Lessons Learned from a Career in Neonatal Research

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Lessons Learned...

- Seize opportunities and energetic mentorship
- Hang in there and formulate the next question
- Lessons learned from animal models
- Take opportunities to engage in clinical trials
Maureen Hack, M.D., Marshall H. Klaus, M.D., Avroy A. Fanaroff, M.D.
ABSTRACT

“...Continuous monitoring of respiration in small infants is now clinically feasible.”

Pediatrics 1969
Effect of CPAP on Incidence of Apnea

(p<0.02)

Kattwinkel 1975
Effect of CPAP on Respiratory Timing

Martin et al: J Appl Physiol 1978
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Mixed Apnea

<table>
<thead>
<tr>
<th>HEART RATE (BPM)</th>
<th>180</th>
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<tbody>
<tr>
<td></td>
<td>120</td>
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<td>60</td>
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<tr>
<th>CHEST WALL MOVEMENT</th>
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10 sec.
Nasal CPAP for Neonatal Apnea

- Decrease in upper airway resistance
- Increase in FRC
- Improvement in oxygenation
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Mexico
[undated]
CO₂ Threshold of Respiratory Muscles

Carlo: J Appl Physiol 1988
Respiratory Control and LES Pressure

DIA EMG (AU)

PLES (mmHg)

Hypoxia-induced apnea

Kiatchoosakun, Pediatr Res 2002
LES Pressure Associated with Apnea Onset

LES Pressure

Apnea

Time Relative to Apnea Onset (sec)

Omari, J Pediatr 2009
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Lessons from Clinical Trial Opportunities

- HIFI Study, NEJM 1989
- CHIME Study, JAMA 2001
- NO CLD, NEJM 2006
- PreVent, 2016-
HFOV to Prevent BPD

HIFI Study Group, 1989
Lessons from Clinical Trial Opportunities

- HIFI Study, NEJM 1989
- CHIME Study, JAMA 2001
- NO CLD, NEJM 2006
- PreVent, 2016-
Infants with $\geq$ One Extreme Event per 20,000 Monitor Hours

CHIME Study: JAMA 2001
Lessons from Clinical Trial Opportunities

- HIFI Study, NEJM 1989
- CHIME Study, JAMA 2001
- NO CLD, NEJM 2006
- PreVent, 2016-
Proposed Effects of Nitric Oxide on the Development of the Respiratory System

“Available evidence does not support use of iNO in routine care of premature infants who require respiratory support”.

“Future research should seek to understand the gap between benefits on lung development and function suggested by basic research and animal studies, and the results of clinical trials to date”.

Pediatrics 2011
Lessons from Clinical Trial Opportunities

- HIFI Study, NEJM 1989
- CHIME Study, JAMA 2001
- NO CLD, NEJM 2006
- PreVent, 2016-
Prematurity-related Ventilatory Control [PreVent] 2016-

An NHLBI sponsored multicenter observational study to investigate mechanisms of ventilatory control that contribute to the risk of respiratory morbidity in preterm infants

Case Western • Northwestern • UAB
Univ Miami • Washington Univ • UVA
So…

*Does Apnea of Prematurity Still Matter?*

- Serves as a biologic link between the lung and brain
- May contribute to pulmonary morbidity via need for increased respiratory support
- May contribute to neurodevelopmental morbidity via intermittent hypoxic episodes
- Prolongs hospitalization and cost