

A PREEMINENT RESEARCH UNIVERSITY

"COVID- 19- Vaccines and Therapeutics: Trust But Definitely Verify!"

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Executive Director, WE-CARE

Continuing Education Title: The SARS-CoV-2 Pandemic: The Virus' Characteristics - The

Therapeutics - The Impacts on Communities

Learning Objectives

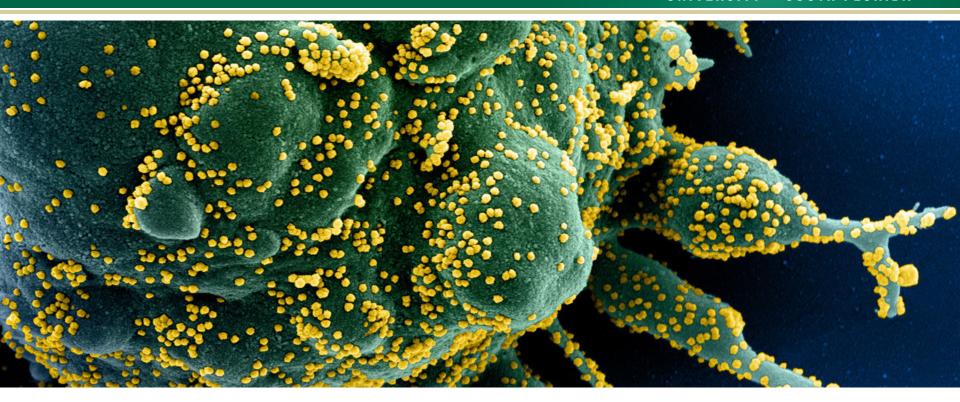
- 1. Review the characteristics of the SARS-CoV-2 virus, including emerging variants
- 2. Identify common myths about vaccines and other therapeutics designed to prevent and treat SARS-CoV-2 infection, including vaccine development.
- 3. Incorporate relevant educational strategies to address youth concerns about vaccines.



WHAT IS THE CORONAVIRUS? SARS-COV-2? WHAT ARE ITS CHARACTERISTICS?

Coronaviruses – A Family Affair

- Coronavirus Four types (Common cold/ flu)
- Severe Acute Respiratory Syndrome (SARS- 2002)
- Middle East Respiratory Syndrome (MERS- 2012)- 10 yrs
- Novel Coronavirus (SARS-CoV-2 {COVID-19} 2019)- 7 yrs
- NEXT Coronavirus (?????) 4/5 yrs



What is the SARS CoV-2 virus

Immune hunters called T cells can seek and destroy a cell (green) infected with and making copies of SARS-CoV-2 (yellow).

NIAID



Where Did SARS-CoV-2 Originate?

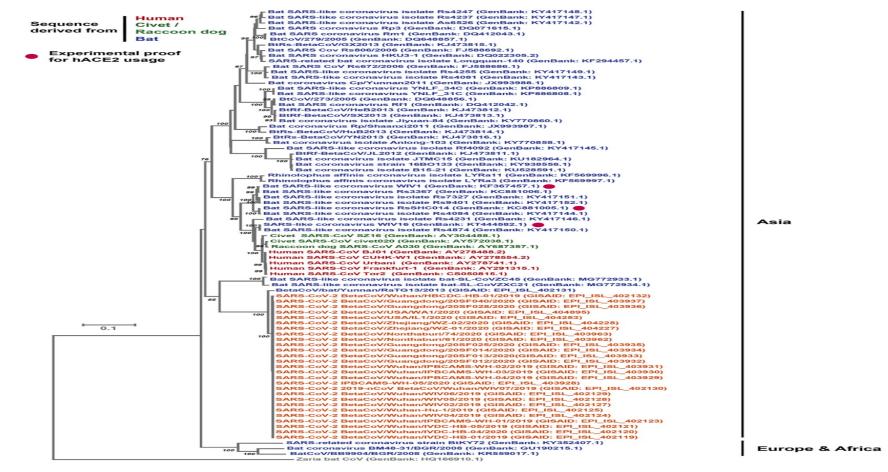
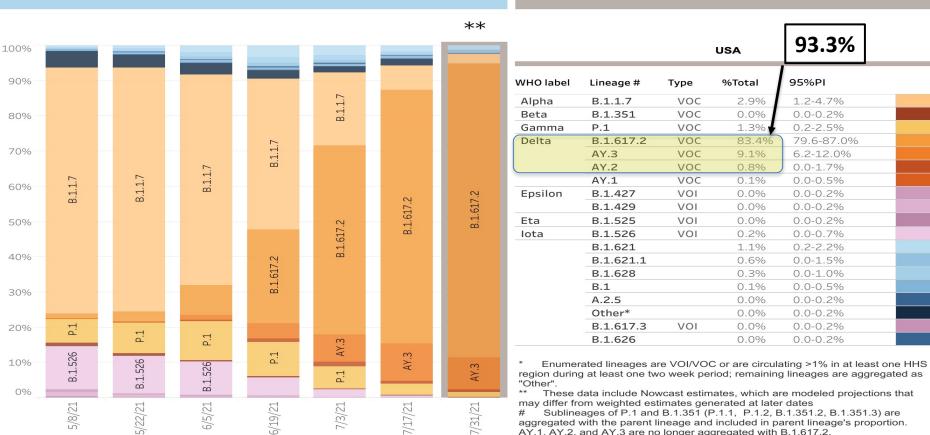


Figure S2. Extended Version of the Phylogenetic Tree, Related to Figure 2B

Please cite this article in press as: Hoffmann et al., SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor, Cell (2020), https://doi.org/10.1016/j.cell.2020.02.052

United States: 4/25/2021 - 7/31/2021

United States: 7/18/2021 - 7/31/2021 NOWCAST



AY.1, AY.2, and AY.3 are no longer aggregated with B.1.617.2.

Sublineages of P.1 and B.1.351 (P.1.1, P.1.2, B.1.351.2, B.1.351.3) are aggregated with the parent lineage and included in parent lineage's proportion.

Importance of Vaccinating NOW!

Vaccines Are Effective Today!!

Vaccine Efficacy or Effectiveness (VE) Against Variants

Vaccine	Study type	VE
Pfizer	Post-EUA	 90% against B.1.1.7 in Qatar* 100% for severe/critical disease
Janssen	Pre-EUA	 74% in U.S. 66% in Brazil 52% in S. Africa 73-82% for severe/critical disease in each country
Novavax	Pre-EUA Pre-EUA	96% against non-B.1.1.7 in UK86% against B.1.1.7 in UK51% against B.1.351 in S. Africa
AstraZeneca	Pre-EUA Pre-EUA	84% against non-B.1.1.7 in UK75% against B.1.1.7 in UK10% against B.1.351 in South Africa*

*>85% in UK & Israel (predominate B.1.1.7): https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html
Abu-Radad and Butt. Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants | NEJM

Novavax.: https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3

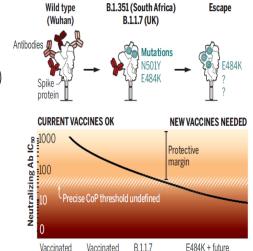
Madhi et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant | NEJM

mary et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7):- The Lancet **mild/moderate illness

Vaccine-Induced Antibody Protection and Variants

Approaching Escape Threshold?

- Robust correlation between vaccine efficacy (VE) versus:
 - Neutralizing titer (ρ= 0.79)
 - Binding antibody titer ($\rho = 0.93$)
- Correlate of protection, or threshold that protects against SARS-CoV-2, not yet determined
- Variants result in reduced protective antibody levels
 - Lower VE and increased breakthrough infection?
 - Shorter duration of immunity?



elderly

escape mutants?



Discuss the vaccines and therapeutics designed to prevent and treat SARS-CoV-2 infection, including vaccine research and development

The Covid-19 Vaccine-Development Multiverse Penny M. Heaton, M.D.

The rapid pace of development of vaccines against Covid-19 is enabled by several factors:

- 1. **Prior knowledge** of the role of the spike protein in coronavirus pathogenesis and evidence that neutralizing antibody against the spike protein is important for immunity;
- 2. Evolution of **nucleic acid vaccine technology platforms** (Moderna & Pfizer) that allow creation of vaccines and **prompt manufacture of thousands of doses** once a genetic sequence is known; and
- 3. Development activities that can be <u>conducted in parallel, rather than</u> <u>sequentially, without increasing risks for study participants</u>.

November 12, 2020 N Engl J Med 2020; 383:1986-1988



The Vaccines Seemed to have been produced **TOO** quickly, Right?

Current Vaccine Clinical Trials

Vaccine Company	Clinical Trial Phase	Target Number to be Enrolled
University of Oxford and AstraZeneca	Phase 3	30,000
Moderna Therapeutics	Phase 3 (EUA – 12/2020)	30,000 (11,000 POC)
BioNTech and Pfizer	Phase 3 (EUA – 12/2020)	44,000
Novavax	Phase 2/3 (Nov 2020) - USF Health	30,000
Eli Lilly (AB formula)	Phase 3	400

500

Phase 3

Regeneron (AB Formula)

	יו	ALUA	. J vacci	1163 7	uverse Li	ilects
Adverse Reaction	\/ ! 4 - k			Pfizer Vaccine 2nd	Pfizer Placebo	J&J Vaccine 1st

41.9

47.4

1.2

14.0

3.7

21.3

25.4

24.5

7.3

5.9

0.4

12.7

62.8

67.6

21.3

48.3

17.4

6.1

35.4

38.5

9.4

9.2

0.9

23.7

Headache

Fatigue

Nausea/

Vomiting

Chills

Fever

Myalgia

FDA FIIA COVID-19 Vaccines - Adverse Effects

51.7

59.4

1.9

35.1

15.8

37.3

24.1

22.8

1.2

3.8

0.5

8.2

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38.9

38.2

14.2

N/A

9.0

33.2

J&J **Placebo**

23.7

21.5

9.7

N/A

0.6

12.7

What is in the Pfizer Vaccine?

- The Pfizer-BioNTech COVID-19 Vaccine is a:
- white to off-white,
- sterile,
- preservative-free, frozen suspension.
 - Contains a nucleoside-modified messenger RNA (modRNA)
 - encodes the <u>viral spike glycoprotein (S)</u> of SARS-CoV-2.
- The vaccine also includes the following ingredients:
 - lipids ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide,
 - 1,2-distearoyl-sn-glycero-3-phosphocholine, and cholesterol),
 - potassium chloride,
 - monobasic potassium phosphate,
 - sodium chloride,
 - dibasic sodium phosphate dihydrate, and
 - sucrose

What is in the Moderna Vaccine?

- The Moderna COVID-19 Vaccine is a:
- white to off-white,
- sterile,
- preservative-free frozen suspension.
- Contains a synthetic messenger ribonucleic acid (mRNA)
 - encodes the stabilized spike glycoprotein (S) of the SARS-CoV-2 virus.
- The vaccine also contains the following ingredients:
 - lipids (SM-102, 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 [PEG2000-DMG],
 - cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]),
 - tromethamine,
 - tromethamine hydrochloride, acetic acid, sodium acetate, and
 - sucrose.

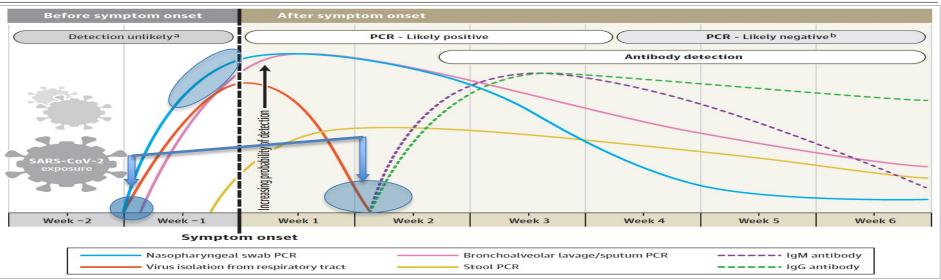


How do the Vaccines Work? (Pre-req: Cell/ Molecular Biology ©)



Interpreting Diagnostic Tests for SARS-CoV-2

Figure. Estimated Variation Over Time in Diagnostic Tests for Detection of SARS-CoV-2 Infection Relative to Symptom Onset



Estimated time intervals and rates of viral detection are based on data from several published reports. Because of variability in values among studies, estimated time intervals should be considered approximations and the probability of detection of SARS-CoV-2 infection is presented qualitatively. SARS-CoV-2 indicates severe acute respiratory syndrome coronavirus 2; PCR, polymerase chain reaction.

- ^a Detection only occurs if patients are followed up proactively from the time of exposure.
- ^b More likely to register a negative than a positive result by PCR of a nasopharyngeal swab.

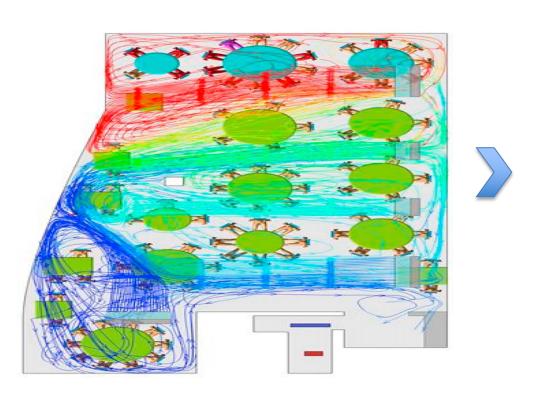
JAMA Published online May 6, 2020

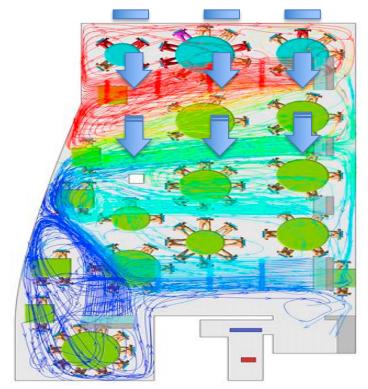


Communicating with our Young(<u>er</u>) People about SARS-CoV-2

Clinical impact of SARS-CoV-2, including longterm clinical challenges- and their concerns

SARS-CoV-2 Spread in Closed Spaces





https://doi.org/10.1016/j.buildenv.2021.107788

Science

RESEARCH ARTICLES

Cite as: M. Monod et al., Science

10.1126/science.abe8372 (2021).

Age groups that sustain resurging COVID-19 epidemics in the United States

SARS-CoV-2 transmission is sustained primarily from

age groups 20-49 in the first locations in the model, the percent contribution

to onward spread was 41.1% [40.7%-41.4%] from individuals aged 35-49, compared to 2.1% [1.6%-2.8%] from individuals aged 0-9, 4.0% [3.5%-4.6%] from individuals aged 10-19, vaccination with transmission-blocking vaccines, could bring

34.7% [33.9%-35.5%] from individuals aged 20-34, 15.3% [14.8%-15.8%] from individuals aged 50-64, 2.5% [2.2%-2.9%] deaths. from individuals aged 65-79 age group, and 0.3% [0.3%-0.3%]

from individuals aged 80+ (table S4). Spatially, the contribution of adults aged 35-49 were estimated to be remarkably homogeneous across states, whereas the estimated contributions of young adults aged 20-34 to COVID-19 spread tended

to be higher in Southern South-western and Western re-

evaluated was highest from individuals aged 35-49 (1.39 [1.34-1.44]) and 20-34 (1.29 [1.24-1.36]), and around one for age sible SARS-CoV-2 lineages have not yet established, addi-

2020, the estimated reproduction number across all locations

tional interventions among adults aged 20-49, such as mass

resurgent COVID-19 epidemics under control and avert

Conclusions This study provides evidence that the resurgent COVID-19 epidemics in the US in 2020 have been driven by adults aged 20-49, and in particular adults aged 35-49, before and after school reopening. Unlike pandemic flu, these adults ac-

Post-acute COVID-19 syndrome

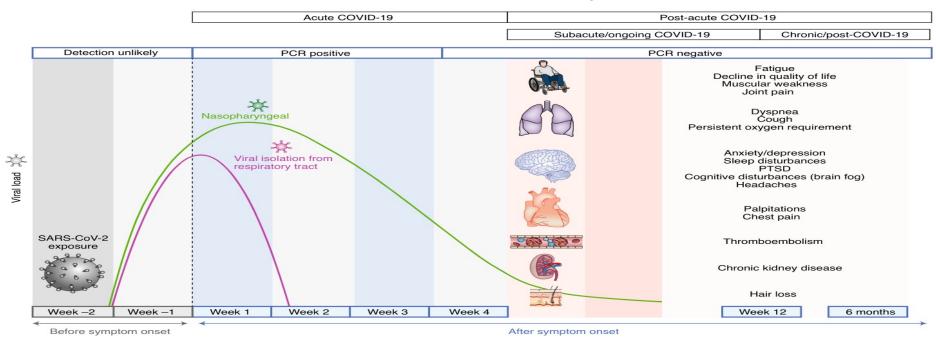


Fig. 1 | Timeline of post-acute COVID-19. Acute COVID-19 usually lasts until 4 weeks from the onset of symptoms, beyond which replication-competent SARS-CoV-2 has not been isolated. Post-acute COVID-19 is defined as persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms. The common symptoms observed in post-acute COVID-19 are summarized.

6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records



Maxime Taquet, John R Geddes, Masud Husain, Sierra Luciano, Paul J Harrison

1000	
Oa.	

	All patients	Patients without hospitalisation	Patients with hospitalisation	Patients with ITU admission	Patients with encephalopathy
Cohort size	236 379 (100.0%)	190 077 (100.0%)	46 302 (100.0%)	8945 (100.0%)	6229 (100-0%)
Demographics					
Age, years	46 (19.7)	43.3 (19.0)	57 (18.7)	59.1 (17.3)	66.7 (17.0)
Sex					
Othe estimate	236379 pated incidences in the constant of t	ce of a <u>ne</u> u	<u>ırological</u>	or <u>psychia</u>	atric (0·2%)
Unk 6 33-17	7–34·07), w	ith 12-84%	10) 71 (22 . 7 /0)	2104 (24.470)	1) 12 (24: 7/0)
ні _{sp} their. firs	st such dia		8617 (18.6%)	2248 (25·1%)	895 (14·4%)
Not Hispanic or Latino	134 075 (56-7%)	106 844 (56-2%)	27 231 (58.8%)	5041 (56.4%)	3873 (62-2%)
Unknown	64532 (27.3%)	54078 (28.5%)	10 454 (22.6%)	1656 (18.5%)	1461 (23.5%)

What was found with the J&J Vaccine

Reporting rates of TTS after Janssen COVID-19 vaccine

- 7.98 million vaccine doses administered*and 15 confirmed TTS cases[†] as of April 21, 2021
 - Some age- and sex-specific doses administered data were imputed
 - Additional potential TTS cases under review, including potential male cases

	Females			Males			
Age group	TTS cases	Doses admin	Reporting rate [‡]	TTS cases	Doses admin	Reporting rate [‡]	
18-49 years old	13	1,866,294	7.0 per million	0	1,977,330	0 per million	
50+ years old	2	2,125,239	0.9 per million	0	2,010,144	0 per million	

^{*} Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations; † One case was excluded from the final analysis: a female aged <50 years who had concurrent diagnosis of COVID-19 and TTS following receipt of Janssen vaccine; † Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered

Rare complication of COVID-19 presenting as isolated headache

Rehan Asif, ¹ Marcella Sinead O' Mahony²

SUMMARY

An 18-year-old man presented with persistent isolated headache 2 weeks after recovering from acute COVID-19 illness. Extensive cerebral venous sinus thrombosis (CVST) was detected on CT venogram despite him having no other thrombotic risk factors. CVST can complicate COVID-19. A high index of clinical suspicion is warranted as it can often have a subtle presentation with paucity of neurological symptoms.

Rare complication of COVID-19 presenting as isolated headache

Rehan Asif, ¹ Marcella Sinead O' Mahony²



Figure 1 Plain CT of the head showing suspicious hyperdense area (arrow), raising the possibility of venous sinus thrombosis.

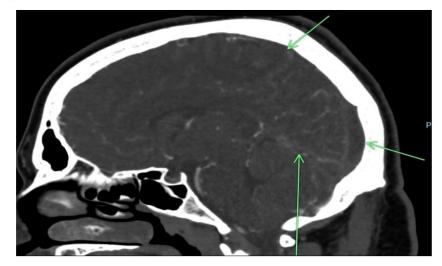


Figure 2 CT venogram showing filling defects throughout straight and superior sagittal sinuses (arrows), confirming cerebral venous sinus thrombosis.

Asif R, O' Mahony MS. BMJ Case Rep 2020;13:e239275. doi:10.1136/bcr-2020-239275

MRNA Vaccines – Myocarditis in Young Adults?

Preliminary myocarditis/pericarditis reports to VAERS following dose 2 mRNA vaccination, Exp. vs. Obs. using 7-day risk window (data thru Jun 11, 2021)

		Females		Males			
Age groups	Doses admin	Expected*,†	Observed*	Doses admin	Expected*,†	Observed*	
12–17 yrs	2,189,726	0–2	19	2,039,871	0–4	128	
18–24 yrs	5,237,262	1–6	23	4,337,287	1–8	219	
25–29 yrs	4,151,975	0–5	7	3,625,574	1–7	59	
30–39 yrs	9,356,296	2–18	11	8,311,301	2–16	61	
40–49 yrs	9,927,773	2–19	18	8,577,766	2–16	34	
50–64 yrs	18,696,450	4–36	18	16,255,927	3–31	18	
65+ yrs	21,708,975	4–42	10	18,041,547	3–35	11	
Not reported	-	_	1	-	_	8	



*Assumes a 7-day post-vaccination observation window (i.e., symptom onset from day of vaccination through Day 6 after vaccination)

*Based on Gubernot et al. U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccine. 2021 May 14:502644.00(21)0578-8. Expected counts among females 12-29 years adjusted for lower prevalence relative to males by factor of 1.7 (Fainweather, D. et al., Curr Probl Cardiol. 2013;38(1):

Preliminary myocarditis/pericarditis reports to VAERS following dose 2 mRNA COVID-19 vaccination, Exp. vs. Obs. using 21-day risk window (data thru Jun 11, 2021)

	Females			Males			
Age groups	Doses admin	Expected*,†	Observed*	Doses admin	Expected*,†	Observed*	
12-17 yrs	2,189,726	1–7	20	2,039,871	1–12	132	
18-24 yrs	5,237,262	2–18	27	4,337,287	2–25	233	
25–29 yrs	4,151,975	1–15	11	3,625,574	2–21	69	
30–39 yrs	9,356,296	5–54	14	8,311,301	5–48	71	
40–49 yrs	9,927,773	6–57	23	8,577,766	5–49	40	
50–64 yrs	18,696,450	11–108	25	16,255,927	9–94	34	
65+ yrs	21,708,975	12–125	17	18,041,547	10–104	16	
Not reported	_	_	1	_	_	9	



^{*} Assumes a 21-day post-vaccination observation window (i.e., symptom onset from day of vaccination through Day 20 after vaccination)

Based on Gubernot et al. U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. Vaccine. 2021 May 14:50264-410X(21)00578-8. Expected counts among females 12-29 years adjusted for lower prevalence relative to males by factor of 1.7 (Fairweather, D. et al. Curr Probl Cardiol. 2013-38/11)7-46).

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

Study of 2 COVID-19 Vaccines Show Positive Safety Results With Pregnancy

April 28, 2021 Jennifer Gershman, PharmD, CPh



Preliminary study results showed no safety concerns among pregnant women that received Pfizer-BioNTech and Moderna COVID-19 vaccines.

New evidence supports pregnant women receiving coronavirus disease 2019 (COVID-19) vaccines.

No Effect on Male Fertility

Letters

RESEARCH LETTER

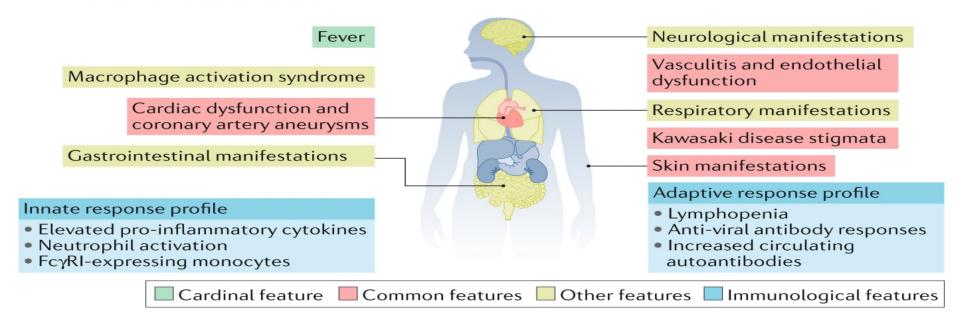
Sperm Parameters Before and After COVID-19 mRNA Vaccination

Discussion | In this study of sperm parameters before and after 2 doses of a COVID-19 mRNA vaccine, there were no significant decreases in any sperm parameter among this small cohort of healthy men. Because the vaccines contain mRNA and not the live virus, it is unlikely that the vaccine would affect sperm parameters. While these results showed statistically signifi-

Time to vaccinate Children? Was it studied?

Fig. 1: Emerging clinical and immunological features of MIS-C.

From: MIS-C: early lessons from immune profiling



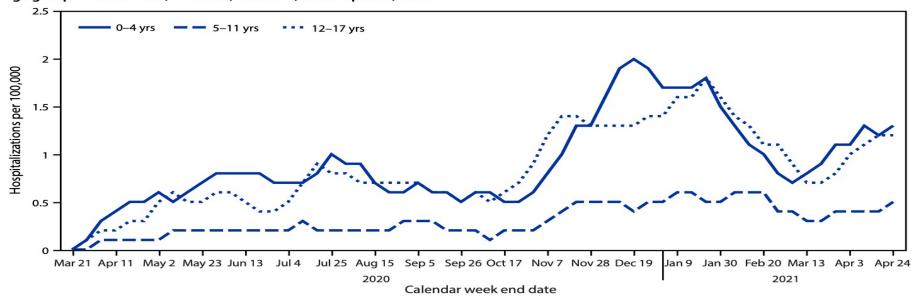
Children 2020, 7(7), 69; https://doi.org/10.3390/children7070069

NATURE REVIEWS | RHEUMATOLOGY

Morbidity and Mortality Weekly Report

Hospitalization of Adolescents Aged 12–17 Years with Laboratory-Confirmed COVID-19 — COVID-NET, 14 States, March 1, 2020–April 24, 2021

FIGURE 1. Three-week moving average COVID-19-associated hospitalization rates* among children and adolescents aged <18 years, by age group — COVID-NET, 14 states,† March 1, 2020-April 24, 2021



Abbreviation: COVID-NET = Coronavirus Disease 2019-Associated Hospitalization Surveillance Network.

^{*} Number of patients with laboratory-confirmed COVID-19-associated hospitalizations per 100,000 population.

[†] COVID-NET sites are in the following 14 states: California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.

Myths and Facts about COVID-19 Vaccines

Updated July 7, 2021

Languages ▼

Print

How do I know which COVID-19 vaccine information sources are accurate?

Accurate vaccine information is critical and can help stop common myths and rumors.

It can be difficult to know which sources of information you can trust. Before considering vaccine information on the Internet, check that the information comes from a credible source and is updated on a regular basis. Learn more about finding credible vaccine information.

Is it safe for me to get a COVID-19 vaccine if I would like to have a baby one day?

Yes. If you are trying to become pregnant now or want to get pregnant in the future, you may get a COVID-19 vaccine when one is available to you.

There is currently no evidence that COVID-19 vaccination causes any problems with pregnancy, including the development of the placenta. In addition, there is no evidence that female or male fertility problems are a side effect of any vaccine, including COVID-19 vaccines.



CDC Provides Transparent Information to the Public about Issues with Vaccines

CDC educational materials*

Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination

Updated May 27, 2021 Languages ▼ Prin

What You Need to Know

- More than 165 million people have received at least one dose of COVID-19 vaccine in the United States, and CDC continues to monitor the safety of COVID-19 vaccines for any health problems that happen after vaccination.
- Since April 2021, there have been increased reports to the Vaccine Adverse Event Reporting System (VAERS) of cases
 of inflammation of the heart—called myocarditis and pericarditis—happening after mRNA COVID-19 vaccination
 (Pfizer-BioNTech and Moderna) in the United States.
- These reports are rare, given the number of vaccine doses administered, and have been reported after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults.
- CDC and its partners are actively monitoring these reports, by reviewing data and medical records, to learn more
 about what happened and to see if there is any relationship to COVID-19 vaccination.
- Most patients who received care responded well to medicine and rest and quickly felt better.

Clinical Considerations: Myocarditis and Pericarditis after Receipt of mRNA COVID-19 Vaccines Among Adolescents and Young Adults

Summary

Since April 2021, increased cases of myocarditis and pericarditis have been reported in the United States after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults. There has not been a similar reporting pattern observed after receipt of the Janssen COVID-19 Vaccine (Johnson & Johnson).

In most cases, patients who presented for medical care have responded well to medications and rest and had prompt improvement of symptoms. 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 and its partners are investigating these reports of myocarditis and pericarditis following mRNA COVID-19 vaccination.

CDC continues to recommend <u>COVID-19 vaccination</u> for everyone 12 years of age and older given the risk of COVID-19 illness and related, possibly severe complications, such as long-term health problems, hospitalization, and even death.





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