Perinatal SARS-CoV-2

What do we think we know?

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OKAPI CLINIC
Ongoing Care of Congenital and Perinatal Infections

UT Health San Antonio

Questions

- What are the risks for congenital and perinatal transmission?
  - What percentage of infants born to COVID+ mothers will be infected?
  - Can infants be infected transplacentally? And if so, what does that mean?
  - How can we safely deliver these infants?
  - Do we need to separate mother and baby?
  - Can mother breastfeed?
  - When does maternal antibody protect the baby?
  - How long does infant immunity last after maternal infection?
  - How long does infant immunity last after maternal immunization?

What percentage of infants will be infected?

- What we thought we knew:
  - Worst case scenario: *Listeria* (>50% attack rate)
  - Untreated HIV – 25-30%
  - Hepatitis C – 5%
  - Best-case scenario: ~0.5-1% (minimal rate for most viral pathogens)

  - Probably depends on viral load/shedding and whether or not infection can be spread hematogenously or just perinatally

Current knowledge: Incidence

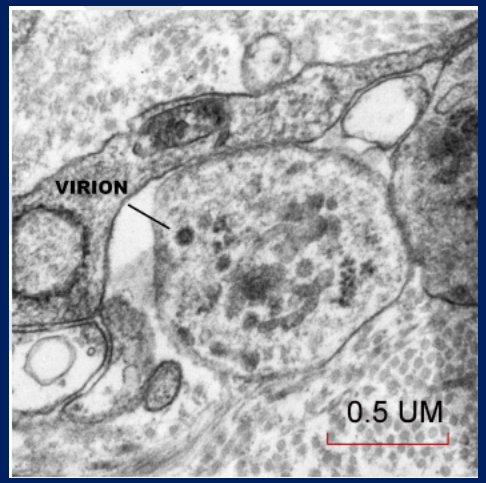
- Based on AAP collaborative (294 sites, 7168 dyads, ~1 year):
  - 1.5-2%
  - Primary risk factor seem to be timing of maternal infection (more later) and severity of maternal infection
  - Sort of best-case scenario!

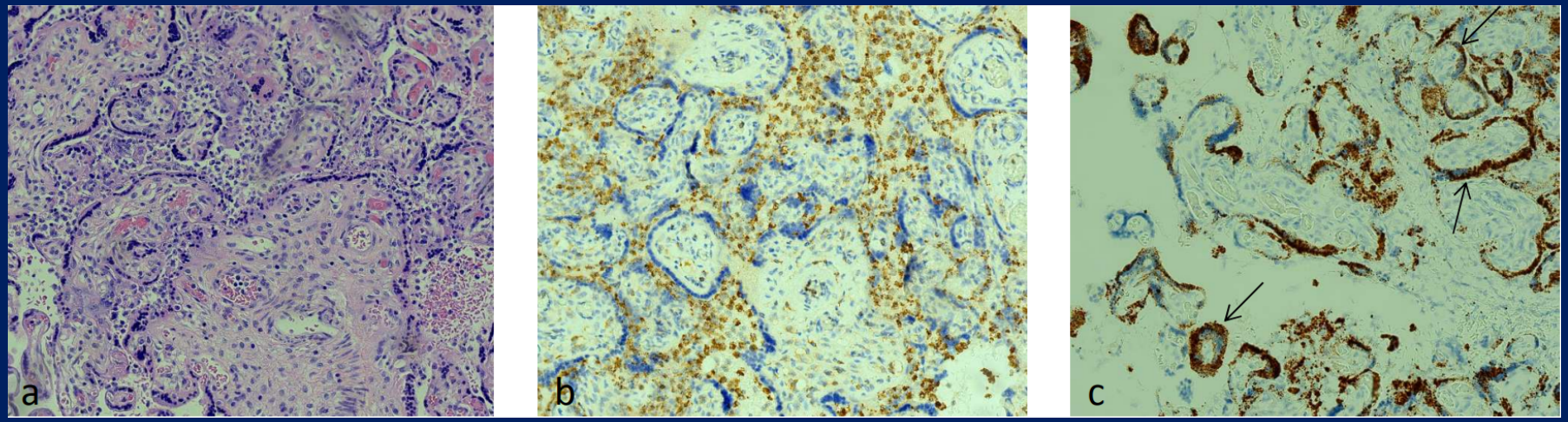
Can infants be infected transplacentally?

- What we thought we knew:
  - Almost certainly, since SARS-CoV-2 can be detected in blood and any pathogen that can reach the maternal bloodstream can theoretically infect the fetus
  - Late congenital infection probably looks like perinatal/postnatal disease
  - Early congenital infection???

Current knowledge: Transplacental infection

- Congenital infection with immediate separation, positive placenta, positive infant has been reported
  - England
  - France
  - Dallas

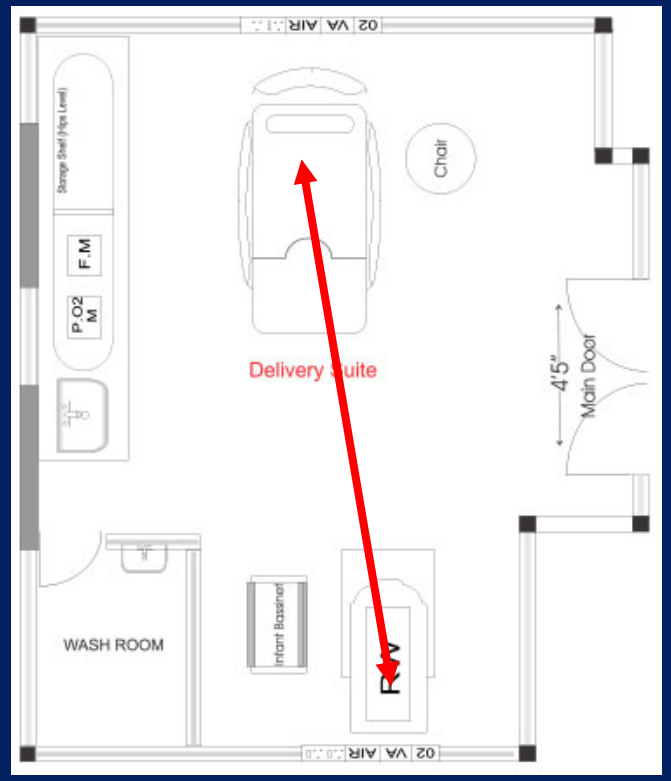




Current knowledge: Transplacental infection

- No evidence so far of 1st trimester teratogenicity (as in congenital rubella syndrome, cytomegalovirus infection, etc)
- Continued surveillance needed to see if there are late effects of this respiratory viral infection during pregnancy (eg, influenza's controversial association with schizophrenia)

How can we safely deliver these infants?



- What we thought we knew:
  - SARS-CoV-2 is transmitted by both droplets (~6 feet) and aerosols (which diffuse into the shared airspace and can float for hours)
  - Sustained vocalization and higher volume increases droplet shedding
  - Increased intrathoracic and intra-abdominal pressure increases droplet shedding

Current Knowledge – Delivery

- Current CDC guidance states that “forceful exhalation during the second stage of labor would not be expected to generate aerosols to the same extent as procedures more commonly considered to be aerosol generating (such as bronchoscopy, intubation, and open suctioning)”
- However, the CDC does recommend airborne precautions (including N95 mask and eye protection) for clinicians delivering COVID+ mothers

Do we need to separate mother and baby?

- What we thought we knew:
  - If mother is COVID+, it might protect the infant to separate the infant during immediate postnatal care and, if possible, the nursery stay

- However
  - No evidence of benefit in separation with seasonal OR pandemic influenza
  - Real concerns about maternal/infant bonding, breastfeeding
  - Real concerns about workflow in hospitals that do not have a 24/7 newborn nursery (eg, would separation require NICU admission?)

Current Knowledge - Separation

- AAP and CDC recommendations changed several times
- AAP Perinatal Collaborative ultimately demonstrated that there was **NO DIFFERENCE** in neonatal infection rate (~1.5-2%) regardless of whether infant was separated or not
- Current recommendations:
  - **Do not separate** mother and baby unless mother is too sick to care for infant
  - Hand hygiene should be encouraged before and after handling baby
  - Until she has recovered (>10 days from positive test AND symptoms improved/resolved), mother should mask while directly caring for baby

Can mother breastfeed?

- What we thought we knew:
  - SARS-CoV-2 virus can be detected in breast milk
  - MERS-CoV can be detected in fresh milk and unpasteurized camel milk was a significant source of transmission during MERS epidemic

- As a result:
  - WHO always recommended breastfeeding
  - CDC had interim recommendations that offered “pump-and-dump” as an interval strategy
  - Separation of infant was often a barrier to breastfeeding regardless

Breastfeeding

- Chambers C, et al. Evaluation of SARS-CoV-2 in breast milk from 18 infected women. *JAMA* 2020. 324(13): 1247-48.
  - 64 samples from 18 COVID19+ mothers
  - 63 of 64 samples negative by PCR
  - The one positive sample did not grow in viral culture
- Tam PC, et al. Detectable SARS-CoV-2 in human breast milk of a mildly symptomatic patient with COVID-19. *Clin Infect Dis* 2021. 72(1): 128-130.
  - 6 samples from 1 mother
  - 1 sample positive by PCR
  - No recovery in culture
- Kumar J, et al. SARS-CoV-2 detection in human milk: a systematic review. *J Mat Fetal Neonatal Med*. 2021; February 8th.
  - Review of 34 studies including 116 lactating women
  - RNA detection was ~2% of samples, no culturable virus
- Conclusion: **No infectious virus shed in breast milk**

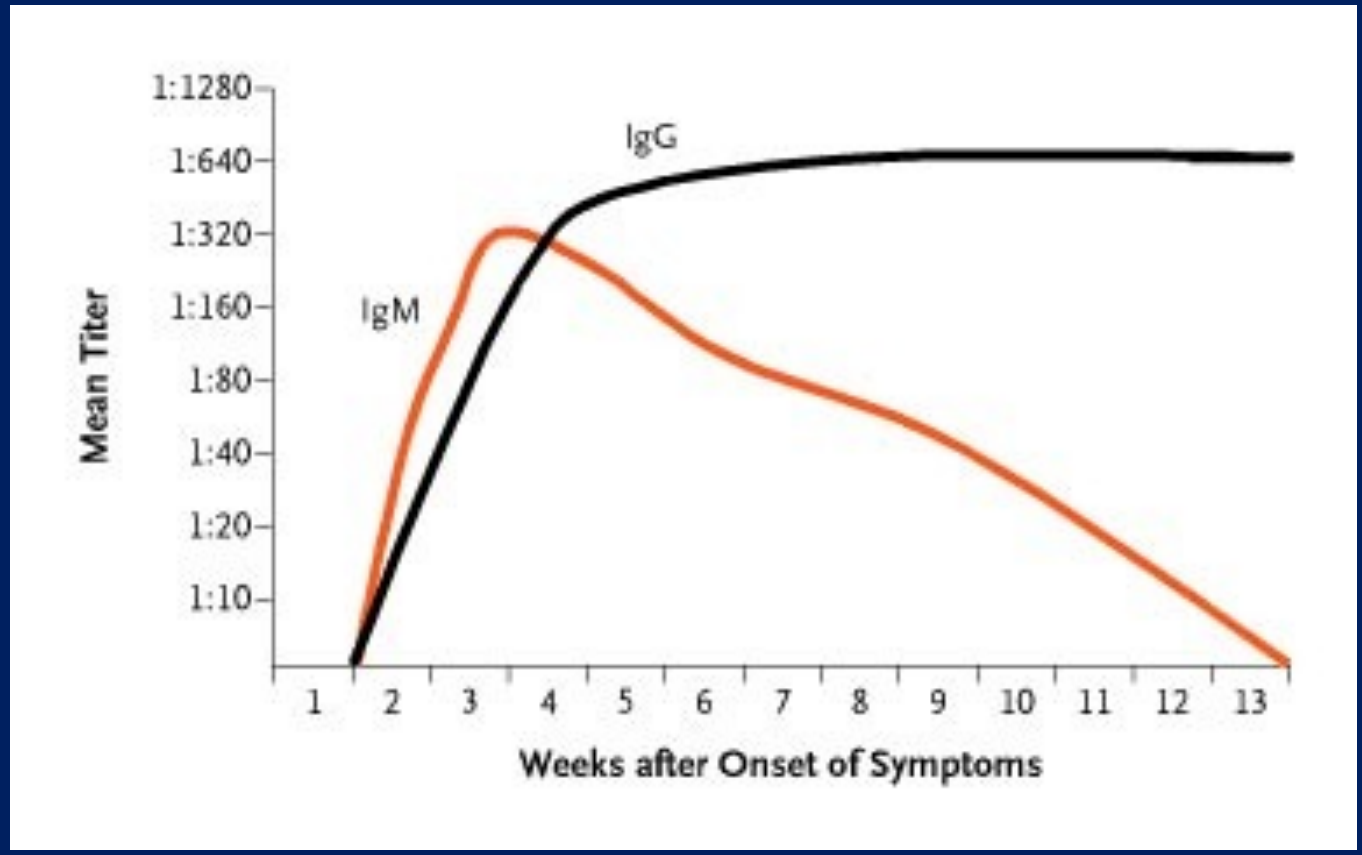
Current Knowledge - Breastfeeding

- RNA detection of virus is scant, and no one has been able to recover viable (eg, culturable) virus from breastmilk
- Translational data demonstrating that anti-SARS-CoV-2 IgA appears in breastmilk along with virus, suggesting a protective effect
- Strictly from a viral standpoint, benefit of breastfeeding exceeds risks (never mind all the other benefits too!)
- Data from the AAP collaborative support these conclusions – no increased risk for infants who are breastfeeding versus formula-fed
- In addition, higher rates of postpartum depression for women prevented from breastfeeding during pandemic!

- **Conclusion: Breastfeeding should be encouraged and supported**

When does maternal antibody protect the baby?

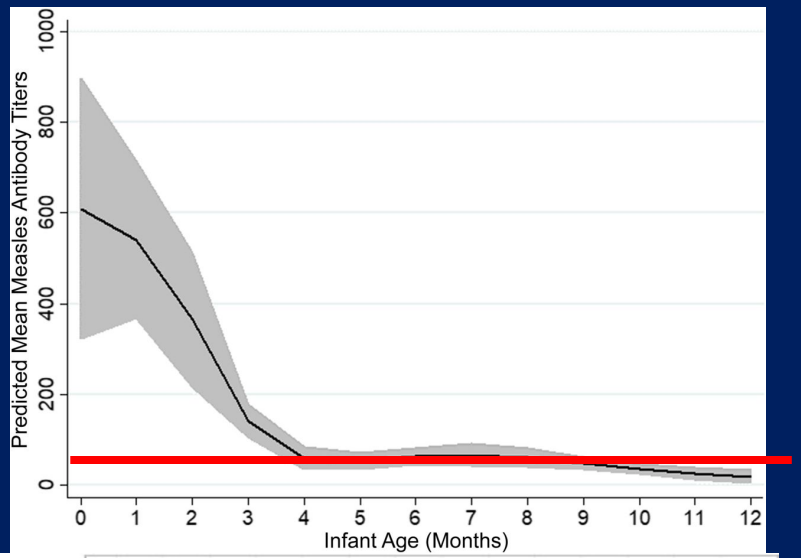
- What we thought we knew:
  - Based on our experience with other perinatal viral infections, especially varicella, we assumed that maternal infection >7 days before delivery would equate to infant protection

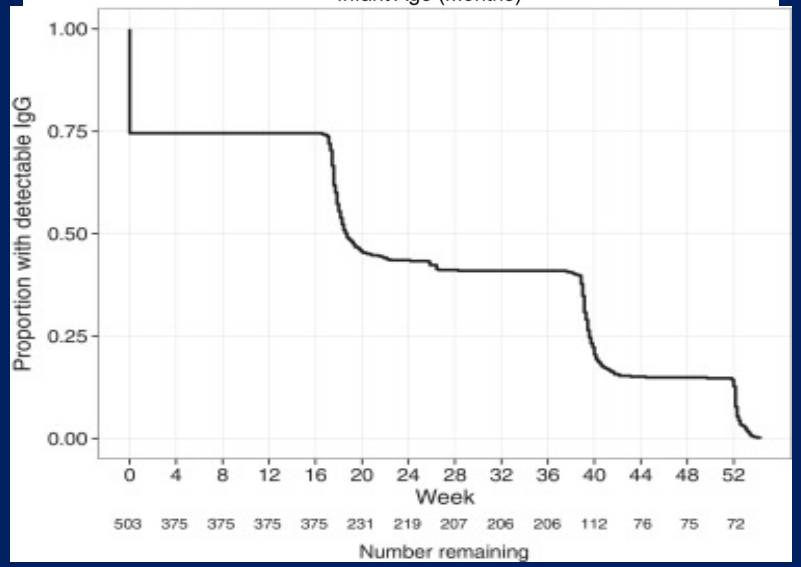


Current Knowledge – Maternal Antibody

YUP		Maternal symptoms		
		Hospitalized for COVID	Symptomatic at home	Asymptomatic
Maternal testing date	≥8 days before	0%	0.9%	0.4%
	7-4 days before	9.1%	4.1%	5.2%
	3 days before to 3 days after	0%	3.8%	2.2%

How long does infant immunity last?





- What we think we know:
  - Maternal immunization against influenza, pertussis lasts up to 4-6 months on average
  - Timing of immunization matters; immunization in the 2nd trimester seems to be optimal (as opposed to 3rd trimester or postpartum)

Current Knowledge – Duration of Antibody

Pfizer

moderna
messenger therapeutics

AstraZeneca

Johnson & Johnson

Summary

- What percentage of infants born to COVID+ mothers will be infected? → **~1-2% overall, with risk peaking at 5-10% for infection 4-7 days before delivery**
- Can infants be infected transplacentally? And if so, what does that mean? → **Yes, and TBD**
- How can we safely deliver these infants? → **PPE as per any other positive patient**
- Do we need to separate mother and baby? → **NO – do not separate**
- Can mother breastfeed? → **YES – breastfeed!**
- When does maternal antibody protect the baby? → **Probably as early as 7 days after infection – and in breast milk too!**
- How long does infant immunity last after maternal infection? → **Probably 6-ish months??? Prospective study needed**
- How long does infant immunity last after maternal immunization? → **Probably 6-ish months??? Prospective study needed**

Questions?

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