# HHP Care Model and Disease Management Webinar Series

## Pregnant and Having a Baby During COVID-19

Thursday, October 28, 2021
5:30pm – 6:30pm

HAWAIʻI PACIFIC HEALTH | KAPIʻOLANI PALI MOMI STRAUB WILCOX

# Moderator

**Andy Lee, MD**
Medical Director, *Hawai‘i Health Partners*
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Hawai‘i Pacific Health

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# Disclaimer:

- The following is intended as information resource only for HHP/HPH providers, clinicians, administrative and clinical leaders.

- Specific areas may not pertain directly to your clinical practice area and/or may not be applicable to your practice based on your existing workflows, infrastructure, software (e.g. EHR), and communications processes.

# Webinar Information

- You have been automatically muted.
  You cannot unmute yourself.
- You will be able to submit questions via the Q&A section.
  - Due to time constraints, any unanswered questions will be addressed this week and posted on the HHP website
- A recording of the meeting will be available tomorrow on the HHP website and intranet.

# Disclosures

- The planners and presenters of this activity report no relationships with companies whose products or services (may) pertain to the subject matter of this meeting

# Pregnant and Having a Baby During COVID-19

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# Pregnant and Having a Baby …
# During COVID-19


- Rodolfo E Bégué, MD
- Pediatric Infectious Diseases
- University of Hawaii, JABSOM
- Kapi'olani Medical Center Women and Children

- October 28th, 2021

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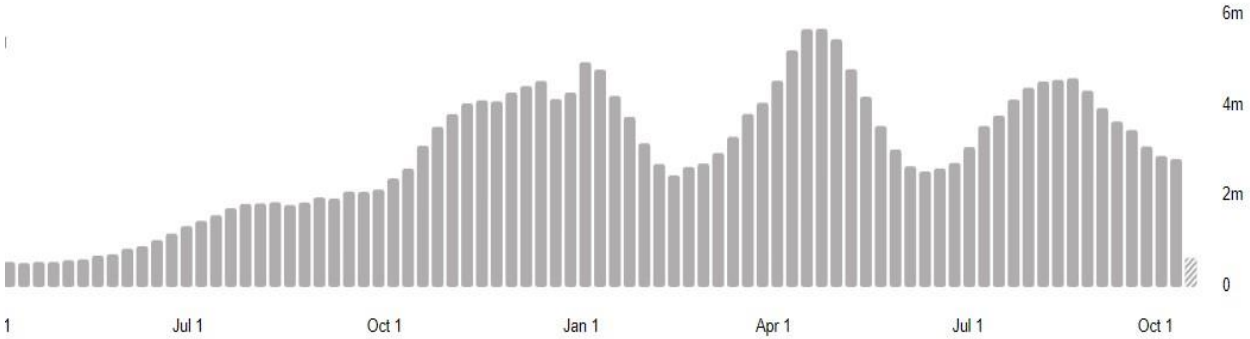
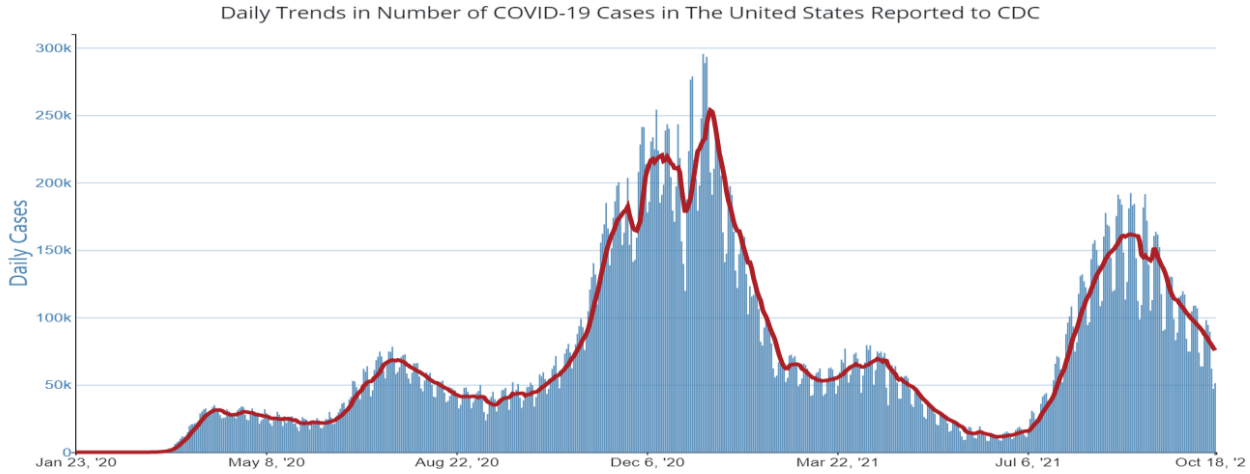



**World**
**241 M**




**USA**
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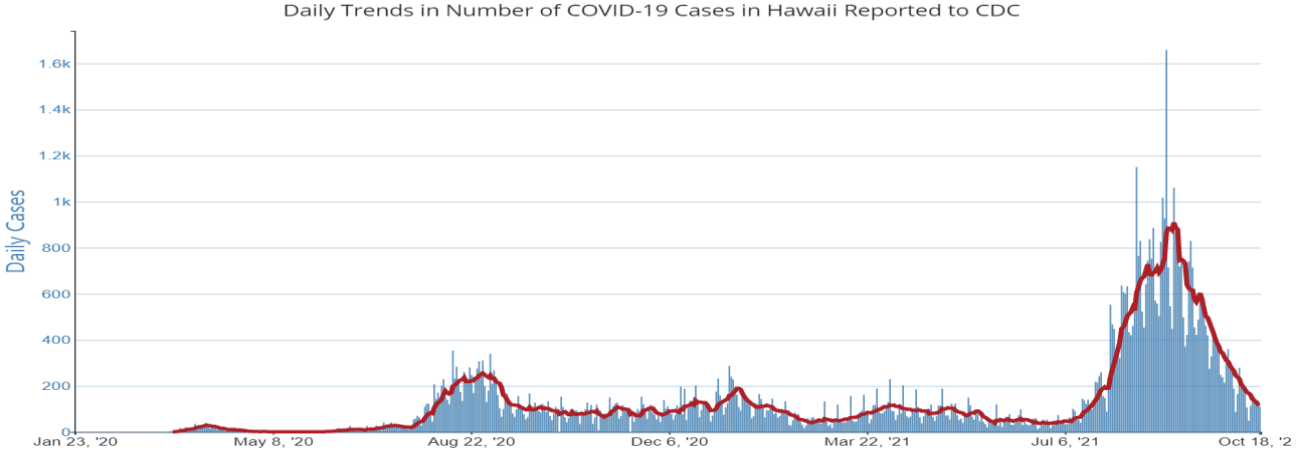


**Hawai'i**
**79.8 K**

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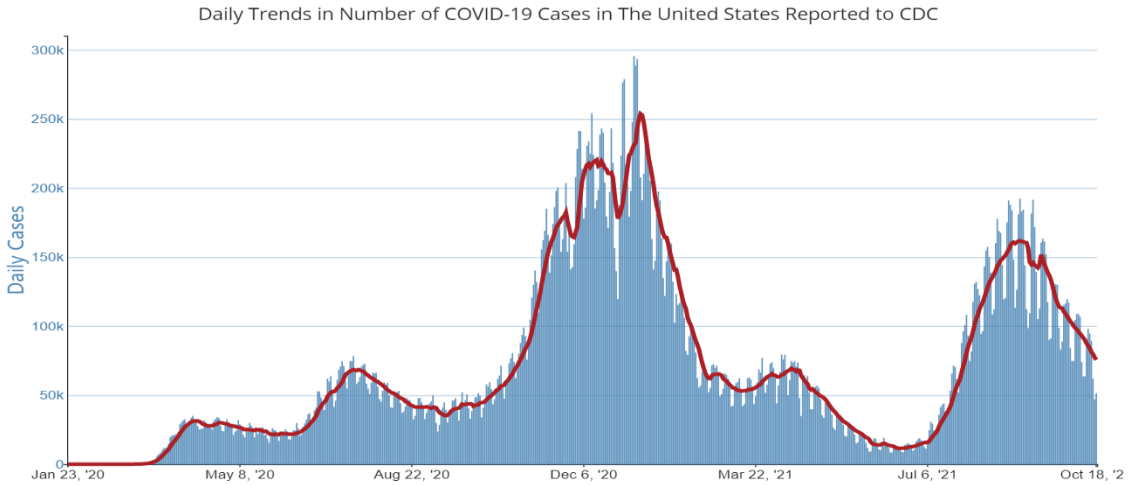
# Outline

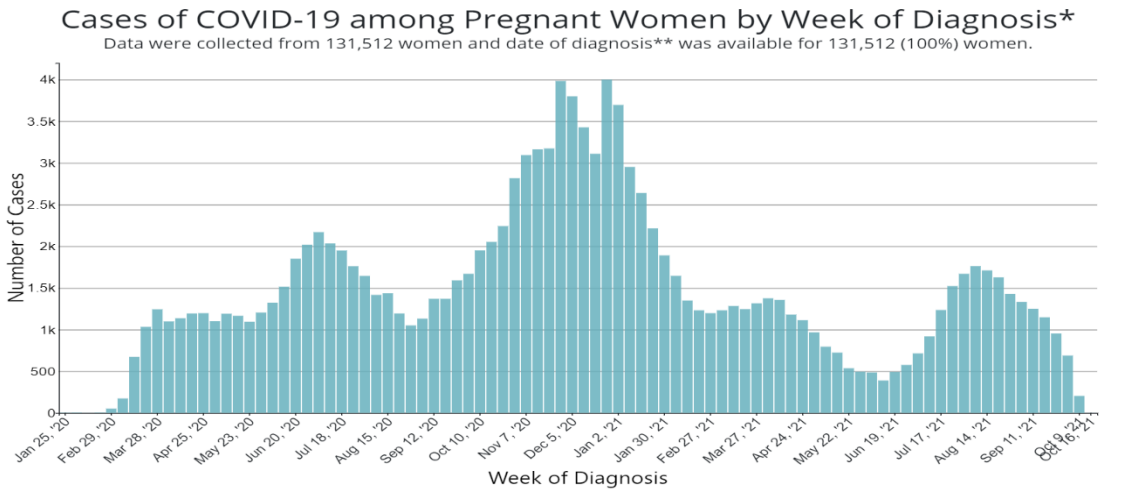
- Impact of SARS-CoV-2 in pregnant person
- Impact of SARS-CoV-2 in the neonate
- Recommendations
- SARS-CoV-2 vaccine for pregnant persons

# WHAT ABOUT MOM?

# Susceptibility During Pregnancy

- Pregnant persons are **not more** susceptible to SARS-CoV-2 infection, BUT they are not immune either




**CDC (as of 10/19/2021)**

**Total: 44,979,605**

**Pregnant: 131,512**

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# What About Severity?

- Physiologic and immunologic changes during pregnancy
- Any febrile illness can initiate labor
- SARS-CoV-2 infection can lead to viremia → 15%?
- SARS-CoV-2 “infects” the placenta but does not cross the placenta
- SARS-CoV-2 causes micro thrombosis in all organs and can cause placenta insufficiency
- The result of all this would be negative outcomes for the mom and the baby!

# COVID-19 in Pregnancy - CDC

- Ellington et al MMWR June 26, 2020;69(25):769-75 (Jan 22-June 7, 2020)
- Zambrano et al (CDC) MMWR Nov 6,2020;69(44):1641-47 (→ Oct 23, 2020)

  National Notifiable Disease Surveillance (NNDSS)
- All SARS-CoV-2 (+)
  91,142 (9% pregnant) → 461,825 (5.7% pregnant)

| | SARS-CoV-2 (+) | |
|---|---|---|
| | Pregnant | Nonpregnant |
| **Cough** | **51.8 %** | **53.7 %** |
| **Shortness of Breath** | **30.1 %** | **30.3 %** |
| **Muscle aches** | **38.1 %** | **47.2 %** |
| **Fever** | **34.3 %** | **42.1 %** |
| **Diarrhea** | **14.3 %** | **23.1 %** |

**X 1,000 pop**

| | SARS-CoV-2 (+) | |
|---|---|---|
| | Pregnant | Not-pregnant |
| **Be admitted to PICU** | **10.5** | **3.9** |
| **Require invasive ventilation** | **2.9** | **1.1** |
| **Require ECMO** | **0.7** | **0.3** |
| **death** | **1.5** | **1.2** |

**~ 1.5-3.0 X**

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# Maternal Outcomes – US (U of California)

- Chinn et al. JAMA Open 2021;4(8):e2120456
  - 499 US academic centers (review adm database captures 95% US pop)
  - 869,079 pregnant women → 18,715 (2.2%) SARS-CoV-2 (+)

| | Pregnant | |
|---|---|---|
| | SARS-CoV-2 (+) | SARS-CoV-2 (-) |
| **C-section** | **32.5%** | **32.3%** |
| **PT birth** | **16.4%** | **11.5%** |
| **ICU admission** | **5.2%** | **0.9%** |
| **Mechanical Ventilation** | **1.5%** | **0.1%** |
| **Mortality** | **0.1%** | **<0.01%** |

# COVID Mat/Neo Outcome - International

- Villar et al. JAMA Pediatrics April 22, 2021
  - 43 Institutions, 18 countries (International)
    706 (+), 1,424 (-)

- Increased risk of

| | (+) | (-) | OR |
|---|---|---|---|
| Pre-/eclampsia | 8.4 | 4.4 | 1.76 |
| Severe infection | 3.6 | 1.1 | 3.38 |
| ICU | 8.4 | 1.6 | 5.04 |
| Maternal mortality | 1.6 | 0.1 | 22.3 |
| PT birth | 22.5 | 13.6 | 1.59 |
| Severe Neonatal morbidity | 6.2 | 2.3 | 2.66 |
| Severe Perinatal morbidity | 17.0 | 7.9 | 2.14 |

Fever and SOB of any duration associated with:
increased maternal complications (2.56)
increased neonatal complications (4.97)

# The bottom line …

- … When pregnant persons are infected by SARS-CoV-2
- Clinical presentation is similar to non-pregnant
  - 33%-50% may be asymptomatic

- Most of them (~80-90%) do well … but SARS-CoV-2 makes complications TWICE AS BAD !

- Risk Factors:
  - Age
  - Underlying medical conditions (maybe 2nd part of pregnancy)

# What to do when pregnant and infected?

- Treat same as for  non-pregnant people
- Monoclonal antibodies
- $O_2$, supportive care
- Dexamethasone
- Antivirals: Remdesivir
- Immune modulators: Tocilizumab, Baricitinib
- Anticoagulation, other
- Obstetric: MgSO4, antenatal glucocorticoids, delivery (as indicated)

IDSA Guidelines on the Treatment and Management of Patients with COVID-19

# Would C/Section help?

- NO, actually it may be bad
- In Spain, C-section was associated with clinical deterioration
  - Martinez-Perez et al. JAMA 324(3):296-299
  - 78 pregnant with COVID-19 asymptomatic or mild
  - 41 VD, 37 C/S
    Clinical deterioration C/S: 8/37 (22%) vs VD: 2/41 (5%)

- … and surgery when with SARS-CoV-2 may have more complications
  - COVID Surg Collaborative. Lancet 2020;July 4, 396(10243):27-38
  - 235 hospitals, 29 countries
  - 1,128 patients SARS-CoV-2 (+) who had surgery
    - pulmonary complications → 51.2%
    - 30-day mortality → 23.8%

# WHAT ABOUT THE BABY?

# Impact of SARS-CoV-2 in the fetus/neonate

- Any complication of pregnancy will affect the fetus/neonate
- Prematurity (15%), Small Gestational Age (10%)
- In addition, 2-3 % neonates can get infected (17/263 = 2.6%)
- If infected, is it serious?
  - Not terribly →
    - children < adults
    - infants > older children
    - neonates > infants
- 67 neonates:
  - respiratory distress (18%)
  - asphyxia (2%)
  - fever (15%)
  - rash (3%)
  - DIC (3%)
  - deaths (3%)

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# How is the baby being Infected?

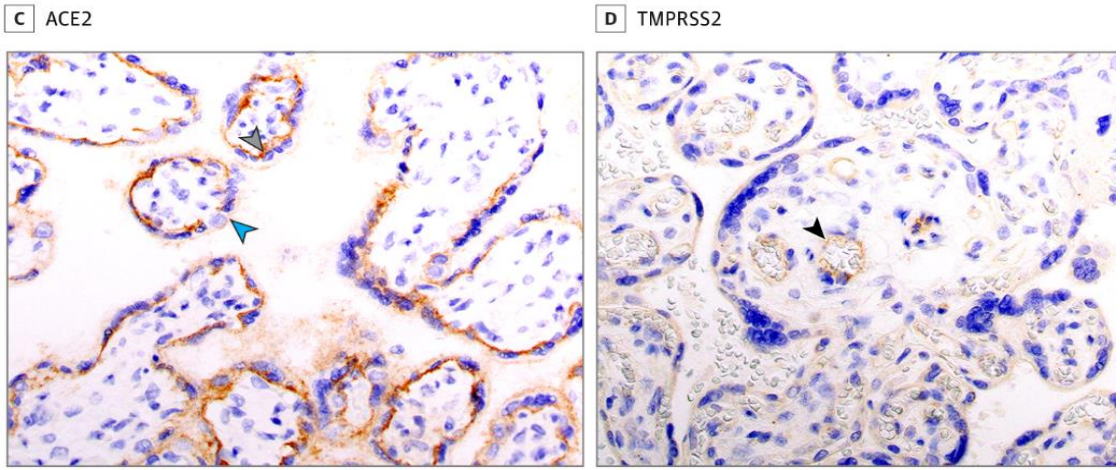
The options are:

- Trans-placentally
- Vaginal secretions
- Breast Milk
- Respiratory secretions

# Is it through the Placenta?

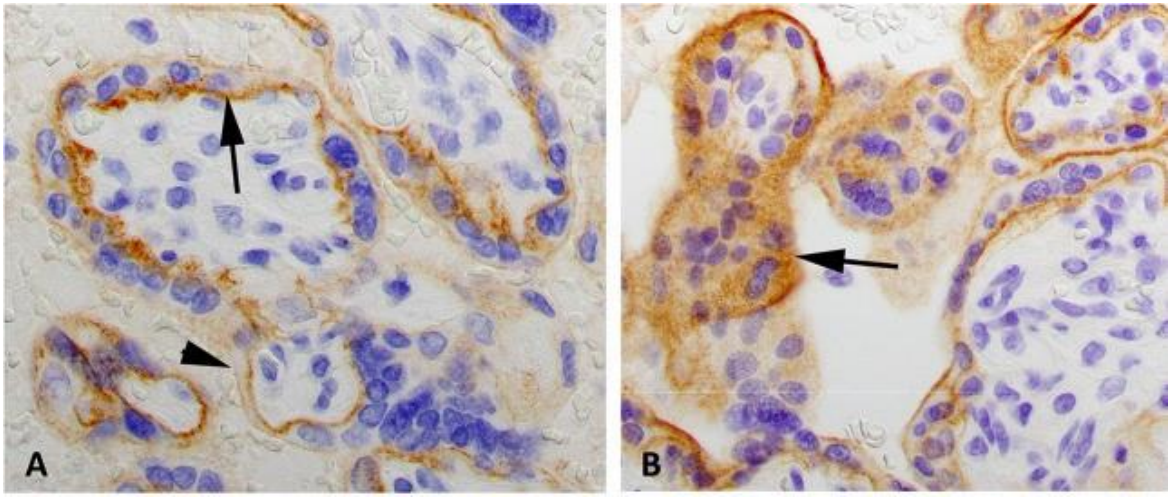
- Probably not: Placenta is not permissive of SARS-CoV-2

- Edlow et al. JAMA-Open Dec 22, 2020 (USA, Massachusetts)
  - 127 pregnant people with SARS-CoV-2 infection
  - 88 placentas → no SARS-CoV-2 detected
    - some expression ACE2 (mainly maternal side)
    - weak expression TMPRSS2
    - no co-expression



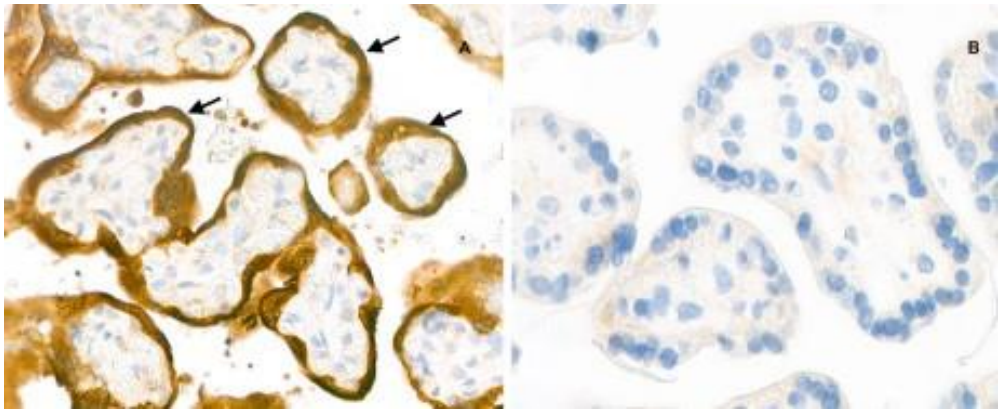
# Transplacental Transmission:

- Hecht et al. Mod Pathol 2020 (Nov);33(11):2092-2103 (USA)
- 19 placentas
- some ACE2,
  weak TMPRSS2,
  no co-expression
- 2/19 placentas SARS-CoV-2 RNA
  mainly maternal site



# Transplacental Transmission: Exceptions!

- Vivanti et al Nature Comm 2020;11:3572 (France)
  - Single case: 35 WGA COVID-19
  - $O_2$ at birth, d3 NICU, intubated, extubated d6, d/c d16
  - Placenta (+) SARS-CoV-2
  - Inflammation and fibrin deposition
  - Mom (+): NPA, vaginal, placenta, AF, blood
  - Neonate (+): NPA, blood, rectal



# “Probable” Vertical Transmission

| | | | | |
|---|---|---|---|---|
| **Demirjian et al PIDJ 2020 (Sept)** | **UK** | **1 case** | **C/S** | **5 d** |
| **Marzollo et al PIDJ 2020 (Sept)** | **Italy** | **1 case** | **VD** | **36 hr** |
| **Sisman et al PIDJ 2020 (Sept)** | **US** | **1 case** | **VD** | **24 hr** |
| **Van Kohorn et al JPIDS 2020 (Dec)** | **US** | **1 case** | **C/S** | **49 hr** |
| **Correia et al PIDJ 2020 (Dec)** | **Portugal** | **1 case** | **C/S** | **30 min** |

# What about vaginal secretions?

- Also seems extremely unlikely!
- C/S not superior to VD for outcomes
- Other CoV (SARS, MERS) have not been identified in vaginal secretions
- SARS-CoV-2 has not been identified in vaginal secretions
  - Schwartz et al. Arch Pathol Lab Med 2020:doi.5858/arpa.2020-0901
  - Simões et al. Front Pediatr 2020;8:276
  - Wu et al. BJOG 2020;127(9):1109-1115
- **Exception:** Vivanti et al Nature Communications 2020;11:3572
  - **BUT:** it has been identified in fecal samples, though

# What about BM?

- Highly unlikely!!
- Other CoV (SARS or MERS) have not been detected in BM
- Good et al (preprint bioRxIV)
  - Mammary gland luminal epithelial cells express ACE2 poorly
  - Only 5% expressed ACE2
  - None co-expressed ACE2 with TMPRSS2

# SARS-CoV-2 (RNA) in Breast Milk

- Tam et al. CID 2021 (Jan 1st)
  - Mom delivered → 3 d later Sx → SARS-CoV-2 (+)
  - Baby tested 1 day later and (+)
  - 1 BM mom (+) RNA, Ct 33, no culture obtained

- Chambers et al. JAMA 2020;324(13):1347-8
  - 64 human milk from 18 SARS-CoV-2 infected women
  - Only 1/64 SARS-CoV-2 (+) by RNA
  - 26 were cultured and all negative

- Conclusion: SARS-CoV-2 in BM: very rare, only RNA, likely not viable

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# Transmission while Breast Feeding

- Shlomani et al. Pediatrics 2021 (July) Israel,
  - 763 newborns of SARS-CoV-2 (+) moms
  - BF allowed in all, with precautions → hand/breast hygiene, mask
  - all NB negative

**Conclusion:**
BF is an unlikely source of infection and should be allowed

# Then, how are they infected?

- Knowing what we know of SARS-CoV-2,
  The most likely mode of transmission of SARS-CoV-2 to neonates is horizontal, from infected close contacts (mom or other)

# Recommendations

# “Expert Opinion”

- ACOG (www.acog.org)
  Novel Coronavirus 2019 (COVID-19)

- SMFM (www.smfm.org)
  Management Considerations for Pregnant Patients with COVID-19

- AAP (www.aap.org):
  Management of Infants Born to Mothers with suspected or Confirmed COVID-19 (online)

- CDC (www.cdc.gov):
  Coronavirus disease 2019 (COVID-19)

# During Pregnancy

- Pregnant people should avoid SARS-CoV-2 as much as possible (NPI, vaccination)
- Pregnant people should be educated on how to avoid SARS-CoV-2 and the symptoms of COVID-19
- If symptomatic → get tested!
- If infected → call your doctor! → mAb!
- Family can be reassured (80-90% will do fine) but must monitor closely during illness and for at least 2 weeks after resolution of symptoms (US?)
- COVID-19 is not a reason to change delivery plans

# During Labor

- Most centers do universal testing (on all admits)
- If positive, admit to negative pressure room
  - or single-patient room with door closed
- Mom should wear mask (as tolerated)
- OB personnel should wear full protection: gloves, face mask (N95), eye protection (or air-purifying respirator)
- OB care as usual: MgSO4, antenatal glucocorticoids
- No reason to delay or induce delivery

# Baby Birth

- No preference for mode of delivery (as clinically indicated)
- When attending baby-birth of COVID-19 mom:
  - OB/Peds personnel → gown, gloves, N95 and eye protection
- OB/Peds care (delayed-cord clamping, skin-to-skin contact practices, neonatal resuscitation) → as usual
- Bath baby after birth to remove virus potentially present on the skin
- Allow mom (wearing mask) to hold baby in Delivery Room

# Baby-Mom

- Mom is infected, so she should be in isolation
- Baby is considered “exposed” and should be quarantined
- As much as possible, baby room-in with mom
- Infected neonates that require mechanical ventilation needs full isolation and HCWs in NICU need full protection
- If mom-baby together: physical barrier, 6-feet away, isolette, mom wearing mask, strict hand-washing
- Maternal COVID-19 is not a contraindication for breastmilk feeding
- If mom elects direct feeding, she should wear mask and practice strict hygiene (hands and breast)
- Alternatively, express breastmilk and feed by uninfected care-giver
- Test baby by RT-PCR (not antibodies!) nasopharynx/oropharynx at 24hr and 48hr

# Visitors

- Limit visitors

- Only one (same one)
  - tested negative (better if vaccinated)
  - restrict wandering/mingling around

- SARS-CoV-2 positive persons should not enter the NICU

# After Discharge

- Discharge as clinically indicated

- Monitor baby/mom daily for 14 days (over the phone)

- Precautions discontinuation:
  - Mom (infected): 10 days after start symptoms or positive test*
  - Baby (exposed): 10 days from last contact with mom or 1st day mom considered not infectious **
  - Other close contacts in household: similar as baby, above
    - alternatively: test negative x 2 (24 hours apart)
    - alternatively: test negative on day 5-7

# Neonate Protection from Infected Mother - NY

- Salvatore et al. Lancet Child Adolescent 2020 Oct vol 4:721-727

- Infants roomed in with their mothers in a closed isolette and mothers used a surgical mask and careful hand and breast hygiene before BF and other interactions with the baby

- 1,481 deliveries
  - 116 (8%) mothers SARS-CoV-2 (+)
  - 120 neonates → all negative up to 14 days of life

# VACCINE

# SARS-CoV-2 vaccines

**Vaccine Efficacy**:

| | | | |
|---|---|---|---|
| **mRNA** | **BNT162b2** | **Pfizer/BNT** | **95%** |
| **mRNA** | **mRNA1273** | **Moderna** | **94.1%** |
| **Adenovirus** | **Ad26. CoV2.S** | **J&J/Jansenn** | **66.9%** |

# Concerns …

- Will the vaccine make me sick?
- Will I loose my baby?
- Will it make my baby sick?
- Will it work?
- Will it make me infertile?

# How much data we have?

- Limited
- Preclinical animal data for mRNA vaccines were promising
- Pregnant people were excluded from RCTs
  But few were inadvertently enrolled
- After EUA, many pregnant/lactating persons (mainly HCWs) have received vaccines
- Formal studies are now being conducted or planned by all vaccine manufacturers

# Vaccine Evaluation

- Adverse Effects (reactogenicity)
- Immunogenicity (antibodies, others)
- Efficacy (prevention)

# Adverse Effects

- Shimabukuro et al NEJM 2021;384(24):2273-82 (v-safe, VAERS)
  - 35,691 pregnant and vaccinated
- Local reaction (injection site)
  → more frequent
- Systemic reactions (headache, myalgias, chills, fever)
  → less frequent

| | Pregnant | Lactating | None |
|---|---|---|---|
| **Number** | **30** | **16** | **57** |
| **Fever post 1st dose** | **0/30** | **0/16** | **1/52** |
| **Fever post 2nd dose** | **4/29 (14%)** | **7/16 (44%)** | **27/52 (52%)** |

Collier et al. JAMA 2021

# Adverse Effects – CDC (v-safe)

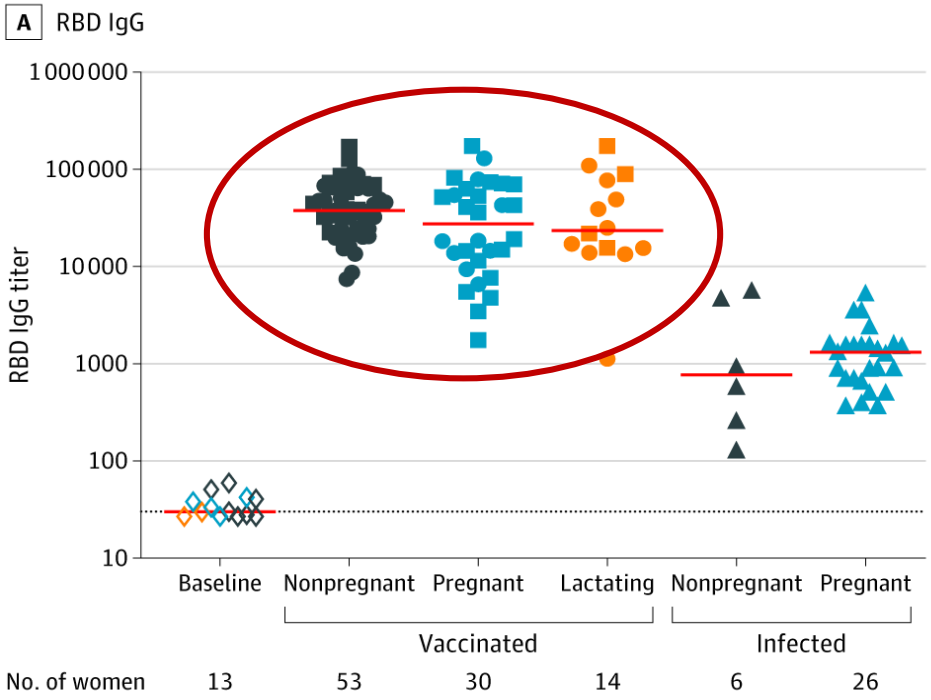
- Of those who completed pregnancy:
  - Losses (12.8%); live born (87.2%)
  - Prematurity(6.5%), SGA (2.8%)
  - NICU admission (9.7%)
  - No deaths

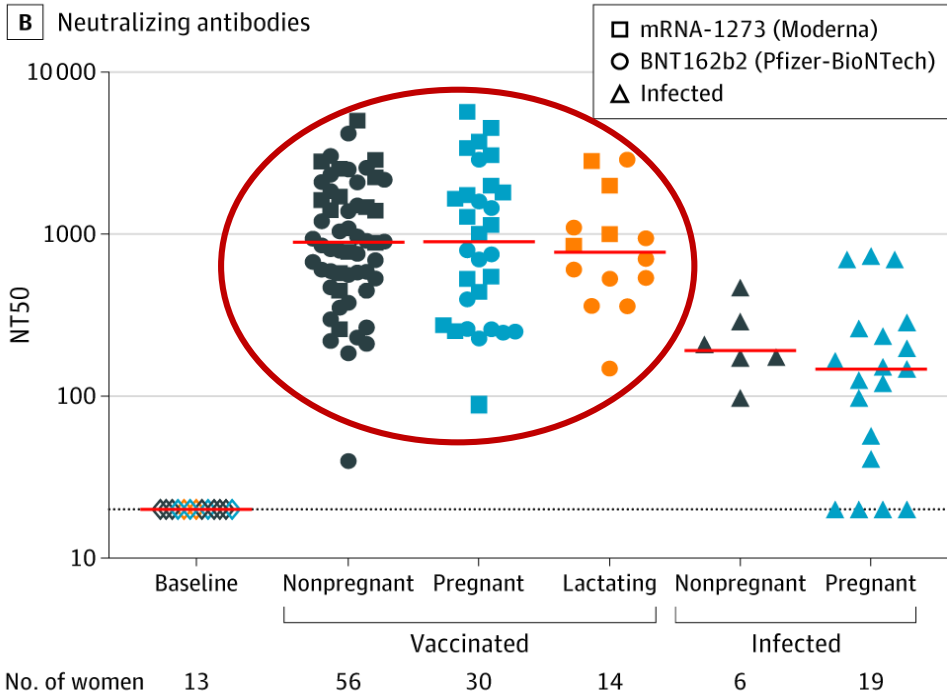
- Of those pregnant and receiving vaccine <20 weeks gestational age
  - Spontaneous loss (12.8%)
  - Malformations (0.2%)

- Conclusion:
  - Pregnant tolerate vaccine as well as non-pregnant (even better?)
  - Vaccine has no consequence in their pregnancy outcome

# Immunogenicity

- 30 pregnant, 16 lactating; 57 none
- NT Abs, nNT Abs, T cell
- Similar in all 3 groups




Collier et al JAMA 2021

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# Antibody (Abs) Transfer Mom-Baby

- Blood:
  - At the time of birth, mom transfers Abs (IgG) to the newborn
    - Rate 80-90%
    - Transfer is better if vaccinated 1st or 2nd T > 3rd T
- Breast Milk:
  - Abs (IgG and IgA) are detectable in BM
  - Level of Abs in BM are lower than serum (~100X) and unclear their role
- Vaccine mRNA is not detected in BM

Prabhu et al. Obst Gynecol 2021
Collier et al JAMA 2021
Beharier et al JCI 2021

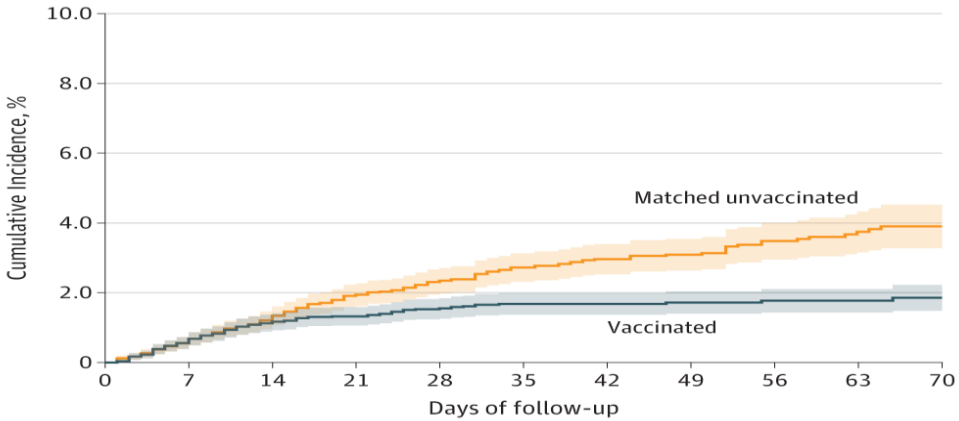
Perl et al JAMA 2021
Romero et al Pediatrics 2021
Golan et al JAMA Peds 2021

# mRNA Vaccines and Sterility …

- “Anecdotal” reports of menstrual cycle changes in vaccinated women
- HPV vaccine has been associated to menstrual changes
- Is it an unspecific response to vaccines (immunologic?)
- Unfortunately, RCTs did not monitor menstrual cycle changes
- It does not necessarily mean that it will affect fertility
- For most, regularity returns after 1 cycle
- In RCTs, unintentional pregnancies occurred with equal frequency among vaccine and placebo recipients
- Survey of fertility clinics has not shown a spike in requests by vaccinated persons
- NIH has initiated a project to evaluate this problem

# Vaccine Efficacy BNT – Pregnancy - Israel

- Goldstein et al. JAMA 2021 (July 12th, 2021)
- Population-based study (not HCWs)
  - 7,530 vaccinated and 7,530 matched unvaccinated
  - 1st T (21%), 2nd T (46), 3rd T (33)
- Cases SARS-CoV-2 day 28-70 post vaccination
  - 10 infected among vaccinated group (0.33%)
  - 46 infected among unvaccinated group (1.64%)
  - VE = 78% (57-89%)




| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No. at risk | | | | | | | | | | | |
| Matched unvaccinated | 7530 | 7446 | 6825 | 5661 | 4788 | 4023 | 3376 | 2327 | 1748 | 1295 | 955 |
| Vaccinated | 7530 | 7446 | 6825 | 5661 | 4788 | 4023 | 3376 | 2327 | 1748 | 1295 | 955 |
| Cumulative No. of events | | | | | | | | | | | |
| Matched unvaccinated | 0 | 51 | 99 | 137 | 158 | 175 | 184 | 188 | 196 | 200 | 202 |
| Vaccinated | 0 | 51 | 87 | 97 | 109 | 115 | 115 | 116 | 117 | 117 | 118 |

# Recommendation …

SARS-CoV-2 vaccine(s) should be offered to pregnant or lactating women

- American College of Obstetricians & Gynecologists (ACOG)
- Society Maternal-Fetal Medicine (SMFM)
- Centers for Disease Control and Prevention (CDC)
- American Academy of Breast Feeding Medicine (ABM)
- American Academy of Pediatrics (AAP)

- Yet, only ~33% vaccinated!

# Summary

- While most pregnant persons infected by SARS-CoV-2 will do well, the infection increases (2-5 times) the risk of adverse outcomes for both the mom and the product, especially when underlying medical conditions exist
- Pregnant persons should do their best to avoid SARS-CoV-2 infection including NPIs and vaccination
- While data is imperfect, it continues to improve and points towards no significant adverse effect and much benefit of vaccination for pregnant and lactating women
- Pregnant and lactating persons with COVID-19 should be managed same protocols as for others, including supportive care, steroids, antivirals and others
- During labor and delivery for a pregnant person with SARS-CoV-2, OB and pediatric personnel should follow full precautions, regardless of degree of symptoms
- The baby should be cared as usual, room-in with mom and breastfeed, with precautions
- Mom should follow rules for isolation and baby follow rules for quarantine

Thank you

Questions
Comments

# Q&A

Next Webinar:

# HHP/HPH Community Webinar

**Next week:**

## FRIDAY, November 5, 2021

## 12:00 pm – 1:00 pm

# Thank you!

- A recording of the meeting will be available afterwards.
- Unanswered question?
  - Contact us at info@hawaiihealthpartners.org

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