Pediatric Acute Respiratory Distress Syndrome (PARDS): Do we have consensus?

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Conflicts to Disclose

- I am a consultant for Discovery Laboratories
- No other conflicts
Consensus?
“Of course we value your experience. I swear, nobody around here refers to you as a ‘dinosaur’!”
Pediatric Acute Lung Injury Consensus Conference (PALICCC)

Four years ago in a galaxy far away . . .

The Organizing Committee!
Stated Goals

1. To develop a taxonomy to define pediatric ARDS, specifically predisposing factors, etiology, and pathophysiology

2. To offer recommendations regarding therapeutic support of the child with PARDS

3. To identify priorities for future research in PARDS (and probably equally to bring investigators together for future research)
Pediatric Acute Lung Injury Consensus Conference (PALICC)

Subtopics
1. Definition, incidence, & epidemiology
2. Comorbidities & assessment of severity
3. Ventilatory support
4. Pulmonary specific ancillary treatments
5. Non-pulmonary treatment
6. Monitoring
7. Non-invasive support
8. Extracorporeal support
10. Pathobiology
Proposed Timeline

Organizing committee (n=3)
- Define the methodology
- Define the agenda
- Define the organization
- Topic selection (n=9)
- Expert selection (n=27)

1st meeting
- Starting meeting

1st draft
- Recommendation Creation
- Experts group work
- Standardized literature review
- 1st draft of the recommendations
- 1st draft of the argumentations

2nd meeting
- Recommendations review
- 2nd experts meeting
- Harmonization of the recommendations with the whole group of experts

Rating
- (2 rounds) Rand/UCLA

3rd meeting
- Finalization
- 3rd experts meeting
- Presentation of agreed recommendations
- Discussion on disagreements
- 3rd rating round if necessary
- Finalization of the Recommendations (short text) with argumentations (9 long texts)
- Priorization of research

4th step
- Diffusion

Presentations:
- PALISI, SCCM, ESPNIC, ANZICS, GFRUP, CCCTG & WFPICCS meetings

Publications:
- Pediatr Crit Care Med on-line ± paper (according to fundings) & other journals

Since March 14th 2012 (PALISI meeting)
- Chicago October 2nd 2012
- Montreal April 18th-19th 2013
- Paris (ESICM) October 9th 2013
- 1st presentation at PALISI meeting March 2014

Manuscripts are accepted and will be published this year in PCCM!
The Team!
Pediatric Acute Lung Injury Consensus Conference (PALICC)

First task was to agree on a name!

- Pediatric acute lung injury
- Pediatric acute hypoxemic respiratory failure
- Pediatric ALI/ARDS
CONSSENSUS

THIS WOULD WORK A LOT BETTER IF YOU'D JUST AGREE WITH ME.
PARDS: What’s in a name?

- Initial “Adult respiratory distress syndrome” (Ashbaugh 1967)
  - “severe dyspnea, tachypnea, cyanosis that is refractory to oxygen therapy, loss of lung compliance, and diffuse alveolar infiltrates on CXR”

- Murray—lung injury score
  - Included PaO2/FiO2, compliance, lung quadrants, PEEP -- refined the definition, scored 0-4

- AECC—operational definition
  - Separated “ALI” and “ARDS”

- Berlin conference—refinement of definitions
  - Abandoned “ALI” in favor of “mild-moderate-severe” ARDS
# Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

<table>
<thead>
<tr>
<th>Berlin Definition</th>
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</thead>
<tbody>
<tr>
<td><strong>Acute Respiratory Distress Syndrome</strong></td>
</tr>
<tr>
<td><strong>Timing</strong></td>
</tr>
<tr>
<td><strong>Chest imaging</strong></td>
</tr>
<tr>
<td><strong>Origin of edema</strong></td>
</tr>
<tr>
<td><strong>Oxygenation</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td><strong>Mild</strong></td>
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<tr>
<td><strong>Moderate</strong></td>
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<tr>
<td><strong>Severe</strong></td>
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**Abbreviations:** CPAP, continuous positive airway pressure; FiO$_2$, fraction of inspired oxygen; Pao$_2$, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.<br/><sup>a</sup>Chest radiograph or computed tomography scan.<br/><sup>b</sup>If altitude is higher than 1000 m, the correction factor should be calculated as follows: $[\text{PaO}_2/\text{FiO}_2 \times (\text{barometric pressure}/760)]$.<br/><sup>c</sup>This may be delivered noninvasively in the mild acute respiratory distress syndrome group.
But nothing about kids!
Why do we need a specific definition for kids?

- Epidemiology (currently reported incidence of ARDS in children varies from 2-12.8/100,000 person years)
- Demographics—which children are at risk for PARDS?
- Prognosis: Is it different from that in adults?
- Treatment?
- Future progress and study?
Pediatric Acute Respiratory Distress Syndrome (PARDS)

Consensus Definition

- **Acute onset:** < 7 days from acute insult (most on admission, 95% within 3 days, all within one week)
- **Age:** 0 - 18 years (exclude neonatal lung injury)
- **Infiltrates on CXR** have to be new, **but not bilateral**
- **Oxygenation disturbance (OI* or OSI** rather than PaO2/FiO2)
  - **Mild PARDS** \( 4 \leq OI < 8 \) or \( 5 \leq OSI < 7.5 \)
  - **Moderate PARDS** \( 8 \leq OI < 16 \) or \( 7.5 \leq OSI < 12.3 \)
  - **Severe PARDS** \( OI \geq 16 \) or \( OSI \geq 12.3 \)

\[ *OI = FiO2 \times Paw \times 100/PaO2 \]

\[ **OSI = FiO2 \times Paw \times 100/SpO2 \]
Special Populations (not considered in previous definitions)

Non-invasive ventilation (HFNC, CPAP, BIPAP, etc.)
  - Full face-mask bi-level or CPAP $\geq 5$ cmH20
    P/F ratio $\leq 300$ or S/F ratio $\leq 264$

Cardiac Patients
  - Standard criteria w/ acute deterioration in oxygenation not explained by cardiac disease or LV dysfunction

Chronic Lung Patients
  - Standard criteria w/ acute deterioration in oxygenation not explained by previous lung disease
Why “Mild-moderate-severe” using OI makes sense

Figure 1: Distribution of initial Oxygenation index and mortality from CHLA dataset (n=397). Mortality increases as OI increases, but there appear to be cut-points in which mortality is similar (OI <4, 4-8, 8-16, > 16)
Data from CHOP Yehya et al. CCM 2015

Figure 2. Classification of patients into Berlin (A–C) and Pediatric Acute Lung Injury Consensus Conference (D–F) oxygenation categories based on initial $\text{Pao}_2/\text{Fio}_2$ (PF) (A) or oxygenation index (OI) (D) at time of acute respiratory distress syndrome diagnosis, the value 24 hr after diagnosis (B and E), and the worst value in the first 24 hr (C and F). Mortality is plotted for each group. $p$ Values represent a nonparametric test for trend, testing if mortality increases across worsening oxygenation categories.
Pop Quiz

What is the advantage to using “oxygenation index (OI)” as opposed to “hypoxemia index” (P/F)?

1. The oxygenation index curve is linear within the clinical range as opposed to the hypoxemia index which is exponential.

2. The OI takes into account mean airway pressure. Mean airway pressure can actually change the P/F ratio.

3. No advantage in kids, but the adult intensivists have actually shown OI to be a better prognosticator than P/F ratio in adult ARDS.
Why Use OI instead of P/F?

- P/F ratio can be manipulated by changing PEEP or Paw (e.g., same degree of injury can “look different” by changing PEEP)
- Adult intensivists tend to be more uniform in their approach to positive pressure—e.g., use of the ARDSnet FiO2/PEEP grid, don’t use HFOV—so P/F works for them.

<table>
<thead>
<tr>
<th>Lower PEEP/higher FiO2</th>
<th>FiO₂</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
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<th>0.5</th>
<th>0.6</th>
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<td>12</td>
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<tr>
<td>FiO₂</td>
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<td>0.9</td>
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<tr>
<td>PEEP</td>
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<td>16</td>
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<td>18-24</td>
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</table>

<table>
<thead>
<tr>
<th>Higher PEEP/lower FiO₂</th>
<th>FiO₂</th>
<th>0.3</th>
<th>0.3</th>
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<th>0.3</th>
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<th>0.5</th>
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<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
<td>8</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>FiO₂</td>
<td>0.5</td>
<td>0.5-0.8</td>
<td>0.8</td>
<td>0.9</td>
<td>1.0</td>
<td>1.0</td>
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<tr>
<td>PEEP</td>
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<td>20</td>
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Pop Quiz #2

The Oxygen-Hemoglobin Dissociation Curve:

1. Is linear throughout its range
2. Relates oxygen and carbon dioxide partial pressure
3. Is fairly flat above an oxygen saturation of 96%
4. Is directly affected by cardiac output
5. 1 and 2
Use of S/F and OSI instead of P/F and OI

- Decreasing use of arterial catheters so we frequently don’t measure PaO2
- If you substitute SpO2 for PaO2, need to titrate down FiO2 until SpO2 < 97% because the oxyhemoglobin curve is flat at SpO2 > 95% and SpO2 won’t change much until you turn down the FiO2 to get to the linear part of the curve
- Why keep the SpO2 > 97% anyway?
New Definition Problems

- P/F ratio still has to be used in non-intubated kids and, even at that, difficult to know actual FiO2
- Judgment will be required to identify PARDS in kids with CHD and CLD
- We will have to convince colleagues to turn down the FiO2 so that SpO2 < 97% in order to make the diagnosis of PARDS using S/F ratio or OSI
Biggest Definitional Problem

Pneumonia  Trauma  Sepsis  RSV

drowning  Etc., etc.

PARDS
Pediatric Acute Respiratory Distress SYNDROME

PARDS

Acute Onset
New Pulmonary Infiltrates
OI > 4
Consensus? Common Pathophysiology

Common Mechanisms

- Loss of alveolar-capillary integrity
- Inflammation
- Increased lung water
- Surfactant dysfunction
- Decreased compliance, V/Q mismatch, hypoxia, respiratory failure (and then we add on mechanical ventilation)
Hypoxia is the primary physiologic disturbance in PARDS and is a consequence of shunt & V/Q mismatch from loss of lung volume (i.e., atelectasis). But dead space in some references is a better predictor of outcomes.
Consensus? Treatment

[Image: Cartoon of a bridge labeled "YOU FIRST." with "LEFT" and "RIGHT" on the sides and a "MIDDLE" section where a "AREA OF AGREEMENT." is located.]
Pop Quiz #3

Tidal volumes of 6-8 mls per kilogram (ideal body weight) have been shown to be associated with improved outcomes in PARDS

1. True
2. False
PALICC Consensus: Mechanical Ventilation

- Anytime you have 3 intensivists in a room you have at least 5 different “best” ways to ventilate a patient!

**Weak agreement only**
- No recommendation on ventilator mode
- Vt 5-8 ml/Kg ideal body weight
- Ideal SpO2 level 92-97%, no specific lower SpO2
- Keep PIP or plateau pressure < 29-32 cmH$_2$O!
- Moderately elevated PEEP (10-15 cmH2O) titrated to oxygenation & hemodynamics!
- Could not recommend recruitment maneuvers
- Could not recommend HFOV in moderate to severe PARDS, although stepwise titration of HFOV when used produced strong agreement
Consensus: Mechanical Ventilation (continued)

- **Strong Agreement**
  - Markers of oxygen delivery, compliance, and hemodynamics should be monitored as PEEP is increased.
  - Could not recommend HFJV, high frequency percussive ventilation, or liquid ventilation.
  - Cuffed endotracheal tubes
  - Permissive hypercarbia, although only weak agreement on pH 7.15-7.30
  - No bicarb
Mechanical ventilation recommendations . . . bottom line

Avoid VILI and do the right thing!
Consensus: Monitoring in PARDS

- Consensus that HR, BP, RR, SpO2 should be monitored with appropriate alarms in place.
- On the ventilator: Vt, PIP (or plateau), PEEP, FiO2, flow, pressure, & volume-time with appropriate alarms.
  - Expired Vt should be monitored at the end of the ETT and normalized to ideal body weight.
- Continuous monitoring of EtCO2 should be standard.
- Measurement of ABGs should be adjusted to severity of PARDS, ongoing non-invasive monitoring, and stage of the disease.
- Recommend arterial catheter in severe PARDS for hemodynamic monitoring.
Weaning and Extubation

- Recommend Spontaneous breathing test (SBT) or Extubation Readiness Test (ERT) be done once patient is breathing spontaneously and on minimal ventilator settings (FiO2 ≤ 0.4, PIP < 20 cmH2O, PEEP ≤ 5)

- No specific recommendations on how exactly these “tests” should be performed.
Extubation Readiness
Agreed that it should be routinely assessed but no specifics on how. *My suggestion*, . . .

- CPAP of 5, FiO2 $\leq 0.4$
- Spontaneous Vt $> 6$ cc/Kg
- Highest RR $< 2$ S.D. for age
- Subjective absence of distress or tiring
- Stable EtCO2 and SpO2
- Consider “leak test”

Consider longer “test” if uncertain. Also, consider ABG if clinical judgment is unclear.
Consensus: Non-pulmonary Rx

1. Sedation
   - Objective assessment (SBS) and nurse-implemented protocol vital
   - Neuromuscular blockade should be used only after adequate sedation/analgesia, with monitoring, and ideally daily holidays
   - Withdrawal requires appropriate consideration, consider objective withdrawal score
   - Remember that over-sedation is the biggest impediment to weaning
Consensus: Non-pulmonary Rx (cont.)

- **Fluid management**
  - Two phases:
    1. Resuscitation from shock (a la Rivers)
    2. Fluid restriction—aim for negative balance
  - Fluid management should be goal directed (Clear evidence that oxygenation, duration of ventilation, and mortality relate to fluid balance)
  - No agreement on colloid vs. crystalloid
  - Use of diuretics to attain fluid balance is unstudied
Consensus: Non-pulmonary Rx (cont.)

- Nutrition
  - Nutrition management should be goal-directed to achieve adequate caloric intake as soon as possible. Inability to achieve 1/3 of energy needs in first 10 days clearly associated with mortality
  - Enteral nutrition is preferable
  - If target nutrition not achieved in 72 hrs, consider parenteral nutrition
Consensus: Non-pulmonary Rx (cont.)

- Transfusion
  - TRIPICU study clearly showed that Hgb 7.0 in a stable PICU patient is not inferior to Hgb 9.0
  - Not at all clear if “new blood” is better than “old” blood (ABC study ongoing)
  - FFP may turn out to be more problematic than we thought (Karam’s study results pending)
Consensus: Specific Pulmonary Treatment
Pop Quiz #4

Which of the following have been shown to be clearly effective in PARDS?

1. Nitric oxide
2. Exogenous surfactant
3. Corticosteroids
4. Prone positioning
5. Chest physical therapy
6. None of the above
Consensus on Treatment for PARDS

**No!**

- Steroids
- Nitric oxide
- Surfactant
- Proning (maybe)
- Routine suctioning
- Chest PT
- Inhaled prostigladin, n-acetylcysteine, beta agonists, etanercept, dornase alpha, heliox, etc.
Consensus: Treatment

Caveats

- Nitric oxide might be used if pulmonary hypertension
- Steroids may have some benefit in “chronic” phase of ARDS
- Latest data in adults shows prone positioning beneficial in severe ARDS
- Surfactant needs more study but some studies show benefit
- Etanercept has shown some benefit in idiopathic pneumonia syndrome (after HSCT)
PARDS: Consensus?
Consensus

- We agree to the name PARDS and definition (a definition that now includes formerly excluded patients)

- We are in general agreement about the essential pathophysiology, although we don’t know much!

- We think we are doing better—and believe both the lower incidence and improved outcomes relate to this

- Much more research is needed (and it is hoped that PALICC is the first step)
The questions are amenable to further study

PARDIE!

(Pediatric ARDS Incidence & Epidemiology)
What we accomplished... 

- PALICC established what we know and don’t know about PARDS (which are “not much” and “much”, respectively)
- Highlighted the differences and similarities between adults and kids
- Brought together investigators from all over the world with the hope of future collaboration
- Has already stimulated further international collaboration!
Plus, I’d never been to Paris!