COVID-19 Vaccination and Reproduction: Pregnancy, Lactation, Fertility, and Family

Sarah L. Berga, MD
Professor and Chair
Department of Obstetrics and Gynecology
Jacobs School of Medicine and Biomedical Sciences | UB SUNY
Medical Director
Obstetrics and Gynecology and Women's Health Program Development
Oishei Children's Hospital | Kaleida Health

JOHN R. OISHEI Children's Hospital | Leading with CARE

Disclosures: Sarah L Berga MD
August 2021

CONSULTING:

Ferring Pharmaceuticals SW Reproductive Health Advisory Board, 10.25.19, Denver, CO

ClearBlue Medical Advisory Board, 11.20.19, Washington DC

EDITORIAL BOARDS & POSITIONS:

American Journal of Obstetrics and Gynecology, Advisory Board: 2003-present *(Gratis)* ***Human Reproduction Update, Associate Editor, 2017 to 2020 (gratis)***

International Society for Gynecological Endocrinology, *Executive Committee Member*: 2004-present (*Gratis)*

Journal of Obstetrics and Gynecology Canada, *International Editorial Board:* 2017-present (*Gratis)*

Mayo Clinic Proceedings*, Editorial Board*: *2019-present (Gratis)*

Menopause*, Editorial Board*: 1999-present (*Gratis)*

UpToDate, *Peer Review Board*: 2005-present

SERVICE:

Member, Board of Trustees, Salem Academy and College, Salem, NC: 2018-present *(Gratis)*

COVID-19 Vaccination and Reproduction: Pregnancy, Lactation, Fertility, and Family

LEARNING OBJECTIVES

- **Understand the risks and benefits of COVID-19 vs COVID-19 vaccination in:**
  - **Men and women with infertility or fertility concerns**
  - **Pregnant women**
  - **Lactating women**
  - **Family members**

COVID-19 Vaccination and Reproduction: Pregnancy, Lactation, Fertility, and Family

- **Vaccination is safer for all aspects of reproductive function than COVID-19 infection**
- Women and men seeking to conceive and those undergoing infertility care should get vaccinated
- Women who are currently pregnant should get vaccinated
- Women who are currently lactating should get vaccinated
- As many family members as are eligible should vaccinated

COVID-19 Vaccination and Reproduction: Pregnancy, Lactation, Fertility, and Family

- **Women and men seeking to conceive and those undergoing infertility care should get vaccinated**
- There is no evidence that **COVID-19 vaccination has any long-term effects on fertility, miscarriage**, oocytes (eggs), or sperm quality and quantity
- **COVID-19 infection may temporarily impair fertility by reducing the brain messages to the ovaries that causes ovulation (folliculogenesis) and the testes that produces sperm (spermatogenesis)**
- Vaccination is clearly better for fertility than COVID-19 infection

COVID-19 Vaccination and Reproduction: Pregnancy, Lactation, Fertility, and Family

- **Immune education:** COVID-19 vaccination is a safer way to build immunity than getting infected, in part because getting infected comes with a high risk of other medical consequences, especially in pregnancy

- Risks for severe COVID-19 illness and mortality far outweigh any benefits of natural immunity

- Immunity produced by vaccination appears to provide better protection than that which follows infection

- The Delta variant seems to be at least as harmful and is more contagious than the Alpha variant

Fertility

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM)
PATIENT MANAGEMENT AND CLINICAL RECOMMENDATIONS DURING THE CORONAVIRUS (COVID-19) PANDEMIC

UPDATE No. 11 – COVID-19 Vaccination

December 16, 2020

Because COVID-19 mRNA vaccines are not composed of live virus, they are not thought to cause an increased risk of infertility, first or second trimester loss, stillbirth, or congenital anomalies.

FAQS: COVID-19 and Reproductive Function

Q: Is it safe to try to conceive or to undergo infertility treatment during or after vaccination?

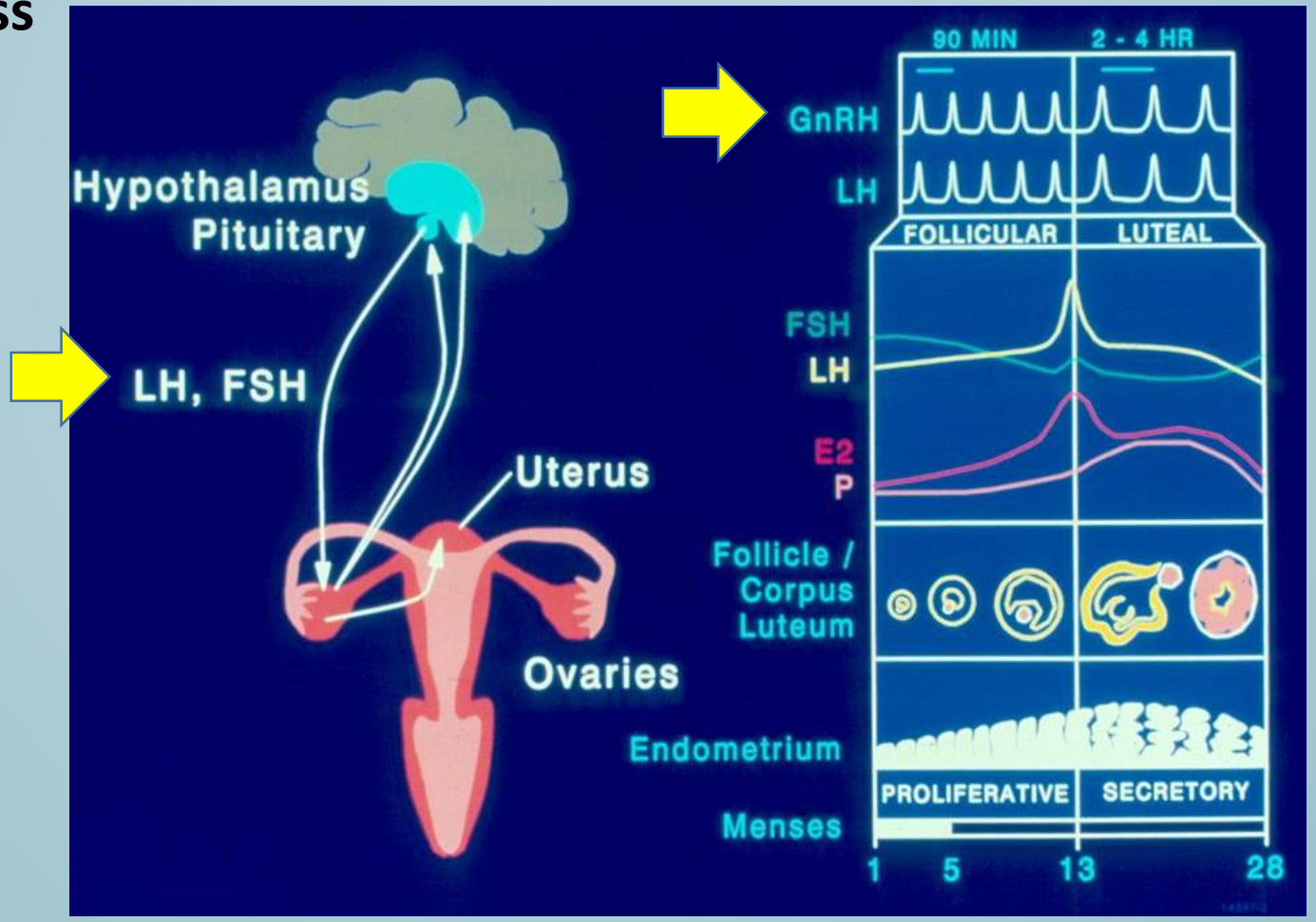
A: It is better to get vaccinated before infertility interventions.

A: COVID-19 infection is likely to compromise fertility; a recent COVID-19 infection may delay in conception or impair outcomes from infertility interventions.

FAQS: COVID-19 and Reproductive Function

Q: By what mechanisms might COVID-19 infection compromise fertility?

-Most likely mechanism is reduced folliculogenesis and spermatogenesis secondary to suppression of hypothalamic GnRH drive to ovaries and testes due to metabolic demand of acute and chronic illness



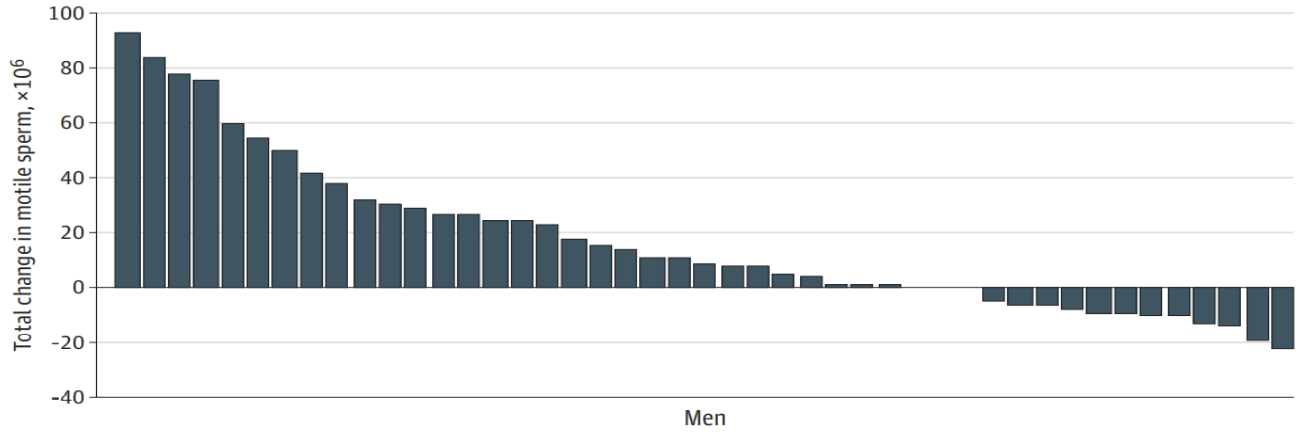
Sperm parameters before and after COVID-19 mRNA vaccination

Table. Change in Semen Analysis Parameters Before and After COVID-19 Vaccination

Parameter	Normal value	Median (IQR)		*P* value
		Baseline	Follow-up	
No. of participants		45	45	
Volume, mL	>1.5	2.2 (1.5-2.8)	2.7 (1.8-3.6)	.01
Sperm concentration, million/mL	>15	26 (19.5-34)	30 (21.5-40.5)	.02
Total motility, %	>40	58 (52.5-65)	65 (58-70)	.001
TMSC, million	>9	36 (18-51)	44 (27.5-98)	.001

Abbreviations: IQR, interquartile range; TMSC, total motile sperm count.

Figure. Waterfall Plot Showing Changes in Total Motile Sperm Count Parameters Within Participants Before and After COVID-19 Vaccination



Each bar represents an individual participant.

FAQS: COVID-19 and Reproductive Function

Q: Many infections persist in semen. Is there COVID-19 in semen?

A: Yes. Incidence unknown.

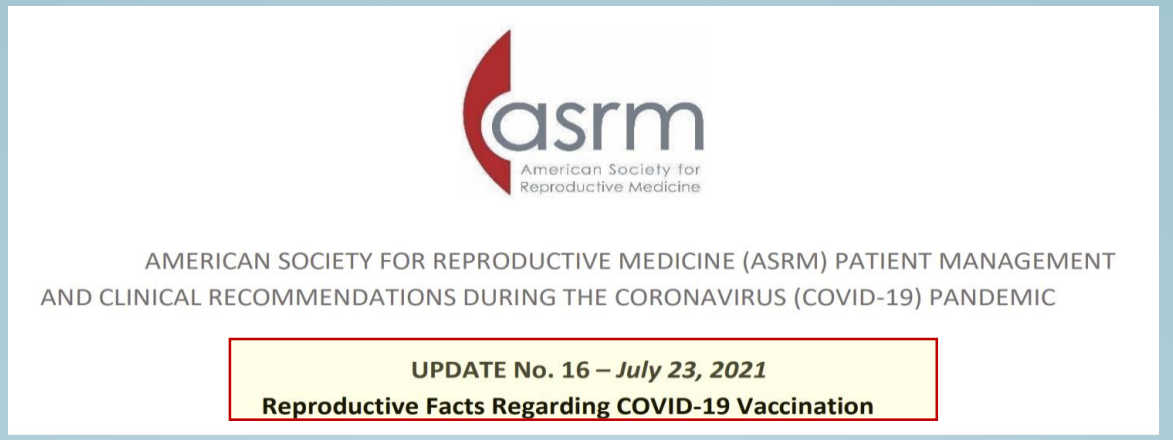
Q: Is semen potentially infectious? If so, does it compromise fertility or outcomes associated with ART?

A: Unknown.

Q: Should men who have had COVID-19 wait to try to conceive or to donate sperm? If so, for how long?

A: Wait at least 90 days.

Reports indicate ↓ sperm concentration and ↓sperm motility for 72–90 days following COVID-19 infection Fertil Steril 2020 113:1140-1149.



COVID-19 VACCINES DO NOT:

- reach or cross the placenta
- induce antibodies against the placenta
- increase the risk of miscarriage
- impact male or female fertility
- impact fertility treatment outcomes

JOHN R. OISHEI Children's Hospital

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM) PATIENT MANAGEMENT AND CLINICAL RECOMMENDATIONS DURING THE CORONAVIRUS (COVID-19) PANDEMIC

UPDATE No. 16 – *July 23, 2021*
Reproductive Facts Regarding COVID-19 Vaccination

- Reproductive endocrinologists should discuss COVID-19 vaccination with all patients and encourage vaccination for all patients during evaluation and treatment for infertility. Vaccination either pre-conception or early during pregnancy is the best way to reduce maternal/fetal complications. Physician counseling has been shown to have significant positive impact on patient willingness to consider vaccination.[9]

- None of the currently available COVID-19 vaccines reach or cross the placenta. The intramuscularly administered vaccine mRNA remains in the deltoid muscle cell cytoplasm for just a few days before it is destroyed.[10,11] However, protective antibodies to COVID19 have been shown to cross the placenta and confer protection to the baby after delivery.[12,13]

- COVID19 vaccination does not induce antibodies against the placenta.[14]

- Existing data suggest COVID19 vaccination during pregnancy does not increase risk of miscarriage.[15]

- COVID19 vaccination does not impact male or female fertility or fertility treatment outcomes.[16-18]

Pregnancy – A Special Opportunity

To Be Vaccinated By Mom

COVID-19 vaccination rates in pregnancy March 13-May 8 – MMWR

Summary

What is already known about this topic?

Pregnant women are at increased risk for severe illness and death from COVID-19.

What is added by this report?

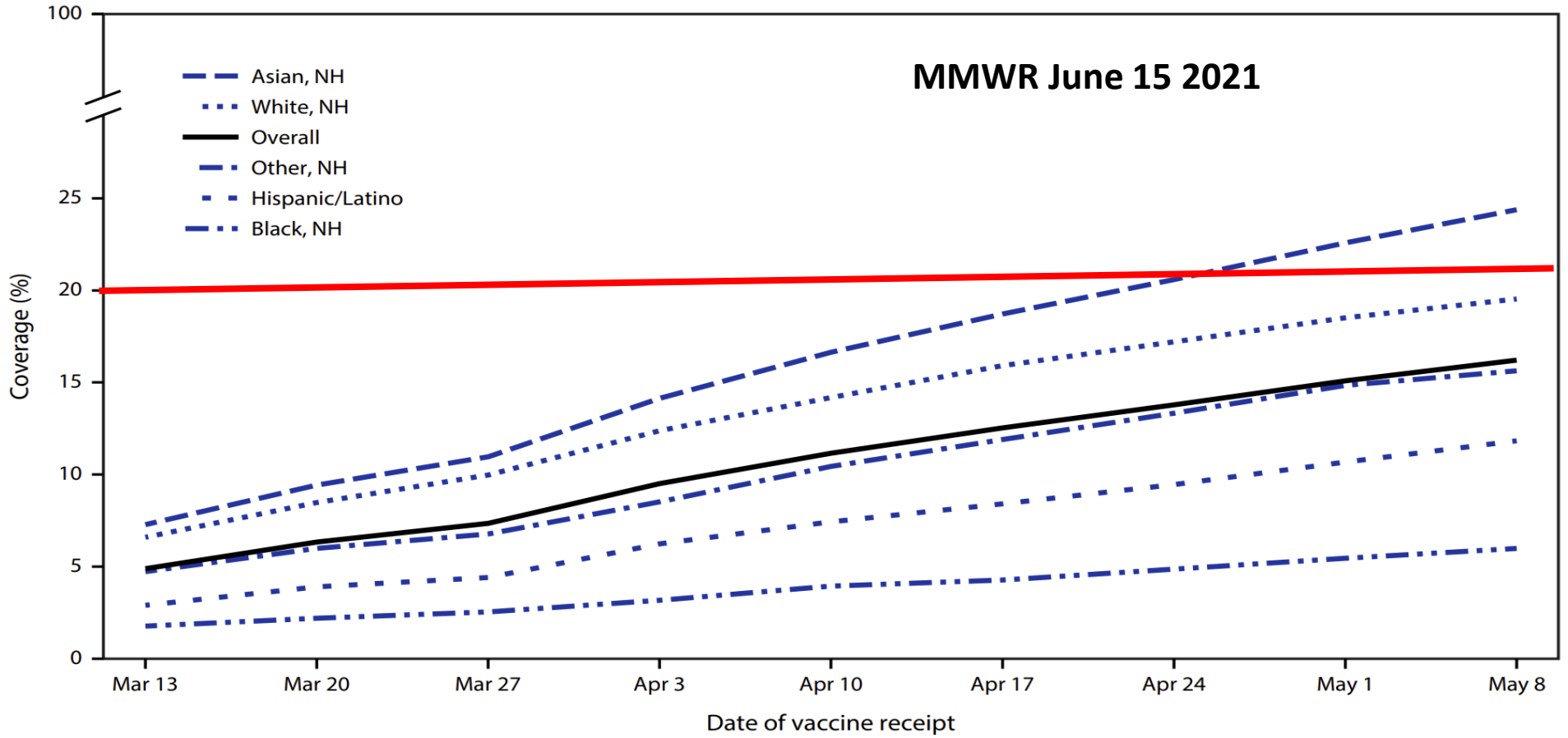
As of May 8, 2021, 16.3% of pregnant women identified in CDC's Vaccine Safety Datalink had received ≥1 dose of a COVID-19 vaccine during pregnancy in the United States. Vaccination was lowest among Hispanic (11.9%) and non-Hispanic Black women (6.0%) and women aged 18–24 years (5.5%) and highest among non-Hispanic Asian women (24.7%) and women aged 35–49 years (22.7%).

What are the implications for public health practice?

Improving outreach to and engagement with health care providers and pregnant women, especially those who are younger and from racial and ethnic minority groups, could increase vaccine confidence and thus coverage of COVID-19 vaccination in this population.

COVID-19 vaccination rates in pregnancy March 13-May 8

FIGURE. Cumulative COVID-19 vaccination coverage (receipt of ≥1 dose*) among pregnant women,† overall and by race and ethnicity§ — Vaccine Safety Datalink, United States, March 13–May 8, 2021¶



Abbreviation: NH = non-Hispanic.

* Receipt of first or second dose of the Pfizer-BioNTech or Moderna vaccines or a single dose of the Janssen (Johnson & Johnson) vaccine.

† All pregnant women identified in the Vaccine Safety Datalink during December 14, 2020–May 8, 2021. These estimates do not exclude pregnant women who completed COVID-19 vaccination before pregnancy.

§ "Other, NH" includes American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and Multiple or Other races.

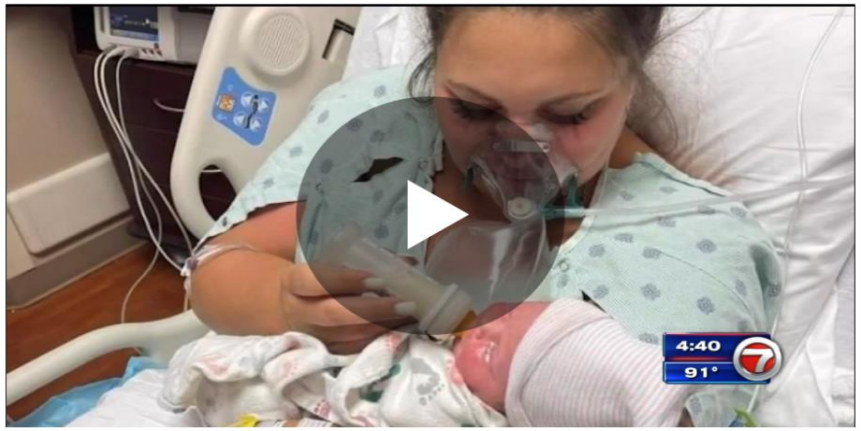
¶ Cumulative vaccination data from the Vaccine Safety Datalink were first reported to CDC on March 13, 2021, and included vaccines administered since December 14, 2020; thus, data reported during December 14, 2020–March 12, 2021, could not be displayed by week.

How harmful is COVID-19 infection during pregnancy?

- Cohort study of pregnant US women compared outcomes in those with and without COVID-19 infection from Mar 1, 2020 to Feb 28, 2021 - before Delta variant predominance
- 869 079 total, 850 364 wo and 18 715 with COVID-19
- Odds ratios (OR)
  - **Preterm delivery**
    - OR < 28 wk **9.22** (3.70-23.01) p<0.001
    - OR 28-31 wk **12.64** (3.79-42.24) p<0.001
    - OR 32-36 wk **22.83** (9.74-53.49) p<0.001
    - OR ≥ 37 wk **0.44** (3.97-27.47) p<0.001
  - **Term delivery**
    - OR ≥ 37 wk **0.44** (3.97-27.47) p<0.001
  - **ICU admission** during delivery 5.2% with vs 0.9% wo; OR **5.84** (5.46-6.25) p<0.001
  - **Resp failure / mechanical vent** 1.5% with vs 0.1% wo; OR **14.33** (12.50-16.42) p<0.001
  - **Death** 0.1% with vs <0.01% wo; OR **15.38** (9.68-24.43) p<0.001

Chinn et al. JAMA Network Open 2021

Florida woman dies from COVID-19 just days after giving birth



MELBOURNE, Fla. (WSVN) — A Florida woman has died from COVID-19 just days after she gave birth to her child.

Fox 35 reports that 30-year-old Kristen McMullen was only able to hold her

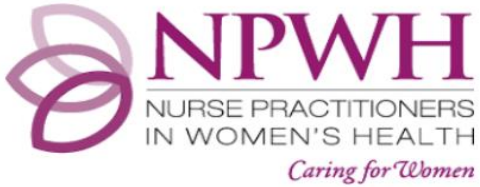
Vaccination in Pregnancy

- Vaccines currently available under the Emergency Use Authorization have not been explicitly tested in pregnant and lactating women
- **At least 139,000** pregnant women have been vaccinated with no excess adversity
- Does the vaccine integrate into our DNA? Does it cause mutations?

  This has not been observed and is unlikely because…..

  -RNA requires a specific enzyme (reverse transcriptase) to integrate into DNA.

  -This enzyme is not present in coronavirus or in humans.



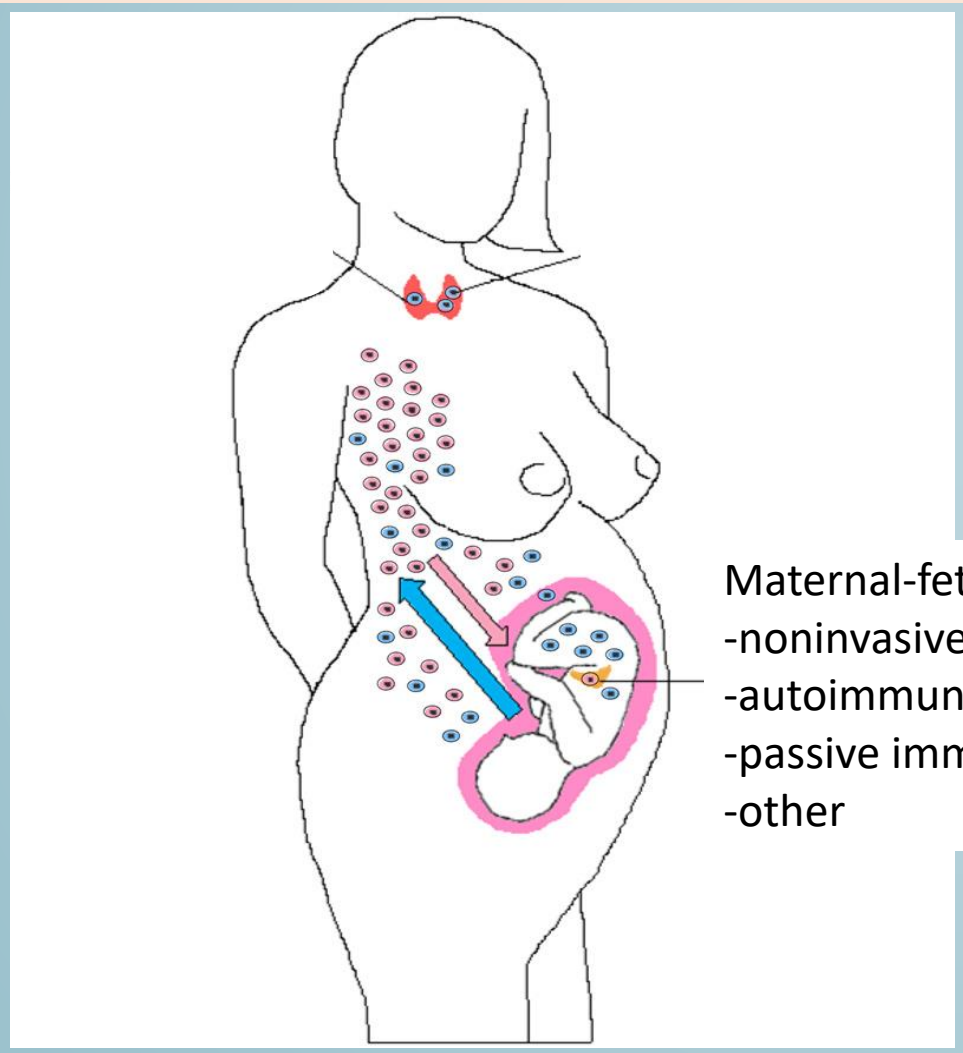
Last updated: July 30, 2021

COVID-19 Vaccination if You Are Pregnant or Breastfeeding

Last updated: July 30, 2021

- Another potential benefit is that getting the vaccine while pregnant may help you pass anti-COVID-19 antibodies to your baby. In numerous studies of vaccinated moms, antibodies were found in the umbilical cord blood of babies and in the mother's breastmilk.
- The Centers for Disease Control and Prevention (CDC), along with other federal partners, are monitoring people who have been vaccinated for serious side effects. So far, more than 139,000 pregnant people have been vaccinated. No unexpected pregnancy or fetal problems have occurred. There have been no reports of any increased risk of pregnancy loss, growth problems, or birth defects.
- A safe vaccine is generally considered one in which the benefits of being vaccinated outweigh the risks. The current vaccines are not live vaccines. There is only a very small chance that they cross the placenta, so it's unlikely that they even reach the fetus. Vaccines don't affect future fertility. The only people who should NOT get vaccinated are those who have had a severe allergic reaction to vaccines in the past or any vaccine ingredients.

Babies cannot be directly immunized…….
but can be “vaccinated” by mom

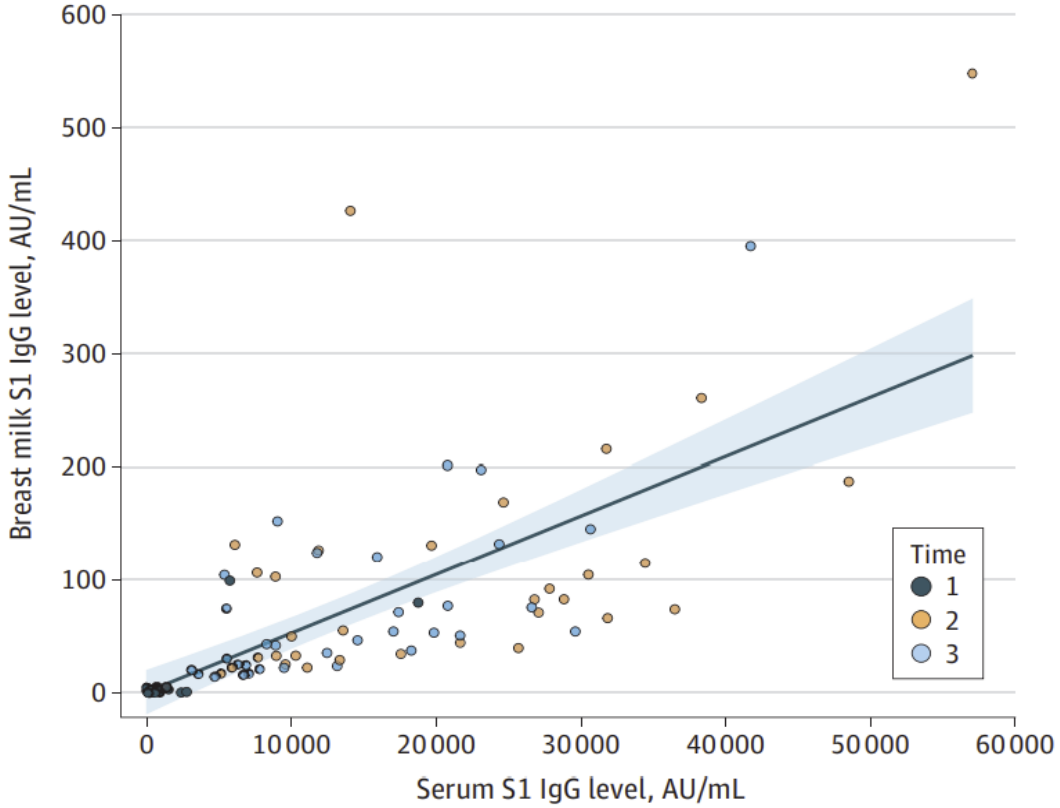


Maternal-fetal bidirectional microchimerism is universal:
-noninvasive prenatal testing (NIPT)
-autoimmune disease in mother and/or offspring
-passive immunization
-other

Lactation

Anti-COVID-19 antibodies correlate in serum and breastmilk

Figure 2. Correlation Between Immunoglobulin (Ig) G S1 Subunit (S1) Levels in Serum and Breast Milk of Vaccinated Participants



AU indicates arbitrary units.

JAMA Network Open. 2021;4(8):e2120575. doi:10.1001/jamanetworkopen.2021.20575

August 11, 2021

Offspring can be “vaccinated” by mom
before, during, and even after pregnancy if mom breastfeeds

COVID-19 Vaccines While Pregnant or Breastfeeding

Updated Aug. 11, 2021

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

-New analysis of registry data
-No increase in miscarriage among pregnant women who got mRNA vaccine before 20 weeks
-Prior findings also showed no safety concerns when vaccinated late in pregnancy or in their infants

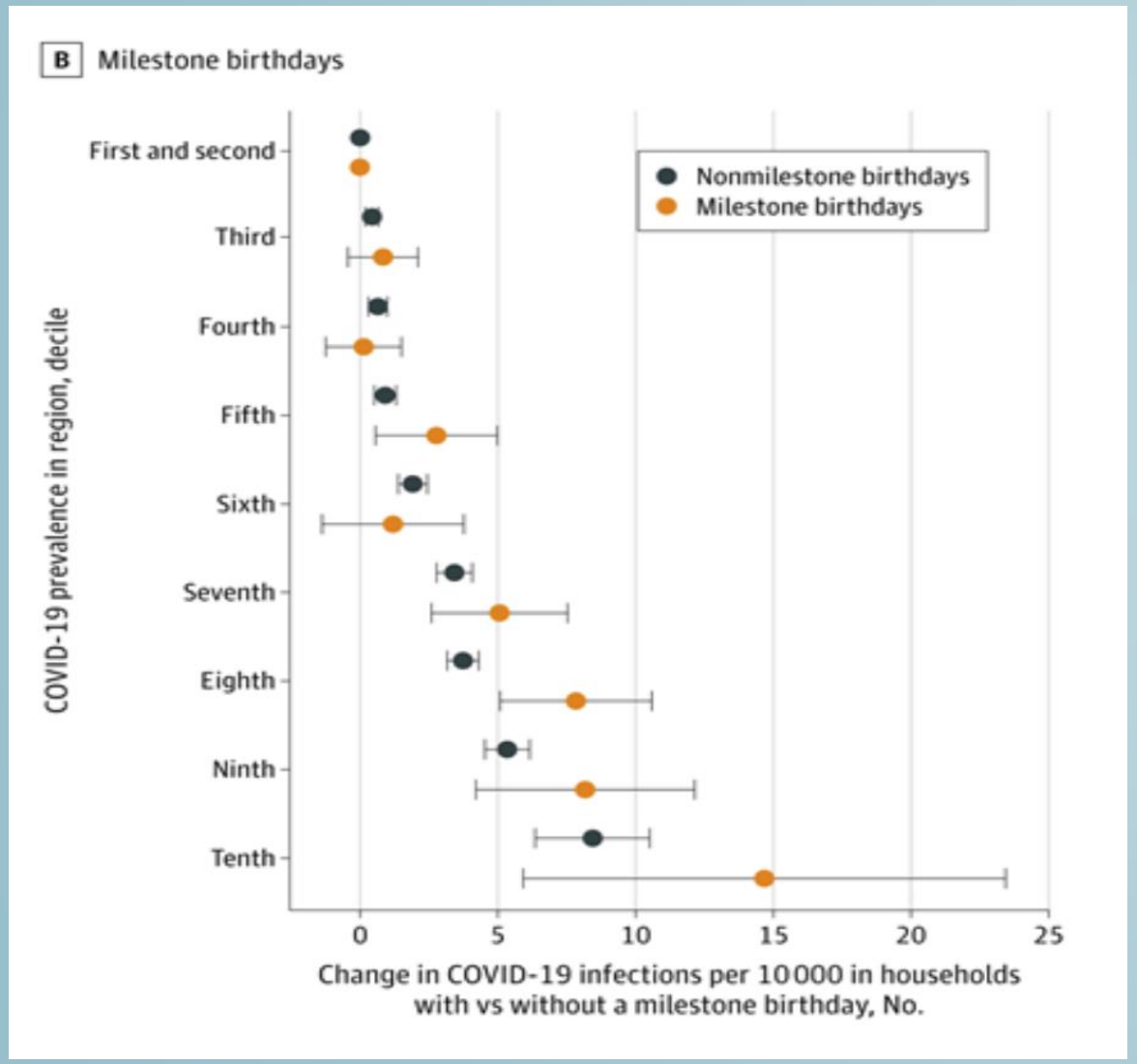
COVID-19 vaccination is recommended for all people aged 12 years and older, including people who are pregnant, breastfeeding, trying to get pregnant now, or might become pregnant in the future. Pregnant and recently pregnant people are more likely to get severely ill with COVID-19 compared with non-pregnant people. Getting a COVID-19 vaccine can protect you from severe illness from COVID-19.

Men Too!

Men are partners and parents too

Men’s fertility needs to be protected too

As children return to school, exposures will increase, so now is the time to vaccinate as many members of the household as possible

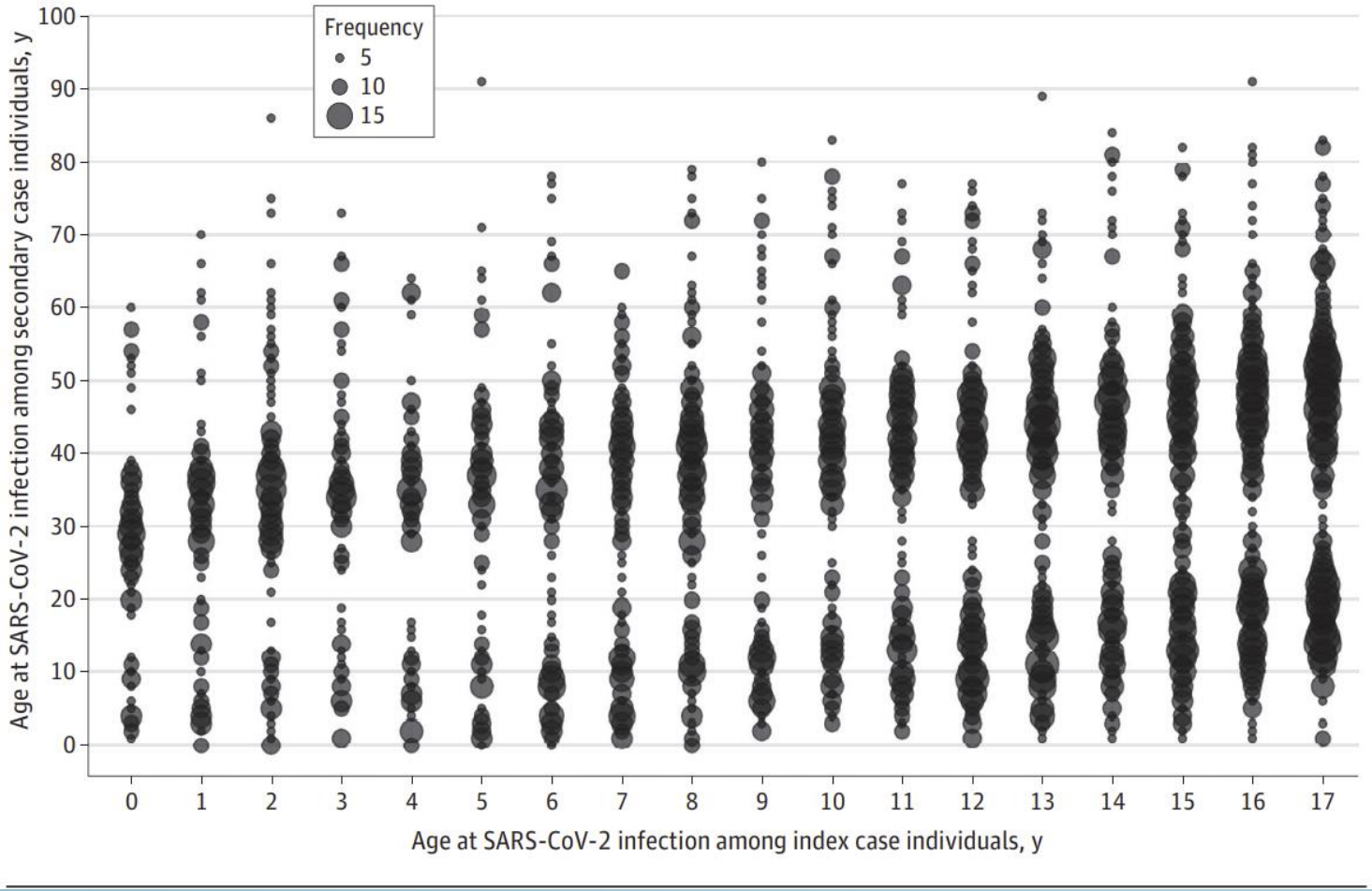


Assessing the association between social gatherings and COVID-19 risk using birthdays

JAMA Intern Med 2021;181:1090-1099

As children return to school, exposures will increase, so now is the time to vaccinate as many members of the household as possible

Figure 2. Bubble Plot of Age-to-Age Transmission



JAMA Pediatrics | Original Investigation

Association of Age and Pediatric Household Transmission of SARS-CoV-2 Infection

Lauren A. Paul, MSc; Nick Daneman, MD; Kevin L. Schwartz, MD; Michelle Science, MD; Kevin A. Brown, PhD; Michael Whelan, MSc; Ellen Chan, MSc; Sarah A. Buchan, PhD

JAMA Pediatr. doi:10.1001/jamapediatrics.2021.2770
Published online August 16, 2021.

This study suggests that younger children may be more likely to transmit SARS-CoV-2 infection compared with older children, and the highest odds of transmission was observed for children aged 0 to 3 years.

COVID-19 vaccination saves lives, protects fertility, and safeguards fetal and infant health