

Audrey Harris Lecture
Covid 19: an Update 9-30-21

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Audrey Harris Vision and Jackson Graves Foundation

Passion for the education of Neonatal Intensive Care Nurses, the backbone of the NICU

Who in turn educate us all

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Disclosures

- None related to COVID-19

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Objectives

- Describe the transmission and spectrum of perinatal disease
- Describe the infectivity of the Delta variant
- Describe methods of control and resilience in context of Covid

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Case

- Prenatal consultation 33 Y/O G3P2 at 27 wks
- Attended Mother's Day event: 18/20 got COVID (all positives unvaccinated)
- On BiPAP, 100% with resp distress
- Mechanical ventilation and delivery day 2
- Mom went on ECMO day 3
- Baby received CMV, surfactant

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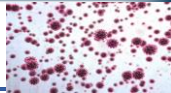
Case Outcome

- Mom on ECMO for 5 days but survived
- Severe respiratory distress and on oxygen at first visit
- Baby did well for first 7 days, then developed ileal perforation, requiring bowel resection
- Mother's and baby's lives are changed forever
- For lack of a small jab.....

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COVID-19



- RNA respiratory virus generally causing URI symptoms
- Officially: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)
- Derived from bats(?), similar to SARS CoV-1 and MERS CoV, but then human transmission
- Originally from Wuhan, China, Dec, 2019
- Lab controversy??



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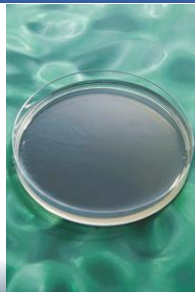
Rapid Spread

- Droplets or secretions ($> 5 \mu\text{M}$), occasionally surfaces
 - Protection: Gown, glove, mask, eye shield
- Aerosolizing procedures (ventilation, flow),
 - Smaller ($< 5 \mu\text{M}$) allowing droplets to stay in air longer
 - Can be taken up by indoor ventilation systems
 - Protection: Above plus N-95 mask



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Exponential growth



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Exponential Growth

- R_0 of the alpha variant was 2.5; Delta is 8!
- Initially, cases double every 6 days
- Start with 10 cases
- How many cases in 30 days?
- Formula: $C_{30} = C_0 \times 2^{30/6}$
- $C_{30} = 10 \times 2^5 = 320$
- For Delta
 - $C_{30} (\text{Delta}) = 10 \times 8^{30/6} = 327,680 \text{ cases!}$



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How to Stop the Growth?

- Vaccine
- Infection
- Death

Which would you pick?



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Covid in Pregnancy

Characteristics	COVID-19	SARS	MERS
Number of cases	15	17	12
Age (years)	32-40	27-44	31-39
Gestational age at infection (weeks)	All were in the third trimester except 2 women who were less than 28 weeks gestation	4-32	4-38
Respiratory complications (n)	None	Asthma (1)	Asthma (1), Pulmonary fibrosis (1)
Symptoms			
Fever (%)	84*	100	58
Cough (%)	28*	76	67
Dyspnea (%)	18*	35	58
Investigations*			
CXR/T evidence of pneumonia	76*	100*	100*
Leukocytosis (%)	38*	40*	50*
Lymphopenia (%)	22*	67*	50*
Thrombocytopenia (%)	13*	36*	50*
Maternal complications			
Mortality (%)	0	14	25
Mechanical ventilation (%)	2	35	41
Fetal complications			
Miscarriage stillbirth (%)	2*	20	10*
ICR (%)	9	13	9*
Preterm birth (%)	25*	23*	23*
Neonatal complications			
Neonatal death (%)	2	0*	0*

* Patients whose data was not reported were excluded from the calculations.

*1 patient who aborted her pregnancy was excluded from the calculations.

*Leukocytosis was defined as a white cell count of more than 11,000 per cubic millimeter. Lymphopenia was defined as a lymphocyte count of less than 100 per cubic millimeter. *Thrombocytopenia was defined as a reduced count of less than 150,000 per cubic millimeter.



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What We Knew with Alpha

- Information about the different routes (transplacental, perinatal, and postnatal) and risks of transmission of COVID-19 disease to newborn infants was limited to case reports (Liu, 2020, 11 neonates; Chen H, 2020, 9 patients) and not population-based studies.
- With few exceptions, all neonates did well
- Those who did not may have been related to prematurity, asphyxia



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Now: Comparative Study

- March to Oct 2020, 706 COVID pregnancies, 43 institutions, 18 countries, matched x2
- COVID + Maternal RR compared to non COVID pregnancies
 - Preeclampsia 1.76
 - Severe infections 3.38
 - ICU admission 5.05
 - Maternal mortality 22.3!!



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Comparative Study

- Neonatal Outcomes RR
 - Preterm birth 1.59
 - Medically indicated PT birth 1.97
 - Severe neonatal morbidity 2.66



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Comparative Study (Generally with Alpha Variant)

Symptomatic Moms

- Severe maternal complications 2.56
- Neonatal complications 4.97

Asymptomatic Moms

- Maternal morbidity 1.24 (Barely significant)
- Preeclampsia 1.63
- Neonatal complications not significantly increased

Take home message: COVID increases maternal and neonatal morbidity, mainly in symptomatic moms

Villar J, JAMA Pediatrics, 2021



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Delta Variant

- New variants emerge with transmission
- Started in India Dec 2020; US in Mar 2021
- Responsible for large upswing in cases, deaths
- In SE US (Alabama with 44% fully vaccinated) vs NE US (Vermont with 76%), rates differ
- Now dominant variant
- What is next???

Del Rio C, JAMA Peds, 2021



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Delta: Severity of Infection

- Cases often present faster and are sicker
- Public Health England Report:
- “significantly increased risk of hospitalization within 14 days of specimen date (HR 2.26, 95% CI 1.32-3.89, p=0.003), and emergency care attendance or hospitalization within 14 days (HR 1.45, 95% CI 1.08-1.95, p=0.015), for Delta cases compared to Alpha cases after adjustment for confounders”

Public Health England Technical Bulletin



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Antenatal Management for PUI/COVID+

- If giving antenatal steroids, consult with MFM
 - Avoid rescue courses and late preterm steroids
 - Pushback from MFM, who advocates for routine steroid administration
- Magnesium for maternal/fetal neuroprotection
 - Use as indicated



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COVID in Pregnancy: ACOG

- Separation for maternal indications (too sick to care for newborn)
- Isolation not mandatory; hygiene is!
- Breastmilk is preferred feeding
- Direct BF is acceptable (mom's choice)
- Many including UAMS are testing all moms

ACOG 2020



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Neonatal Management

- Generally, neonates are spared
- Main danger from maternal infection is to providers, not neonates
- Why not vertical transmission?
 - Placenta has "no (few)" susceptible cells
 - Decreased ACE-2 expression
 - Decreased transmembrane serine protease 2 expression

Dong L, 2020 JAMA; Kirtzman M, 2020, CMAJ; Vivanti, 2020, Nature



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Management Changes

- C-section, isolation for prevention of neonatal disease (Wuhan, China)
- Followed by allowing vaginal delivery
- Followed by isolation of moms from babies (April 2020)
- Followed by allowing rooming in
- Followed by allowing direct breastfeeding
- Followed by discharge to an infected mom

AAP 2020



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Neonatal Management

- Delivery attendance with masking precautions
- 2-5% of newborns will test positive
- Testing, if available 24 and 48 hours
- Rooming in is acceptable with precautions
- Direct breastfeeding with appropriate hygiene
- Discharge to mother or family members is appropriate with education
- No advantage to early discharge

AAP 2020



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NICU Management

- IF on >2 LPM flow, don PPE including N-95 mask or equivalent
- Cohort potentially infected babies
- Visitors to conform with hospital policy for protection of health care workers
 - AT UAMS, we allow 2 visitors (mom + one)
 - One visitor at a time
 - Masks and screening are required

AAP 2020



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Concerns: Breast Feeding

- Positive PCR tests reported from 14 BM samples from 22 women; NO viral replication
- One series of 18 women reported one positive
- Pasteurization results in no positive culture (Donor BM appears safe)
- Small sample sizes

Chambers C, 2020:



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Concerns: Vertical Transmission

- Initial reports revealed positive neonatal PCR tests up to 72 hours (2-5%)
 - 6 of 33 positive antibody tests
 - No symptoms
 - No positive placenta or amniotic fluid cultures
 - Of 33 neonates (Wuhan), 3 non-specific symptoms
 - One with positive IgM, which is non-specific

Dong L, 2020; Yang Z, 2020



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Neonatal Concerns

- Evidence of placental infection present (thrombosis, PCR)
- One neonate with neurological symptoms
- Decreased IgG antibodies to Covid

Vivanti, 2020, Nature, Edlow AG, JAMA, 2020



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Concerns: Vertical Transmission

Positive maternal infection with symptoms

- Positive placental tissue
- Non-specific symptoms (hypoglycemia, hypothermia, feeding difficulties)
- Positive PCR days 2-7
- Decreased antibodies

Positive maternal infection with symptoms

- Positive placental tissue
- Neonatal blood and BAL positive for Coronavirus
- Day 3: irritability, poor feeding, axial hypertonia and opisthotonos
- Gliosis of WM

Kirtsman M, 2020; Edlow AG, 2020

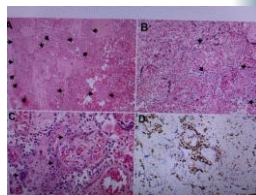
Vivanti AJ, 2020



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Concerns: Vertical Transmission: Rare

- Recently, reports of placental infection with thrombosis, PCR positive tests (CDC)
- One neonate had symptoms consistent with COVID-19

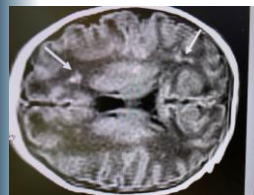


Hosier H, 2020; Penfield CA, 2020; Kirtsman M, 2020



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WM injury



- WM gliosis
- Symptoms resolved at 2 months
- Long term effects unknown
 - Susceptible to seizures?

Vivanti AJ, 2020



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National Registry: SONPM

- Address 3 crucial questions:
 - Likelihood of peri- and postnatal transmission (testing)
 - Assess spectrum of disease and risk factors for severe disease (HMD?)
 - Assess effectiveness of and necessity for infection control practices



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Approach: All Data De-identified

- Invite NICUs nationwide to participate (SONPM, VON, Med NAX)
- Record maternal testing 14 days before and 3 days after delivery
- Record neonatal testing
- Record maternal and infant outcomes
- Record disease severity (or not), isolation procedures, treatment, outcomes, co-morbid conditions



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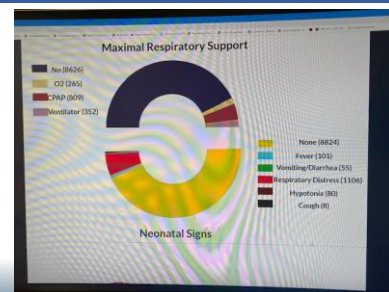
COVID Registry 9-24-21

- 10,188 mother/infant dyads
 - Asymptomatic moms...7872 (78%)
 - Symptomatic.....1909 (19%)
 - Admitted sick.....344 (3%)
- Vag delivery 64%.....C section 36%
- Almost all isolated, BUT
- ONLY 3098 (30%) separated at birth
- 180 of 8273 (2.2%) tested positive



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Neonatal Signs after COVID



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MIS-C

- Occurs 2-4 weeks after COVID infection
- Hyperimmune response
- Cardiac, pulmonary, renal involvement
- Encephalopathy, fever, increased inflammatory markers
- 2-4% mortality
- Several children required ECMO
- Aberrant T and B cell response to COVID??

Levin M, NEJM, 2020



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MIS-N (?)

- Report of 20 neonates from COVID+ mothers
- 19 + for IgG; none + for IgM
- 90% cardiac involvement
- Also, fever, feeding intolerance, renal and respiratory involvement
- Reports from India, not US....yet

Pavar R Children, 2021



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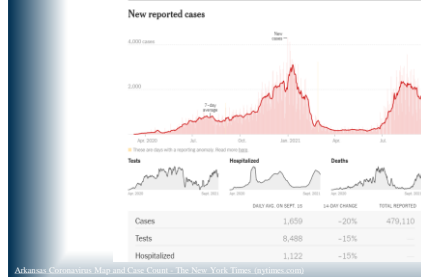
What Do We Do Now?

Vaccinate



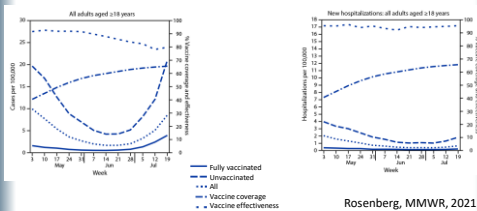
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Reported cases in Arkansas



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Vaccine Effectiveness drifting down overall, but remains high for preventing hospitalization

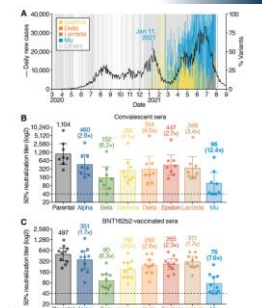


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What about Mu?

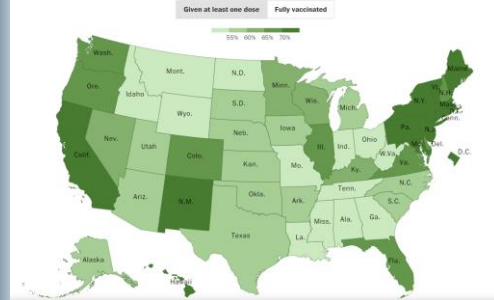
- More resistant to antibody
- Present in 49 states
- Delta remains predominant

Uriu, et al. Ineffective neutralization of the SARS-CoV-2 Mu variant by convalescent and vaccine sera. [bioRxiv.org](https://doi.org/10.1101/2021.09.07.20211111) 9/7/2021



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Share of population:



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What about kids under 12?

- IMMINENTLY UNDER FDA REVIEW!

NEWS HEALTH
Pfizer says they'll be ready to ask for approval of Covid-19 vaccine for kids in a matter of days



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Delta: Vaccine Effectiveness

Table 8. Vaccine effectiveness against symptomatic disease for Alpha and Delta variants

Vaccination status	Vaccine effectiveness (%)	
	Alpha	Delta
Dose 1	49 (45 to 52)	35 (32 to 38)
Dose 2	89 (87 to 90)	79 (78 to 80)

Table 9. Vaccine effectiveness against hospitalisation for Alpha and Delta variants

Vaccination status	Vaccine Effectiveness (%)	
	Alpha	Delta
Dose 1	78 (64 to 87)	80 (69 to 88)
Dose 2	93 (80 to 97)	96 (91 to 98)

Public Health England Technical Bulletin



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Why Is the US Hesitant?

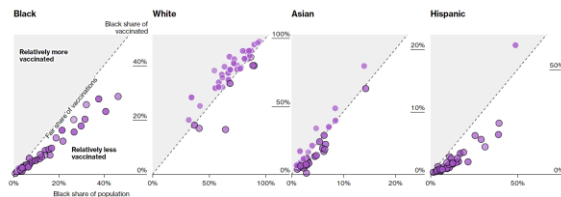
- Polarization
 - Right wing news (Fox, Breitbart), mis-information
 - One of 2 major parties not fiercely advocating
- Contrariness
 - History of personal liberties
- Health insurance
 - Shots free but concern over who is paying for vaccine complications?

Kaiser Foundation, NPR polling, 2021



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Don't assume it is hesitancy – might be an access issue



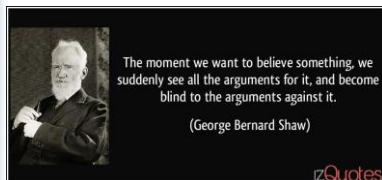
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We know what DOESN'T work in parents already hesitant about vaccines

- Giving information about risks due to vaccine preventable illness
 - Even if delivered by another parent
- Similarly, advocating for herd immunity to protect society does not work particularly well



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Repeating False Information: A Bad Idea

- Repetition increases acceptance (Skurnik 2005)
 - Participants told 3X that a statement was false likely to accept as true than told once
- Repetition spreads misinformation to new audiences
- Myth-busting can convey controversy
- Anecdotes and photographs reinforce the false message (Fagerlin 2005)

Schwartz N, Neuman E, Leach W. Making the truth stick & the myths fade: Lessons from cognitive psychology. Behavioral Science & Policy. 2016;2(1):85-95.

Thanks to Paul Darden for sharing.



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Focus on Building Trust

- Speak up!
 - Ask opened ended questions – don't assume you know what someone's concerns are
 - Share that you're vaccinated and why
 - Share good science
 - Counter myths and misconceptions (but don't repeat them!)
 - Fear based tactics don't work!!
 - Get comfortable explaining how the vaccines work

Wen-Ying SC, 2020, *Health Commun*
 Videos & Animations | The Vaccine Makers Project
www.chen.edu/centers-programs/vaccine-education-center



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Vaccine resistance communication: Key points

- Empathetic and collaborative – use the words “we, protect, their future, prevents cancer”
- Keep it short
- Don't debate
- Don't repeat the myth (autism, infertility, etc.)
- Never close the conversation

Thanks to Paul Darden for this



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Promoting Vaccine Confidence

- Information is necessary but never enough
- Trusted opinion leaders
 - Who do we trust?
 - Physicians, nurses, community leaders
- Lead by example
- Advocate for access



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My Thoughts

- Continue isolation until cases decrease
 - Not overwhelm providers, system
- Resume activities gradually, region specific
- Research on epidemiology, vaccine, treatment
- Testing widely available (active and IgG)
- Lives will change with more taking the jab



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Cultivating Resilience

- The process of adapting well in the face of adversity
- Resilience is neither lucky nor passive. It takes deliberate effort. Inherent in all of us
- Goals:
 - Where do we want to be after this is over?
 - How can we contribute?
 - What have we learned?



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My Personal Journey



- Initially devastated for children and me (no school, peers, sports, I felt unable to contribute)
- Contribution through research, telemedicine
- Learned importance of work, compassion of partners
- Goals: understanding relationships, effects of pandemic, incorporation of telemedicine
- **How wonderful it is that nobody need wait a single moment before starting to improve the world. (Anne Frank)**



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