.3)
Redness	204 097 (5.6)	56 780 (3.4)	147 317 (7.4)	240 265 (12.5)	57 956 (6.0)	182 309 (19.2)
Swelling	379 539 (10.4)	110 077 (6.6)	269 462 (13.6)	348 986 (18.2)	100 430 (10.3)	248 556 (26.2)
Itching	197 441 (5.4)	62 486 (3.8)	134 955 (6.8)	214 658 (11.2)	60 946 (6.3)	153 712 (16.2)
Any systemic reaction[a]	1 823 068 (50.0)	797 410 (48.0)	1 025 658 (51.7)	1 333 931 (69.4)	623 746 (64.2)	710 185 (74.8)
Fatigue	1 127 638 (30.9)	483 146 (29.1)	644 492 (32.5)	1 034 462 (53.9)	464 659 (47.8)	569 803 (60.0)
Headache	943 607 (25.9)	409 359 (24.7)	534 248 (26.9)	897 005 (46.7)	392 266 (40.4)	504 739 (53.2)
Myalgia	705 100 (19.4)	281 743 (17.0)	423 357 (21.3)	845 314 (44.0)	357 381 (36.8)	487 933 (51.4)
Chills	321 009 (8.8)	116 034 (7.0)	204 975 (10.3)	600 354 (31.3)	220 831 (22.7)	379 523 (40.0)
Fever	314 676 (8.6)	116 951 (7.0)	197 725 (10.0)	566 112 (29.5)	208 976 (21.5)	357 136 (37.6)
Joint pain	317 034 (8.7)	123 319 (7.4)	193 715 (9.8)	492 031 (25.6)	192 926 (19.9)	299 105 (31.5)
Nausea	275 423 (7.6)	114 087 (6.9)	161 336 (8.1)	319 248 (16.6)	127 454 (13.1)	191 794 (20.2)
Vomiting	25 425 (0.7)	9966 (0.6)	15 459 (0.8)	31 056 (1.6)	11 276 (1.2)	19 780 (2.1)
Diarrhea	189 878 (5.2)	83 016 (5.0)	106 862 (5.4)	133 877 (7.0)	60 641 (6.2)	73 236 (7.7)
Abdominal pain	111 044 (3.0)	47 096 (2.8)	63 948 (3.2)	117 494 (6.1)	48 129 (5.0)	69 365 (7.3)
Rash outside of injection site	42 409 (1.2)	17 765 (1.1)	24 644 (1.2)	32 686 (1.7)	13 132 (1.4)	19 554 (2.1)

[a] Systemic reactions do not include allergic reactions or anaphylaxis.



Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-CoV-2
April 1, 2021
N Engl J Med 2021; 384:1273-1277
DOI: 10.1056/NEJMc2102131

Preliminary results of the VSD **unvaccinated concurrent comparator** analysis for COVID-19 vaccine safety after either dose of any mRNA vaccine as of February 13, 2021

VSD Rapid Cycle Analysis prespecified outcomes for COVID-19 vaccines	Concurrent comparator analysis	Risk interval	Events in vaccinated	Adjusted expected events in risk interval
Acute disseminated encephalomyelitis	Unvaccinated	1-21 days	0	0
Acute myocardial infarction	Unvaccinated	1-21 days	23	26.0
Acute respiratory distress syndrome	Unvaccinated	N/A	0	N/A
Anaphylaxis	Unvaccinated	0-1 days	20	N/A
Appendicitis	Unvaccinated	1-21 days	31	23.6
Bell's palsy	Unvaccinated	1-21 days	21	20.3
Convulsions/seizures	Unvaccinated	1-21 days	10	9.6
Disseminated intravascular coagulation	Unvaccinated	1-21 days	1	1.1
Encephalitis/myelitis/encephalomyelitis	Unvaccinated	1-21 days	1	.1
Guillain-Barré syndrome	Unvaccinated	1-21 days	1	.6
Thrombotic thrombocytopenic purpura	Unvaccinated	1-21 days	0	0
Immune thrombocytopenia	Unvaccinated	1-21 days	1	1
Kawasaki disease	Unvaccinated	1-21 days	0	0
MIS-C and MIS-A	Unvaccinated	N/A	0	N/A
Myocarditis/pericarditis	Unvaccinated	1-21 days	2	2.1
Narcolepsy and cataplexy	Unvaccinated	N/A	2	N/A
Stroke, hemorrhagic	Unvaccinated	1-21 days	8	10
Stroke, ischemic	Unvaccinated	1-21 days	41	38.8
Transverse myelitis	Unvaccinated	1-21 days	0	0
Venous thromboembolism	Unvaccinated	1-21 days	26	26.3
Pulmonary embolism (subset of VTE)	Unvaccinated	1-21 days	20	21.0

- No statistically significant increased risks detected for any prespecified outcomes

COVID Vaccine-Allergy/Anaphylaxis

Anaphylaxis following mRNA COVID-19 vaccines

Clinical Review & Education

JAMA Insights

Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US—December 14, 2020-January 18, 2021

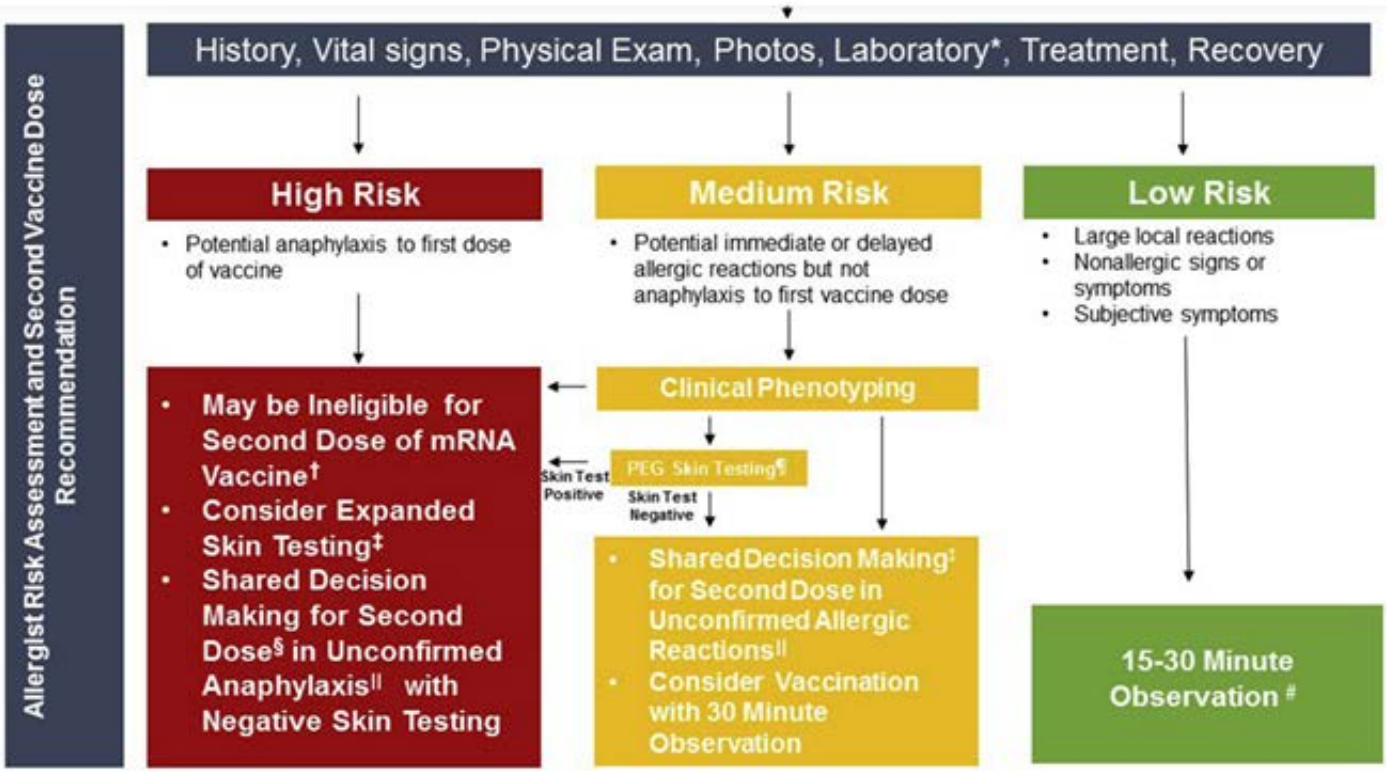
Tom T. Shimabukuro, MD, MPH, MBA; Matthew Cole, MPH; John R. Su, MD, PhD, MPH

Shimabukuro TT, Cole M, Su JR. Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US-December 14, 2020-January 18, 2021. *JAMA*. 2021 Feb 12. doi: 10.1001/jama.2021.1967. Epub ahead of print.

	Pfizer-BioNTech	Moderna
Anaphylaxis reporting rate (cases per million doses administered)	4.7	2.5

Table. Characteristics of Reported Cases of Anaphylaxis Following Receipt of Pfizer-BioNTech (9 943 247 Doses) and Moderna (7 581 429 Doses) COVID-19 Vaccines—Vaccine Adverse Events Reporting System (VAERS), US, December 14, 2020-January 18, 2021

Characteristics	No. (%) of cases	
	Pfizer-BioNTech (n = 47)	Moderna (n = 19)
Age, median (range), y	39 (27-63)[a]	41 (24-63)
Female sex	44 (94)	19 (100)
Minutes to symptom onset, median (range)	10 (<1-1140 [19 h])[b]	10 (1-45)
Symptom onset, min		
≤15	34 (76)[b]	16 (84)
≤30	40 (89)[b]	17 (89)
Reported history[c]		
Allergies or allergic reactions	36 (77)	16 (84)
Prior anaphylaxis	16 (34)	5 (26)
Vaccine dose		
First	37	17
Second	4	1
Unknown	6	1
Brighton Collaboration case definition level[d]		
1	21 (45)	10 (52)
2	23 (49)	8 (43)
3	3 (6)	1 (5)
Anaphylaxis reporting rate (cases per million doses administered)	4.7	2.5



J Allergy Clin Immunol Pract 2020 Dec 31;S2213-2198(20)31411-2

Pregnancy/Breastfeeding/Infertility

Can COVID-19 vaccines cause infertility or miscarriage?

A sophisticated disinformation campaign has been circulating online, claiming that antibodies to the spike protein of COVID-19 produced from these vaccines will bind to placental proteins (syncytin-1) and prevent pregnancy. This disinformation is thought to originate from internet postings by a former scientist known to hold anti-vaccine views (Wolfgang Wodarg, a German politician and physician who left medical practice in 1994)

- COVID-19 infection has not been linked to infertility.
- No other viral infection or vaccination-inducing immunity by similar mechanisms has been shown to cause infertility.
- Antibodies to the spike protein have not been linked to infertility after COVID-19 infection.
- Molecular mimicry between the spike protein and syncytin-1 is not plausible.

JAMA Pediatr. Published online April 22, 2021. doi:10.1001/jamapediatrics.2021.1050

Table 3. Adjusted Associations Between Preexisting Maternal Morbidity or Being Overweight Prepregnancy and Maternal and Neonatal Outcomes According to COVID-19 Diagnosis[a,b]

Maternal COVID-19 diagnosis	No. (%)	RR (95% CI)				
		MMMI[c]	SNMI[d]	SPMMI[e]	Preterm birth[f]	Preeclampsia/ eclampsia/HELLP
Not diagnosed						
No past morbidity	1179 (55.4)	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Past morbidity	245 (11.5)	1.20 (0.92-1.54)	3.04 (1.48-6.28)	1.48 (0.95-2.29)	1.73 (1.26-2.39)	1.86 (1.11-3.12)
Diagnosed						
No past morbidity	547 (25.7)	1.57 (1.33-1.85)	4.02 (2.39-6.76)	2.35 (1.76-3.13)	1.76 (1.40-2.22)	1.88 (1.24-2.86)
Past morbidity	159 (7.5)	1.71 (1.33-2.20)	1.88 (0.74-4.73)	2.29 (1.50-3.51)	1.96 (1.41-2.73)	3.29 (2.03-5.33)
Not diagnosed						
Normal weight	823 (40.3)	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Overweight	554 (27.1)	1.01 (0.81-1.24)	1.56 (0.76-3.20)	1.14 (0.78-1.67)	0.78 (0.59-1.05)	1.37 (0.82-2.30)
Diagnosed						
Normal weight	342 (16.8)	1.28 (1.03-1.58)	2.07 (0.99-4.31)	1.99 (1.38-2.88)	1.42 (1.07-1.90)	1.80 (1.06-3.07)
Overweight	323 (15.8)	1.81 (1.48-2.21)	4.15 (2.15-8.01)	2.44 (1.72-3.48)	1.43 (1.08-1.85)	2.62 (1.57-4.36)

Abbreviations: HELLP, Hemolysis, elevated liver enzymes, low platelet count; MMMI, maternal morbidity and mortality index; RR, relative risk; SNMI, severe neonatal morbidity index; SPMMI, severe perinatal morbidity and mortality index.

[a] All models adjusted for country, month entering study, maternal age, and history of maternal morbidity (including diabetes, thyroid and other endocrine disorders, cardiac disease, hypertension, chronic respiratory disease, kidney disease, malaria, or tuberculosis).

[b] Prepregnancy maternal morbidities included at least 1 of the following: diabetes, thyroid and other endocrine disorders, cardiac disease, hypertension, chronic respiratory disease, kidney disease, malaria, or tuberculosis.

[c] MMMI includes at least 1 of the following complications during pregnancy: vaginal bleeding, pregnancy-induced hypertension, preeclampsia, eclampsia, HELLP, preterm labor, infections requiring antibiotics or maternal death, admission to intensive care unit, or referral for higher dependency care.

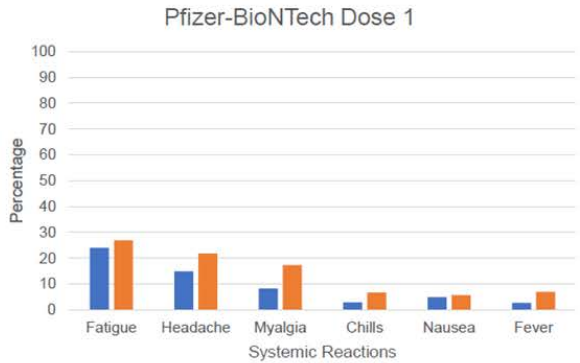
[d] SNMI includes at least 1 of the following morbidities: bronchopulmonary dysplasia, hypoxic-ischemic encephalopathy, sepsis, anemia requiring transfusion, patent ductus arteriosus, intraventricular hemorrhage, necrotizing enterocolitis, or retinopathy of prematurity.

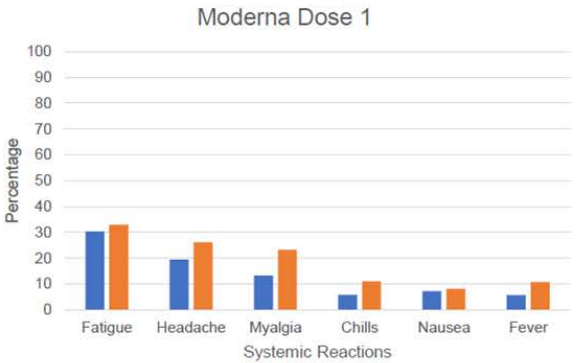
[e] SPMMI includes any of the morbidities listed in the SNMI, intrauterine or neonatal death, or neonatal intensive care unit stay ≥7 days.

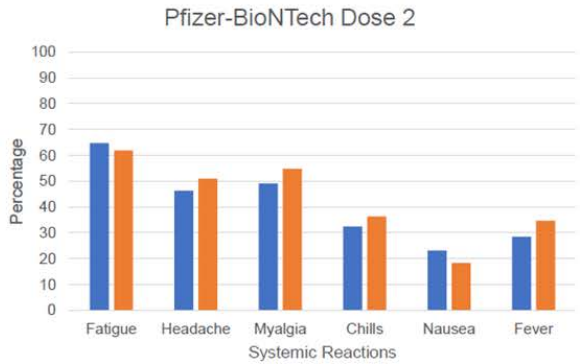
[f] Models for preterm birth also adjusted for history of preterm birth.

COVID vaccine and pregnancy

V-safe: Day 1 post-vaccination systemic reactions in pregnant and non-pregnant women aged 16-54 years*







Pregnant (self-report)
Not pregnant

v-safe℠
after vaccination
health checker

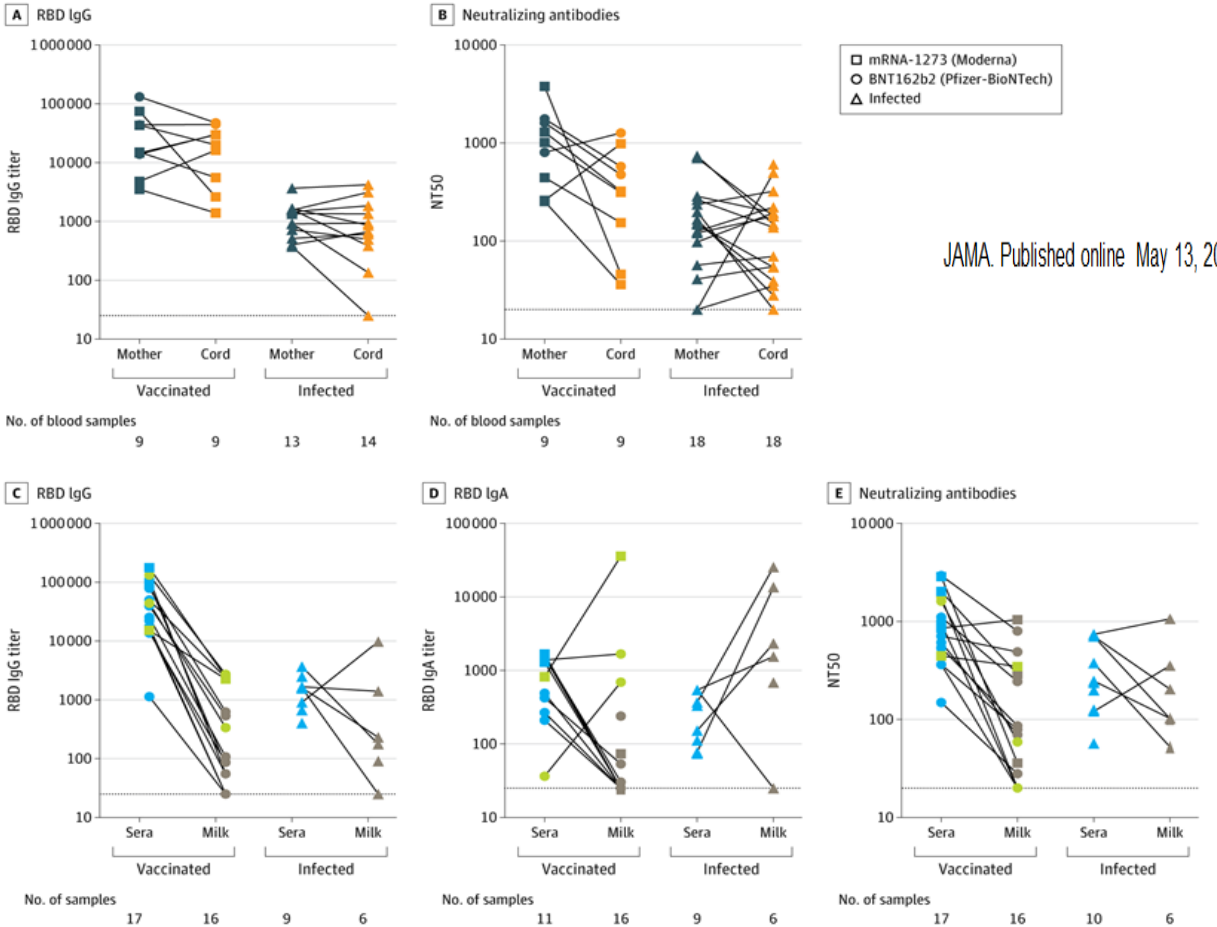
* Source: CDC unpublished **v-safe** data through January 13, 2021

V-safe pregnancy registry outcomes of interest in COVID-19 vaccinated pregnant women as of February 18, 2021*

Outcomes	Background rates*	V-safe pregnancy registry overall
Pregnancy outcome		
Miscarriage (<20 weeks)	26%	15%†
Stillbirth (≥ 20 weeks)	0.6%	1%
Pregnancy complications		
Gestational diabetes	7-14%	10%
Preeclampsia or gestational hypertension§	10-15%	15%
Eclampsia	0.27%	0%
Intrauterine growth restriction	3-7%	1%
Neonatal		
Preterm birth	10.1%	10%
Congenital anomalies‡	3%	4%
Small for gestational age^	3-7%	4%
Neonatal death	0.38%	0%

* Sources listed on slide 33; † 93% of these were pregnancy losses <13 weeks of age; § Pre-eclampsia or gestational hypertension diagnosed during pregnancy and/or during delivery; ‡ Congenital anomalies (overall) diagnosed after delivery only; ^ Birthweight below the 10th percentile for gestational age and sex using INTERGROWTH-21st Century growth standards

From: **Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women**



JAMA. Published online May 13, 2021. doi:10.1001/jama.2021.7563

Does the pause for the J and J show that the vaccines are unsafe?

It shows that millions of people have received the COVID-19 vaccines and these vaccines have undergone the most intense safety monitoring of any vaccines every in the history of the world.

U.S. reporting rates of TTS after Janssen COVID-19 vaccination (as of May 7, 2021)

- 8.73 million total Janssen COVID-19 Vaccine doses administered*

	Females			Males		
Age group	TTS cases	Doses admin	Reporting rate† (per million)	TTS cases	Doses admin	Reporting rate† (per million)
18-29 yrs old	**3**	641,510	4.7	**2**	714,458	2.8
30-39 yrs old	**8**	642,745	12.4	**1**	728,699	1.4
40-49 yrs old	**7**	743,256	9.4	**1**	775,390	1.3
50-64 yrs old	**4**	1,463,416	2.7	**2**	1,505,505	1.3
65+ yrs old	**0**	814,947	0	**0**	697,925	0

* Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations; † Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered

VSD: Cerebral venous sinus thrombosis (CVST) after mRNA COVID-19 vaccination

- 3.3 million doses of Pfizer-BioNTech and 3.0 million doses of Moderna COVID-19 vaccinations administered in VSD as of April 24, 2021
  - 11 total ICD-10 coded CVST diagnoses identified following mRNA vaccines (3 after Pfizer-BioNTech and 8 after Moderna vaccination)
    - 5 ruled out for incident cases (historical n=2, history of head injury n=2, chronic cavernous sinus syndrome n=1)
    - 6 potential CVST incident cases, but all <u>without</u> thrombocytopenia
- <u>No confirmed cases</u> of incident CVST with thrombocytopenia after 6.3 million doses of mRNA COVID-19 vaccines administered in VSD

VSD: Thrombosis events after Janssen COVID-19 vaccination

- 159,885 Janssen COVID-19 Vaccine doses administered in VSD through April 24, 2021
  - No statistical signals detected for any prespecified Rapid Cycle Analysis outcomes
  - No CVST cases identified
- 32 VTE/PE cases identified in the 1–42 days following vaccination (including 3 cases diagnosed with both VTE and PE)
  - 29 of the cases have been quick reviewed to date (3 in progress)

29
- 6 were ruled out as not VTE/PE
- 23 were confirmed VTE/PE cases

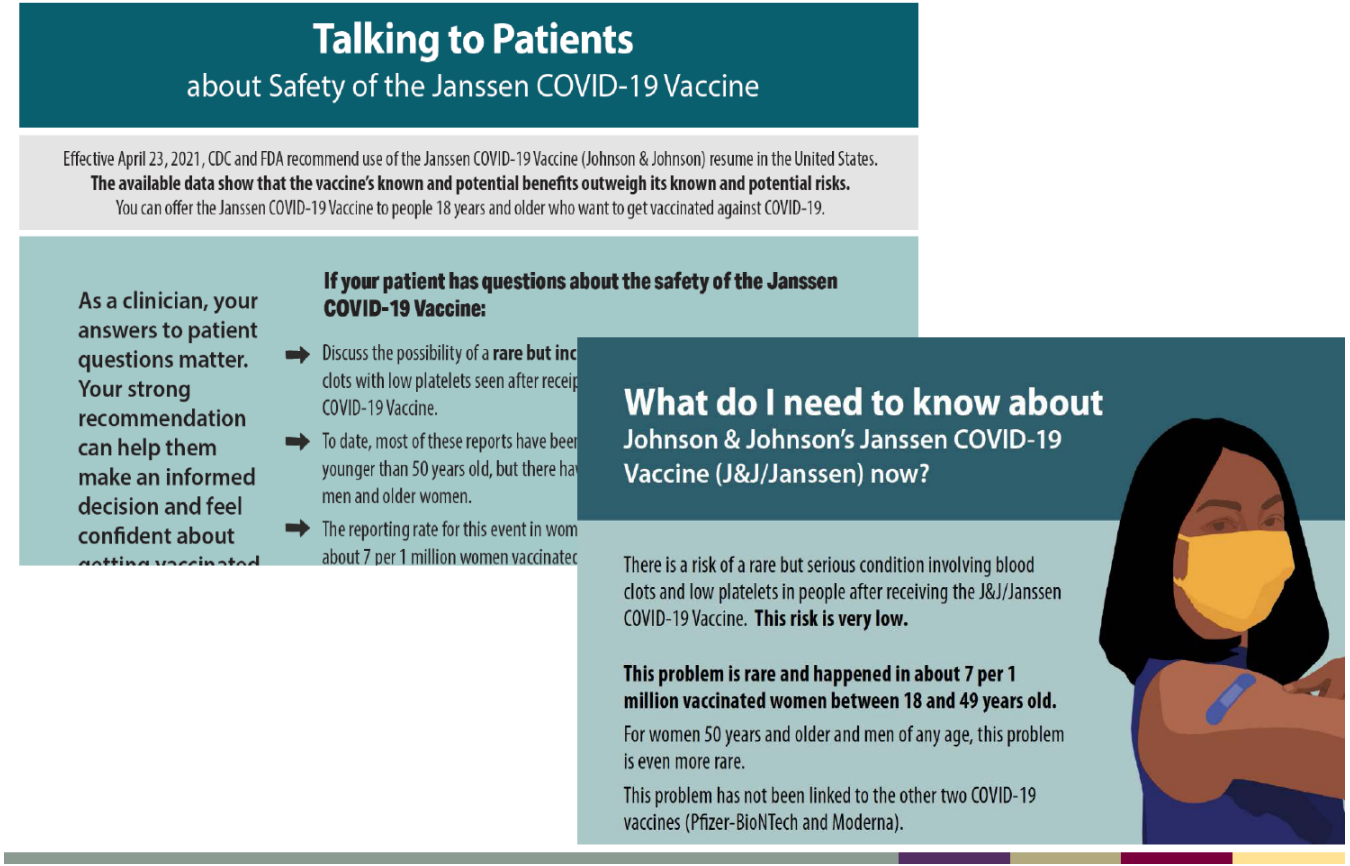
23
- 4 were determined to have symptom onset prior to vaccination
- 1 had an indeterminate symptom onset
- 18 are potential VTE/PE cases with incidence following vaccination

18
- 10 female (5 PE, 5 VTE), 8 males (4 PE, 4 VTE)
- Ages ranged from 30–79
- None with history of COVID-19 infection
- None with thrombocytopenia noted at time of VTE/PE

VTE = venous thromboembolism

PE = pulmonary embolism

- Exquisitely small risk of clotting with the vaccine
- 120 times risk of a clotting event with COVID disease



Talking to Patients
about Safety of the Janssen COVID-19 Vaccine

Effective April 23, 2021, CDC and FDA recommend use of the Janssen COVID-19 Vaccine (Johnson & Johnson) resume in the United States.
The available data show that the vaccine's known and potential benefits outweigh its known and potential risks.
You can offer the Janssen COVID-19 Vaccine to people 18 years and older who want to get vaccinated against COVID-19.

As a clinician, your answers to patient questions matter. Your strong recommendation can help them make an informed decision and feel confident about

If your patient has questions about the safety of the Janssen COVID-19 Vaccine:

- Discuss the possibility of a **rare but inc**
  clots with low platelets seen after receip
  COVID-19 Vaccine.
- To date, most of these reports have beer
  younger than 50 years old, but there hav
  men and older women.
- The reporting rate for this event in wom
  about 7 per 1 million women vaccinatec

What do I need to know about Johnson & Johnson's Janssen COVID-19 Vaccine (J&J/Janssen) now?

There is a risk of a rare but serious condition involving blood clots and low platelets in people after receiving the J&J/Janssen COVID-19 Vaccine. **This risk is very low.**

This problem is rare and happened in about 7 per 1 million vaccinated women between 18 and 49 years old.

For women 50 years and older and men of any age, this problem is even more rare.

This problem has not been linked to the other two COVID-19 vaccines (Pfizer-BioNTech and Moderna).

Myocarditis post vaccination

Common with COVID disease

100 patients recently recovered from COVID-19 identified from a COVID-19 test center, cardiac magnetic resonance imaging revealed cardiac involvement in 78 patients (78%) and ongoing myocardial inflammation in 60 patients (60%), which was independent of preexisting conditions, severity and overall course of the acute illness, and the time from the original diagnosis.

JAMA Cardiol. 2020 Jul 27 : e203557.

VAERS REPORTS

Reported cases have occurred predominantly in male adolescents and young adults 16 years of age and older.

Onset was typically within several days after mRNA COVID-19 vaccination, and cases have occurred more often after the second dose than the first dose.

- CDC continues to recommend COVID-19 vaccination for everyone 12 years of age and older given the greater risk of other serious complications related to COVID-19, such as hospitalization, multisystem inflammatory syndrome in children (MIS-C), or death.

Coadministration

COVID-19 vaccines and other vaccines may now be administered without regard to timing. This includes simultaneous administration of COVID-19 vaccine and other vaccines on the same day, as well as coadministration within 14 days. It is unknown whether reactogenicity of COVID-19 vaccine is increased with coadministration, including with other vaccines known to be more reactogenic, such as adjuvanted vaccines or live vaccines. When deciding whether to coadminister another vaccine(s) with COVID-19 vaccine, providers should consider whether the patient is behind or at risk of becoming behind on recommended vaccines, their risk of vaccine-preventable disease (e.g., during an outbreak or occupational exposures), and the reactogenicity profile of the vaccines.

If multiple vaccines are administered at a single visit, administer each injection in a different injection site.

Summary

- Vaccines have known adverse events
- Vaccines are safe and effective
- COVID vaccines are effective
- COVID vaccines have a good safety profile based on clinical trials and post licensure data

Email with any questions: candice.smith@tannerclinic.com