Delta Variant in Children: what are the risks?

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Discussion will cover

- COVID-19 case presentations and management - Adult versus Pediatric care protocols
- General overview of data in terms of incidence, hospitalizations, severity of illness
- Common myths debunked
- Is in-person school safe
- Vaccine efficacy and safety profile in the pediatric population
The Pandemic from Two Sides

- Managing Acute Hypoxemic Respiratory Failure in Adults vs Kids with COVID-19
  - HFNC considerations
  - Timing of intubation
  - Proning and ideal PEEP strategies
  - When nothing is working: Rescue therapies
  - MISC - challenges in identification and management
Adults: ARDS, but make it COVID

From emerging entity to protocolized practices that continue to evolve

- Experiences of other providers, evidence-scarce zone
- Sticking with the basics of ARDS
- Revisiting new and emerging data
- Continuing to play critical care defense
- Groundhog day with Delta Variant
Pre-Intubation management

• Self-pronning
• Role for HFNC and NIPPV
• Timing of Intubation:

Intubate Early!
• Aerosolization with NIPPV and PPE shortages
• Transfer safety
• Prolonged periods of NIPPV, P-SILI

Delay intubation!
• Concerns about ventilator shortages
• Exposures to high amounts of sedation, paralytics
• Complications on the ventilator
Oxygen therapy escalation algorithm

Assess Patient
Are any of the following signs of pneumonia present? fever, cough, dyspnea, respiratory distress, pulse oximetry (SpO2) <95% on room air, tachypnea, confusion, depressed mental status, or elevated respiratory rate (>30/min, 2-12 months old; >50/2-11 months old; >40 if 1-5 years old; >30 if 5-15 years old; >22 if >15 years old)

Continue Monitoring & Reassess (≥q4h)
Is the patient meeting treatment goals?
- SpO2 (95-100)
- Improving work of breathing, perfusion
- PaO2 >45
- Adequate mental status?
If not, consider alternative therapies, escalation, or transfer to a higher level of care

Titrated & SpO2 Goals
- SpO2 ≥ 95% in adults & children
- SpO2 ≥ 90% in pregnant patients
- SpO2 ≥ 94% for infant or child with signs of multi-organ failure
- Avoid SpO2 >100% to avoid effects of hyperoxia and to conserve O2 supply

Adjuncts
- Ensure adequate personal protective equipment and infection prevention control
- Place surgical mask over nasal cannula in high-flow nasal cannula to decrease risk of droplet and aerosolization
- Proper positioning
- Reposition every 2-3 hours
- Elevate the head of the bed
- Provide chest physiotherapy
- Oral and/or nasal suctioning

Initial Nasal cannula
- 0.5-1 LPM nebulizers; 1-2 LPM infants; 4-6 LPM children; 4-6 LPM adults and school children
- Assess response: Increased SpO2 or decreased work of breathing

Simple face mask
- 5-10 LPM
- Assess response: Increased SpO2 or decreased work of breathing

Non-rebreather mask + reservoir
- 10-15 LPM
- May consider adding nasal cannula (max 45 LPM) especially if device that starts with F10 are on hand
- Assess response: Increased SpO2 or decreased work of breathing

Are Emergency Signs present?
- Restlessness
- Diaphoresis
- Hypotension
- Tachycardia
- Cough
- Crackles
- Rash
- Lethargy
- Focal deficit

Consider 5-20 trial of one of the following based on patient & locum context

CPAP/NIPPV Central Indications
- Aspiration risk
- Inability to protect airway or remove mask
- Hemodynamic instability
- Abnormal mental status
- Need for emergent intubation
- Anatomic variants to mask seal interfere
- Insufficient respiratory drive/effort

NIPPV/BiPAP
- especially if CPAP or left heart failure contribute to respiratory failure
- P0 (AP) 5-15/PEEP (CPAP) 5-15

Assess Response
- NIVt≤2h initially; NIVh=on once stable or improving
- Increased work of breathing
- SpO2 <90%, HR >100
- PaCO2>45, dizziness or altered mental status

Consider
- Max FIO2 50
- OR
- Max F/1h
- OR
- Max FIO2 50
- OR
- Max F/1h

CPAP
- (CPAP in infants & young children) 0.5-10 and/or 0.5-2.0 cmH2O as needed

Assess Response
- Onset of airflow and improved work of breathing
Suggested management of acute respiratory distress and respiratory failure in children with COVID-19
Adapted from current guidelines and expert opinion

Evaluate for respiratory distress in SARS-CoV-2+ children

Signs and symptoms of respiratory distress
i. Tachypnea
   a. > 60/minute for infants ≤ 2 months
   b. > 50/minute for infants 2-11 months
   c. > 40/minute for children 1-5 years
ii. Hypoxemia (SpO₂) ≤ 90%
iii. Lethargy or unconsciousness
iv. Inability to drink or breastfeed
v. Labored work of breathing (grunting, chest in-drawing with retractions, accessory muscle use, head-bobbing, nasal flaring)

Determine appropriate level of support

Initiate LFNC for SpO₂ 90-92% targeting SpO₂ 92%-96%
• Consider HFNC (HFNC is currently recommended as first line therapy in adults)
• Consider self-proning with HFNC

Frequent reassessment at least every hour for clinical deterioration and need for rapid escalation

Evaluate PALICC criteria for PARDS and ESPNIC guidelines for COVID-19 management
a. Respiratory failure not caused by heart failure, fluid overload, or perinatal lung disease
b. Within 1 week of disease onset
c. New unilateral or bilateral pulmonary infiltrates
d. Categorize severity of PARDS
   i. Non-invasive ventilation
      1. PARDS (no severity stratification)
         a. P/F ≤ 300 or S/F ≤ 264
   ii. Invasive mechanical ventilation
      1. Mild
         a. 4 ≤ OI < 8 or 5 ≤ OSI < 7.5
         b. P/F 200-300; S/F 221-264
      2. Moderate
         a. 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3
         b. P/F 100-200; S/F 150-221
      3. Severe
         a. OI ≥ 16 or OSI ≥ 12.3
         b. P/F ≤ 100; S/F ≤ 150

• Consider NIPPV (CPAP or BiPAP) when S/F < 264 but > 221 (or P/F 200-300)
• Consider especially in pediatric patients with co-existent asthma
Delayed Intubation: how to decide

Pre-Intubation management: Intubate... sometime in between?

- Concerns about prolonged periods of NIPPV at high settings
  - P-SILI (patient self-inflicted lung injury)
- Challenging discussion with patients and family members
- If tolerating NIPPV comfortably: **reassuring**
- If can take breaks on HFNC for periods of time: **reassuring**
Sometimes – you are forced to intubate.
Consideration of intubation

Indications to consider intubation and mechanical ventilation
i. Worsening tachypnea
ii. Worsening work of breathing including respiratory mechanics concerning for self-induced lung injury (high minute ventilation achieved by high TV)
iii. Declining mental status or fatigue
iv. P/F < 200 or S/F < 221
v. Inadequate ventilation (pH < 7.2)

Suggested initial ventilator settings utilizing lung protective strategies
1. Expiratory TV 5-7 mL/kg ideal body weight (consider smaller TV if decreased compliance)
2. Plateau pressure of < 28-32 cm H₂O
3. Driving pressure of ≤ 15 cm H₂O
4. Permissive hypercapnia targeting pH > 7.2
5. Initiate PEEP 8-10 cm H₂O
6. Titrate PEEP and FiO₂ for goal SpO₂ 92-96% (moderate) or 88-92% (severe)

Monitor for refractory hypoxemia and need to escalate support

Consider measurement of static respiratory compliance to evaluate for potential recruitability and guide PEEP titration
\[ \text{Crs} = \frac{\text{TV (ml/kg)}}{\text{(Pplat – PEEP)}} \]

Low Compliance
- High elastance, compromised compliance, may require higher PEEP strategy

High Compliance
- Low elastance, preserved compliance, may require more moderate PEEP

Escalation
1. Neuromuscular blockade
2. Prone positioning
3. PEEP/Recruitment maneuvers
4. Inhaled nitric oxide
5. HFOV
6. ECMO

De-Escalation
Follow Local Guidance
**ARDS: Back to Basics in Adults**

- Lung protective ventilation as in Pediatric ARDS management
- PEEP and Driving pressure (ΔP)
  - ARDSNet Tables
  - Driving pressure to determine ideal PEEP
  - Esophageal balloon
  - Stress Index

**Tables**

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<th>0.9</th>
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<td>20</td>
<td>22</td>
<td>22</td>
<td>22</td>
<td>24</td>
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</tbody>
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Prone Positioning
- P:F <150 if ventilated
- goal of prone positioning 16h/day
- work down ventilator settings to low/safe as possible
- Technical considerations if team not familiar with procedure and care
- Challenge of being unable to safely supinate patients

Sedation, Paralytics

What if nothing is working

- Adult vs pediatric thoughts on
  - Tracheostomy
  - iNO, inhaled Epo
  - HFOV
  - ECMO
## Pediatric ECMO

<table>
<thead>
<tr>
<th>Table 2. Relative Contraindications, Conditions With Poor Prognosis (ELSO Red Book, 5th Edition, Chapter 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conditions rendering patient unlikely to benefit from ECLS:</strong></td>
</tr>
<tr>
<td>Large intracranial bleed with mass effect or need for neurosurgical intervention</td>
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<tr>
<td>Hypoxic cardiac arrest without adequate CPR</td>
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<tr>
<td>Irreversible underlying cardiac or lung pathology (and not a transplant candidate)</td>
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<tr>
<td>Pulmonary hypertension and chronic lung disease</td>
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<tr>
<td>Chronic multiorgan dysfunction</td>
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<tr>
<td>Incurable malignancy</td>
</tr>
<tr>
<td>Allogenic bone marrow recipients with pulmonary infiltrates</td>
</tr>
<tr>
<td><strong>Conditions with worse prognosis in respiratory ECLS:</strong></td>
</tr>
<tr>
<td>Hepatic or renal failure</td>
</tr>
<tr>
<td>Pertussis infection in infants</td>
</tr>
<tr>
<td>Fungal pneumonia</td>
</tr>
<tr>
<td>Immunodeficiency</td>
</tr>
<tr>
<td><strong>Relative contraindications:</strong></td>
</tr>
<tr>
<td>Vessel anomalies or having previously been clipped or ligated for prior ECMO</td>
</tr>
<tr>
<td>Localized site infection</td>
</tr>
</tbody>
</table>

CPR, cardiopulmonary resuscitation; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation.
5 year old previously healthy girl presented to outside ED with 5 days of fever, abdominal pain, vomiting, sore throat, new rash.

- Hypotensive, tachycardic, tachypneic on exam, pink maculopapular over trunk
- CXR with bilateral hazy opacities
- COVID-19 nasal swab PCR positive
- Vasopressor support initiated and transferred to UNC
- O2 support initiated in route for hypoxemia
More than One Road to ECMO

Additional laboratory data
- WBC 14.7, 3+ left shift
- ESR 32, CRP 179
- Pro-BNP 10,400
- D-dimer 1209
- Troponin 0.599
- Albumin 2.5, AST 94, ALT 86
- PT 15.4, aPTT 40.4
Multisystem Inflammatory Syndrome in Children (MIS-C)

- Age <21
- Fever
- Lab evidence of inflammation (elevated ESR, CRP, LDH, ferritin, fibrinogen, procalcitonin, IL-6, elevated neutrophils, low lymphocytes, low albumin)
- Clinically severe illness requiring hospitalization
- Multisystem organ involvement

AND

- No alternative plausible diagnosis (may fulfill partial criteria for Kawasaki)
- Positive for current or recent SARS-CoV-2 infection, or exposure to suspected or confirmed COVID-19 case within 4 weeks prior to symptom onset

Management with immunosuppression, and supportive care for organ systems involved

https://www.cdc.gov/mis/hcp/index.html
Severe Acute COVID-19 vs. MISC

- Age can be clue
- Cardiac involvement (+/- respiratory involvement) $\rightarrow$ think MISC
- Mucocutaneous involvement $\rightarrow$ think MISC
- Patients with more comorbidities $\rightarrow$ think severe acute COVID-19
- Patients with neuro, GI, hematological involvement WITHOUT cardiac involvement or mucocutaneous involvement $\rightarrow$ think severe acute COVID-19

Feldstein LR et al. JAMA (2021)
Discussion will cover

- COVID-19 case presentations and management - Adult versus Pediatric care protocols
- General overview of data in terms of incidence, hospitalizations, severity of illness
- Common myths debunked
- Is in-person school safe
- Vaccine efficacy and safety profile in the pediatric population
Multisystem inflammatory syndrome in children (MIS-C)

Last updated with cases reported to CDC on or before August 27, 2021*

<table>
<thead>
<tr>
<th>TOTAL MIS-C PATIENTS MEETING CASE DEFINITION*</th>
<th>TOTAL MIS-C DEATHS MEETING CASE DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>4,661</td>
<td>41</td>
</tr>
</tbody>
</table>

*Additional patients are under investigation. After review of additional clinical data, patients may be excluded if there are alternative diagnoses that explained their illness.

Summary

- The median age of patients with MIS-C was 9 years. Half of children with MIS-C were between the ages of 5 and 13 years.
- 61% of the reported patients with race/ethnicity information available occurred in children who are Hispanic/Latino (1,316 patients) or Black, Non-Hispanic (1,362 patients).
- 99% of patients had a positive test result for SARS CoV-2, the virus that causes COVID-19. The remaining 1% of patients had contact with someone with COVID-19.
- 60% of reported patients were male.

<table>
<thead>
<tr>
<th>Discussion will cover</th>
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<tbody>
<tr>
<td>COVID-19 case presentations and management - Adult versus Pediatric care protocols</td>
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<td>Common myths debunked</td>
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<tr>
<td>Is in-person school safe</td>
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<tr>
<td>Vaccine efficacy and safety profile in the pediatric population</td>
</tr>
</tbody>
</table>
### Vaccines approved in the US

**And pediatric ongoing trials**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Approval age limit</th>
<th>Ongoing trials</th>
<th>Hopeful timeline for further approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna</td>
<td>18</td>
<td>01/2021 – EUA requested (12-17 yo)</td>
<td>For 12-17 likely soon</td>
</tr>
<tr>
<td>Pfizer</td>
<td>12</td>
<td>03/2021 worldwide phase 1/2/3 trials began in 6m-2y, 3y-5y, 5y-11y</td>
<td>EUA request likely towards end of Sept/early Oct and approval likely a few weeks later (towards the end of October for 5 y -11 y)</td>
</tr>
<tr>
<td>Johnson and Johnson</td>
<td>18</td>
<td>Underway</td>
<td>Unsure</td>
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</table>
Pfizer trial details (& why is it taking so long)

• March 24-25 – started enrollment
• 2 doses given at 21 days apart *trialed 3 dose ranges in 3 age ranges
  • Puts us at late April to May to realistically be giving second doses to anyone
• FDA asked for 4-6 months of safety data (adverse event data) before consideration
  • Adult approval was given with 2 months of safety data
• September 27th - Date of final data collection for primary outcome measures
• September 28th - Data submitted to the FDA for EUA
• FDA to scrutinize data
Pfizer data - released September 20 to the public

2,268 children 5-10 y who received a 10microgram dose in a two-dose series

• Neutralizing antibody geometric mean titer was 1,197 – a strong immune response (1 mo post 2nd dose) though unknown protection level
  • The GMT in the 16-25 yo range was 1,146 for comparison when given a 30microgram dose for 2 doses

• Side effect profile seems similar to 16-25 yo age group (control group)
Overview of Moderna COVID-19 Vaccine (mRNA-1273) in adolescents (P203)

Overview
- Phase 2/3, randomized, observer-blind, placebo-controlled study to evaluate the safety and effectiveness of mRNA-1273 in healthy adolescents 12 to <18 years of age

Data updates
- Primary endpoint of non-inferior immunogenicity versus the Phase 3 study adult comparator group was met
- No cases of COVID-19 observed after two doses of vaccine using the primary case definition, consistent with a vaccine efficacy of 100%
- Safety and tolerability generally consistent with Phase 3 COVE study in adults

Regulatory Updates
- Authorized for adolescents in United Kingdom, European Union, Japan, Canada, Switzerland, Taiwan, Saudi Arabia, Australia and the Philippines
- Data submitted in United States and other countries

TeenCove Study
- 100 µg mRNA-1273
  - N=2,486
- Placebo
  - N=1,240

Overview of Moderna COVID-19 Vaccine (mRNA-1273) in children (P204)

Overview
- Phase 2/3 expansion study to evaluate the safety and effective of mRNA-1273 in children aged 6 months to less than 12 years ongoing
  - 2-part, open-label, dose-escalation, age de-escalation, randomized, observer-blind, placebo-controlled

Updates
- We selected a dose and expanded enrollment in the 6 years to less than 12 years old cohort, and Part 2 of the study (Arms 8 & 9) is fully enrolled (N=4,000)
- Dose selection studies are still underway for 2 to <6 years old and 6 months to <2 years

Trial Design
- Arm 1 – 50 µg N ~370
- Arm 2 – 100 µg N ~370
- Arm 3-4 – 50 µg N ~75
- Arm 5 – 25 µg N ~150
- Arm 6 – TBD µg N ~150
- Arm 7 – 25 µg N ~75

- Arm 8-9 – 50 µg N ~4,000 (3000 vaccine, 1000 placebo)
- Arm 10-11 – TBD µg N ~4,000 (3000 vaccine, 1000 placebo)
- Arm 12-13 – TBD µg N ~4,000 (3000 vaccine, 1000 placebo)

Dose selected
Dose selection ongoing
Side effects of COVID vaccines

Side effects after getting a COVID-19 vaccine are **normal signs** that a person’s body is building immunity

- **The most common side effects from the COVID vaccines are**
  - Fatigue
  - Redness/swelling/soreness at site of injection
  - Headache
  - Muscle aches
  - Fever or Chills

- They occur usually within the first week, most common at 1-2 days post receipt

SE in 12-15 yos (Pfizer data)
Injection site pain 91%
Fatigue 77.5%
Chills 49%
Muscle pain 42%
Fever 24%
WHAT TO EXPECT:
PFIZER COVID-19 VACCINE SIDE EFFECTS, AGES 12-15

Frequency of Solicited Local and Systemic Reactions Within 7 Days After Each Vaccination, as Percentage of Phase 2/3 Trial Participants
Uncommon side effects

Rare – but serious

• Acute Allergic reactions including anaphylaxis occurs in 2-5 people per million in the US

• Guillain Barre Syndrome –
  • associated with J&J vaccine
  • 195 cases after 14.5 million doses given
  • Usually, 2 weeks post dose
  • Mostly in men over 50 y

• Thrombosis with Thrombocytopenia Syndrome
  • Associated with J&J (2 cases following 362 million doses of Moderna – not above baseline population rate)
  • 46 cases after 14.5 million doses given
  • Almost exclusively in women under 50 y

• Myocarditis/Pericarditis
Myocarditis and Pericarditis following COVID vaccine

• Associated with mRNA vaccines
• Associated with male adolescents and young adults
• Usually within a few days of the second dose (myocarditis) or further from second dose (pericarditis)
• Almost all patients resolved completely

Symptoms/signs include –
Chest pain
Shortness of breath
Palpitations
ST segment changes
Troponin elevation
Myocarditis, Pericarditis, and Myopericarditis by the most recent numbers

- 2,574 reports in all ages/age groups
  - Myopericarditis: 1,903 reports
  - Pericarditis alone: 671 reports
- Median age
  - Dose 1 – 26 y
  - Dose 2 – 20 y
- Median time to symptom onset
  - Dose 1 – 3 days
  - Dose 2 – 2 days
- Between 72-82% male

<table>
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<tr>
<th>Manufacturer</th>
<th>Reports after dose 1</th>
<th>Reports after dose 2</th>
<th>Reports after unknown dose</th>
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<tr>
<td>Pfizer-BioNTech (n=1,282)</td>
<td>169</td>
<td>922</td>
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<td>Moderna (n=557)</td>
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<td>Janssen (n=49)</td>
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<tr>
<td>Not reported (n=15)</td>
<td>2</td>
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<td>4</td>
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<tr>
<td><strong>Total (N=1,903)</strong></td>
<td><strong>337</strong></td>
<td><strong>1,271</strong></td>
<td><strong>295</strong></td>
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Outcomes after myocarditis/pericarditis

Of those that met CDC case definition *(742)

• 701 were hospitalized
• 667 were discharged
  • 77% of those had recovered
• 18 were still hospitalized

• Thus enhanced monitoring set up within the VAERS system including surveys to determine functional status and ongoing clinical symptoms as well as need for further treatment

• Patients being followed by Cardiology division at BCH
Reporting adverse events

Vaccine providers enrolled in the federal COVID-19 vaccination program are responsible for mandatory reporting of the following events:

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events* (irrespective of attribution to vaccination)
- Cases of multisystem inflammatory syndrome (MIS)
- Cases of COVID-19 that results in hospitalization or death

Where the world comes for answers

https://vaers.hhs.gov/reportevent.html
Thank you for joining us!