Neonatal Airway:
In the Delivery Room and Beyond



CPAP

PEEP

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Objectives

1) Discuss the transition of the lung and airways at birth and the potential for injury
2) Discuss the role of CPAP in this transition and bubble CPAP
3) Nasal interfaces and effects on delivered CPAP pressures
4) How much CPAP pressure should we use in the delivery room?
5) When should we determine that CPAP has failed?
6) What is the role of minimally invasive surfactant therapy with CPAP in the delivery room?
7) Role of High Flow Nasal Cannula in the management of respiratory distress in the delivery room

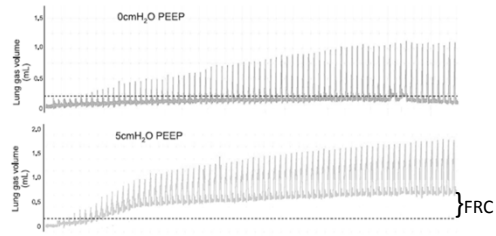
At birth:

- The lung must rapidly clear fluid from airways
- Fluid is driven with each breath into the smaller airways
- Then from the more distal airspaces into the interstitial spaces in the lung parenchyma
- Then slowly absorbed through the lymphatic and capillary system
- Up to 10% of infants need help in this transition

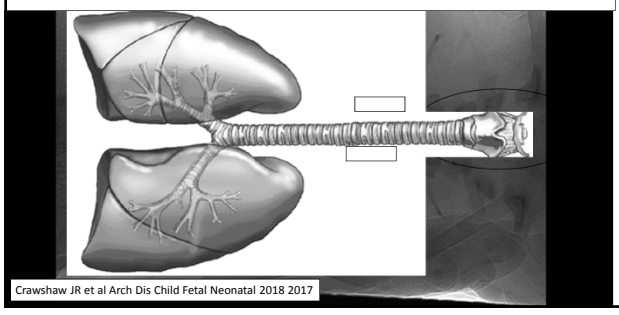
Positive end-expiratory pressure enhances development of a functional residual capacity in preterm rabbits ventilated from birth

J Appl Physiol • VOL 106 • MAY 2009 • www.jap.org

Melissa L. Siew,[1] Arjan B. te Pas,[2] Megan J. Wallace,[1] Marcus J. Kitchen,[3] Robert A. Lewis,[3,4] Andreas Fouras,[5] Colin J. Morley,[2] Peter G. Davis,[2] Naoto Yagi,[6] Kentaro Uesugi,[6] and Stuart B. Hooper[1]

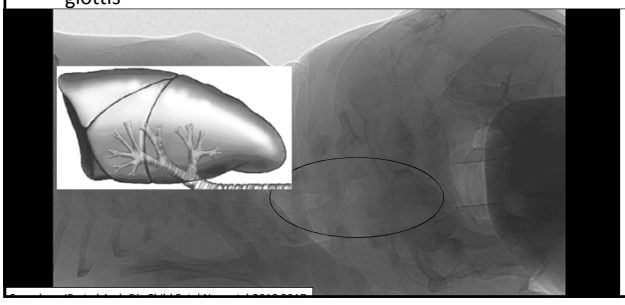


In normal breathing in preterm infant, the glottis remains open for the majority of the breaths. The glottis closes to generate PEEP.



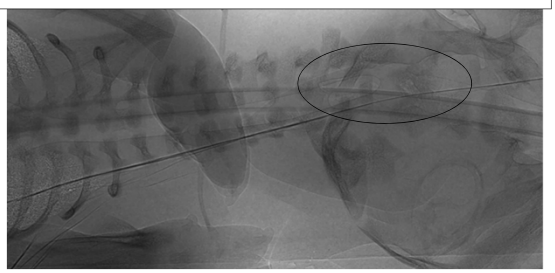
Crawshaw JR et al Arch Dis Child Fetal Neonatal 2018 2017

In the apneic preterm infant, the glottis remains closed
Infants with irregular breathing revert to the fetal condition of a closed glottis



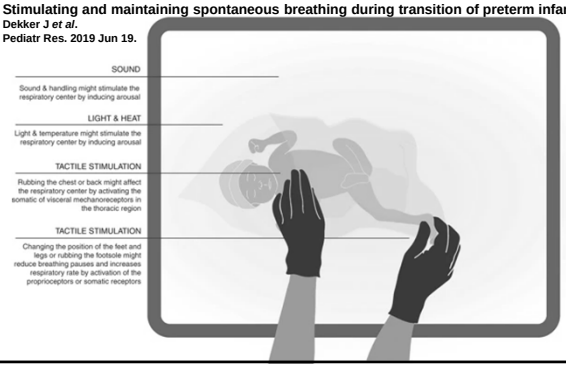
If the glottis is closed, positive pressure breaths cannot get into the lungs, so the infant continues to remain apneic

The



Crawshaw JR et al Arch Dis Child Fetal Neonatal 2018 2017

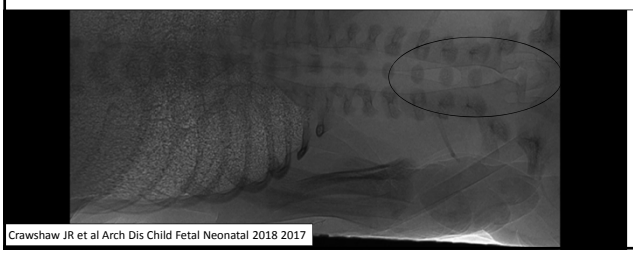
Stimulating and maintaining spontaneous breathing during transition of preterm infants
Dekker J *et al*.
Pediatr Res. 2019 Jun 19.



Continuous Positive Airway Pressure (CPAP) can stabilize the breathing pattern of the infant and increase the time the glottis is open

The

Higher CPAP pressures can cause increased apnea
(> 7 cmH_2O in Rabbit Pups and likely >10 cmH_2O in humans)



Crawshaw JR et al Arch Dis Child Fetal Neonatal 2018 2017

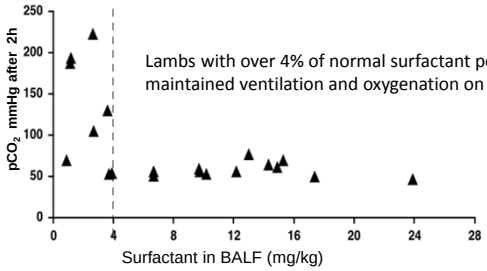
Continuous Positive Airway Pressure

Variables Associated with the Early Failure of Nasal CPAP in Very Low Birth Weight Infants

A Ammari, M Suri, V. Milisavljevic, R. Sahni, D. Bateman, U. Sanocka, C. Ruzal-Shapiro, J. Wung, R. Polin
J Pediatr. 2005 Sep;147(3):341-7.

- 88% of VLBW Infants (<1250g) were placed on nasal CPAP
- 76% were successful on CPAP
- 50% of infants less than 750g failed CPAP

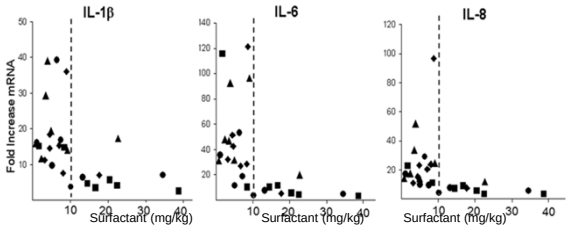
Ventilation on CPAP is dependent of surfactant level



Lambs with over 4% of normal surfactant pool maintained ventilation and oxygenation on CPAP

Mulrooney, N. *Am J Respir Crit Care Med*. March 2005

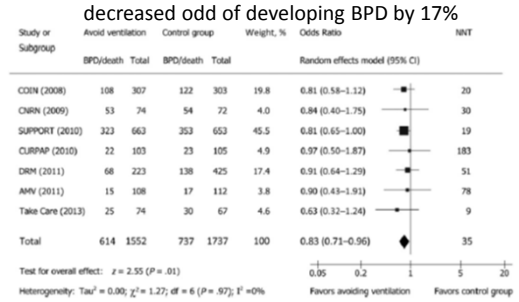
Lung inflammation with mechanical ventilation is dependent of surfactant level



Lambs with > 8% of surfactant have decreased injury

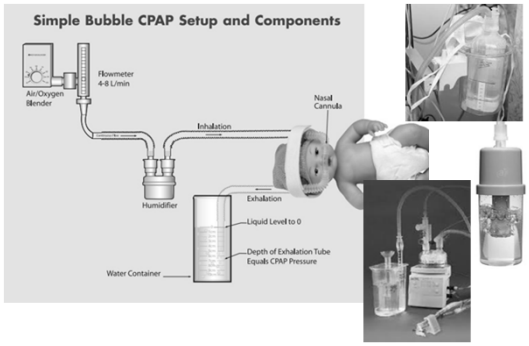
Hillman NH *Respiratory Research* 2010 Oct 29;11:151

Beginning with CPAP versus Immediate Intubation with Surfactant decreased odd of developing BPD by 17%



Fischer *et al* Pediatrics 2013

To bubble or not to bubble?



A comparison of underwater bubble continuous positive airway pressure with ventilator-derived continuous positive airway pressure in premature neonates ready for extubation.
Lee KS - Biol Neonate - 01-JAN-1998; 73(2): 69-75

Randomized crossover study in 10 premature infants ready for extubation

Results:

39% reduction in minute volume ($p < 0.001$)

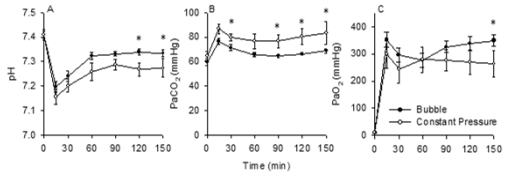
7% reduction in respiratory rate ($p = 0.004$)

No change in tcpCO2 or O2 saturation for infants supported with bubble versus ventilator-derived CPAP.

CONCLUSIONS:

Chest vibrations produced with bubble CPAP may have contributed to gas exchange.

BCPAP verses Conventional CPAP in Preterm Lambs



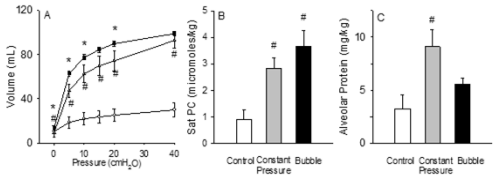
Improved pH in BCPAP lambs

Decreased $PaCO_2$ with BCPAP

Improved oxygenation by 3 hours of life

Pillow JJ. Am J Respir Crit Care Med Vol 176. pp 63–69, 2007

BCPAP verses Conventional CPAP in Preterm Lambs



Improved lung compliance with BCPAP

Larger surfactant pool with BCPAP

Less alveolar damage and protein leak

Pillow JJ. Am J Respir Crit Care Med Vol 176. pp 63–69, 2007

Bubble CPAP versus ventilator CPAP in preterm neonates with early onset respiratory distress--a randomized controlled trial.

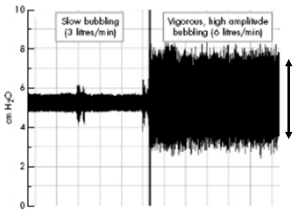
Tagare A1, Kadam S, Vaidya U, Pandit A, Patole S.
J Trop Pediatr. 2013 Apr;59(2):113-9.

TABLE 2
Outcome of CPAP

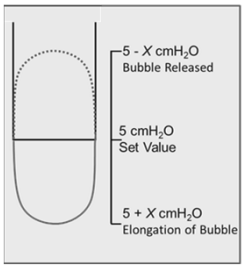
	Ventilator CPAP ($n=57$)	Bubble CPAP ($n=57$)	p-value
Success	36 (63.2)	47 (82.5)	0.03
Duration in CPAP[a] (hr)	30 (2–160)	36 (2–160)	0.22
Morbidity	33 (57.9)	37 (64.9)	0.44
Mortality	5 (8.8)	4 (7.0)	0.89

[a]Values are median (minimum – maximum), p-values by Mann–Whitney U test. The rest of the values are n (%) whose p-values are obtained by χ^2 test if cell frequency is >5, else Fisher's exact test is used.

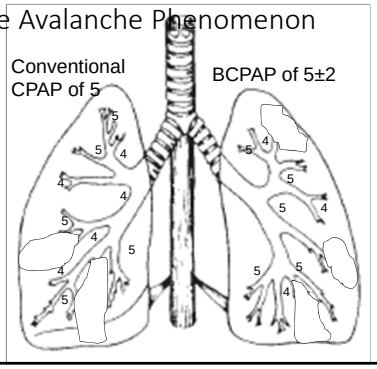
How do we explain the differences seen with BCPAP in preterm lambs?

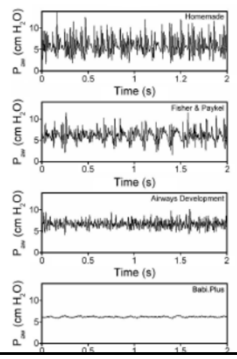


The "noise" of BCPAP



The Avalanche Phenomenon





Volume Oscillations Delivered to a Lung Model Using 4 Different Bubble CPAP Systems

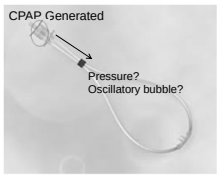
Jonathan A Poli, C Peter Richardson PhD, and Robert M DiBlasi RRT-NPS FAARC
RESPIRATORY CARE • MARCH 2015 VOL 60 No 3

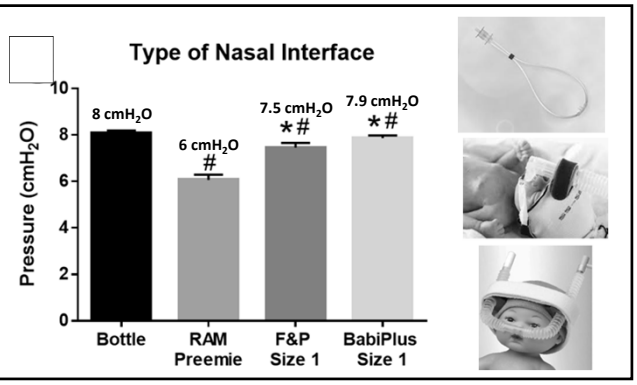


What Type of Nasal Interface should we use with CPAP?

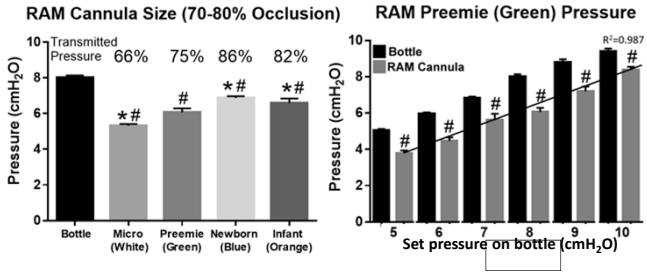








RAM Cannula Pressure transmission is dependent of the Size Cannula used and the % nasal occlusion



How much pressure should we be using in the delivery room?

European Consensus Guideline on the Management of Respiratory Distress Syndrome – 2019 Update (Sweet DG et al . Neonatology June 2019)

"The ideal level of CPAP is not known, but most studies have used at least 6 cmH_2O with some as high as 9 cmH_2O."

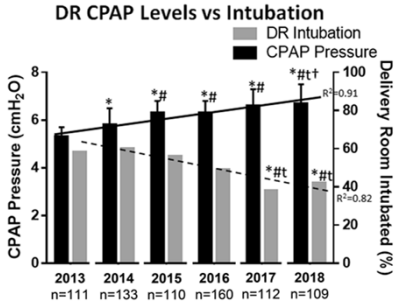
COIN trial (Morley et al. NEJM 2008)
- Infants randomized at 5 minutes of life
- Started CPAP infants on 8 cmH_2O
- CPAP failure/Surfactant Administration was 46% in 5 days
- Pneumothorax rate: 9% (higher than surfactant treatment group)

SUPPORT trial (Finer N *et al*. NEJM 2010)
- Infant randomized prior to delivery, intent to treat analysis
- Started CPAP infants on 5 cmH_2O
- 34% of infants intubated in delivery room
- 67% of infants in CPAP arm received intubation and surfactant
- Pneumothorax rate: 6.8%

VON Delivery Room trial (Dunn *et al*. Pediatrics 2011)
- Started CPAP infants on 5 cmH_2O, then increased to 7 cmH_2O
- 18% of infants intubated in first hour
- 45% of infants in CPAP arm needed surfactant
- Pneumothorax rate: 5.4%

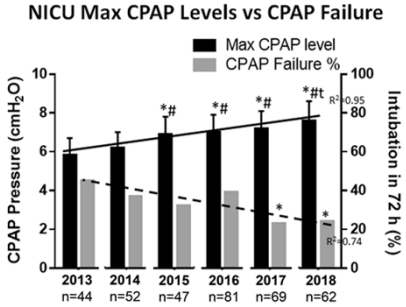
Higher pressures with the RAM cannula was associated with decreased delivery room intubation in infants <1250 grams

<u>WITH A RAM CANNULA</u>
Thus 5.3 cmH_2O (2013) ≈ 4.0 cmH_2O And 6.8 cmH_2O (2018) ≈ 5.0 cmH_2O



Higher pressures with the RAM cannula was associated with decreased CPAP failure within 72 hours in infants <1250 grams

<u>WITH A RAM CANNULA</u>
Thus 5.8 cmH_2O (2013) ≈ 4.4 cmH_2O And 7.6 cmH_2O (2018) ≈ 5.8 cmH_2O



When do we say CPAP has failed and infant needs intubation?

Predictors of early nasal CPAP failure and effects of various intubation criteria on the rate of mechanical ventilation in preterm infants of <29 weeks gestational age.
Fuchs H, Lindner W, Leiprecht A, Mendler MR, Hummler HD.
Arch Dis Child Fetal Neonatal Ed. 2011 Sep;96(5):F343-7. Epub 2011 Jan 30.

- 225 infants (GA 26.2±1.6 weeks)
- 62% were stabilized on nCPAP in delivery room
- 51% failed CPAP and required intubation/surfactant
- A threshold for failure at FiO_2 of ≥0.35-0.40 vs ≥ 0.60 would only increase intubations by 16%

Continuous positive airway pressure failure in preterm infants: incidence, predictors and consequences.
Dargaville PA, Aiyappan A, De Paoli AG, Dalton RG, Kuschel CA, Kamlin CO, Orsini F, Carlin JB, Davis PG.
Neonatology. 2013;104(1):8-14.

- Evaluated CPAP failure rates in 297 infants from 25 to 32 weeks GA
- CPAP was increased to a max of 8 cmH_2O and FiO2 ≥ 0.5 prior to failure
- 22% failed CPAP (45% in infants 25 to 28 weeks, 15% in 29 to 32 weeks)
- A FiO2 > 0.30 in first 2 hours had a >80% chance of failing CPAP

Early predictors of continuous positive airway pressure failure in preterm neonates
Kakkilaya V, Wagner S, Mangona KLM, Steven Brown L, Jubran I, He H, Savani RC, Kapadia VS.
J Perinatol. 2019 Aug;39(8):1081-1088. Epub 2019 May 14.

Table 3 Forward step multivariate stepwise logistic regression model for CPAP failure in both modeling cohort and validation cohort

	Odds ratio (95% CI)	*P*-value
Modeling cohort		
Radiographic severe RDS	3.27 (1.04, 10.28)	0.04
Maximum FiO_2 >0.30	3.89 (1.85, 8.17)	<0.01
a/A PO_2 ≤0.22	4.17 (1.51, 11.54)	<0.01
Validation cohort		
Radiographic severe RDS	21.54 (2.32, 199.91)	<0.01
Maximum FiO_2 >0.30	6.69 (2.13, 21.00)	<0.01
a/A PO_2 ≤0.22	1.62 (0.26, 9.94)	NS

Cannula Type	**RAM Cannula**	**Hudson Prongs/ BabiPlus Prongs/ F & P Flexitrunk**
Starting CPAP (>32 weeks)	6 cmH_2O	5 cmH_2O
If O_2 > 40% to maintain sats > 92 %	Increase to 8 cmH_2O	Increase to 6 cmH_2O
Starting CPAP (<32 weeks)	8 cmH_2O	6 cmH_2O
Max CPAP	10 cmH_2O	7 cmH_2O
Reason for difference	Transmits 65% of the CPAP Pressure to Infant	Transmits the majority of the pressure to infant



Examples of Typical Course of Infants on CPAP

1) 32 week preterm infant with mild RDS
- Admitted on RAM Cannula on CPAP 6 cmH_2O, FiO_2 of 30%
- Infant with mild retractions, FiO2 weaned down to 28% by 20 minutes
- FiO_2 decreases to 25% by 1 hour then continues to decrease
- Infant should remain stable on CPAP and FiO2 improves towards 21%
- Once stable on 21% and breathing comfortably, can be trialed off CPAP

2) 32 week preterm infant with moderate to severe RDS
- Admitted on RAM Cannula on CPAP 6 cmH_2O, FiO_2 of 40%
- Infant with moderate retractions, FiO2 increased to 50%
- CPAP pressure increased to 8 cmH_2O, FiO_2 decreases to 40%
- Infant continues to have retractions, oxygen increases to 43%
- Transport team activated, infant intubated for surfactant treatment

Minimally Invasive Surfactant Therapy (MIST)

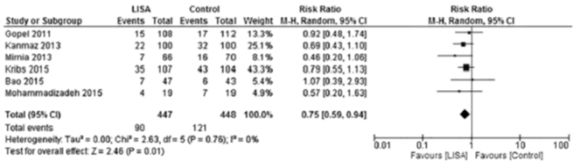
Less Invasive Surfactant Administration (LISA)

Video of MIST procedure

https://www.youtube.com/watch?v=0OmXlOXETZY

https://www.youtube.com/watch?v=IYf92NN1kV0

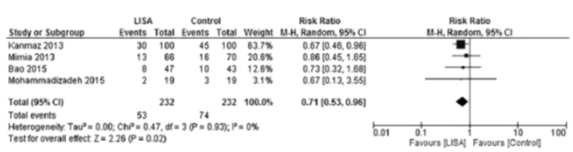
BPD or Death: LISA versus control



Favors LISA 0.75 [0.59, 0.94]

Aldana-Aguirre JC, *et al. Arch Dis Child Fetal Neonatal Ed* 2017;**102**:F17–F23.

Need for Intubation: LISA versus control



Favors LISA 0.71 [0.53, 0.96]

Aldana-Aguirre JC, *et al. Arch Dis Child Fetal Neonatal Ed* 2017;**102**:F17–F23.

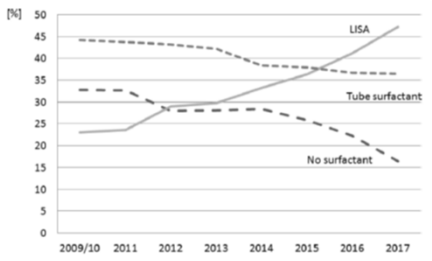


Figure 1 Mode of surfactant administration in the German Neonatal Network. Inclusion limited to infants ≤30 weeks of gestation. LISA, n=4419; tube surfactant, n=5295; no surfactant, n=3514. LISA, less invasive surfactant administration.

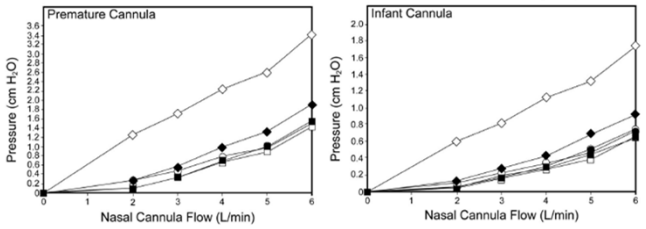
Hertling E, Hartek C, Gopel W Arch Disease Child Fetal Neonatal July 2019

Heated, Humidified High-Flow Nasal Cannula

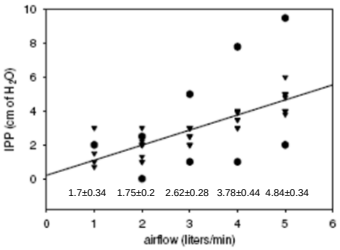
Does is create distending pressure?

High Flow Through a Nasal Cannula and CPAP Effect in a Simulated Infant model
Volsko TA, Fedor K, Amadei J, Chatburn RL
Respir Care. 2011 Dec;56(12):1893-900

- Simulated infant modeling system with compliant lung, respiratory muscles
- Maximal pressure was 3.4 cmH_2O in all models



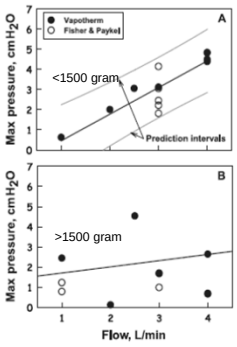
High-flow nasal cannula as a device to provide continuous positive airway pressure in infants
KL Spence, D Murphy, C Kilian, R McGonigle and RA Kilani
Journal of Perinatology (2007) 27, 772–775



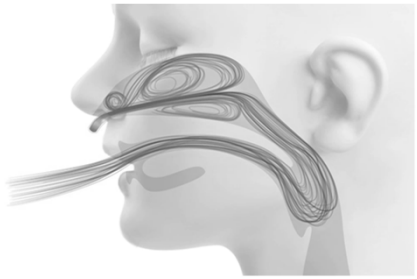
- Intrapharygeal pressures measured
- Stable neonates
- Recorded over 2 to 3 minute period
- Mouths were kept closed by gentle chin support and/or pacifier placement

Heated, Humidified High-Flow Nasal Cannula Therapy: Yet Another Way to Deliver Continuous Positive Airway Pressure?
Zuzanna J. Kubicka, MD, Joseph Limauro, RRT, Robert A. Darnall, MD
PEDIATRICS Volume 121, Number 1, January 2008

- 29.1 to 44 weeks infants, 835 to 3735g
- Flow rates 1L to 5L,
- **No pressure generated with mouth open**

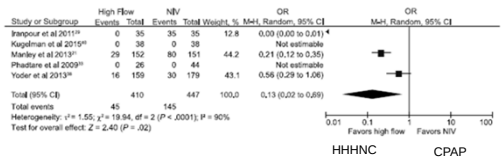


CO_2 Washout with High Flow Nasal Cannula



Vapotherm Illustration

Nasal Trauma



HHHNC CPAP

CPAP is superior to High Flow Nasal Cannula for initial management of RDS

A

Study or Subgroup	nHF Events	nHF Total	CPAP Events	CPAP Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year	Risk Ratio M-H, Fixed, 95% CI
Iranpour 2011	0	35	0	35		Not estimable	2011	
Yoder 2013	6	58	9	67	10.4%	0.77 [0.29, 2.03]	2013	
Lavizzari 2016	17	158	15	158	18.6%	1.13 [0.59, 2.19]	2016	
Roberts 2016	71	278	38	286	46.6%	1.92 [1.34, 2.75]	2016	
Shin 2017	16	42	9	43	11.1%	1.82 [0.91, 3.66]	2017	
Murki 2018	35	133	11	139	13.4%	3.33 [1.76, 6.27]	2018	
Total (95% CI)		**704**		**728**	**100.0%**	**1.83 [1.43, 2.35]**		
Total events	145		82					

Heterogeneity: $Chi^2 = 8.56$, df = 4 (P = .07); $I^2 = 53\%$
Test for overall effect: Z = 4.78 (P <.00001)

0.01 0.1 1 10 100
Favours [nHF] Favours [CPAP]

Hodgson KA, Manley BJ, Davis PG. Clin Perinatol. 2019 Sep

High-Flow Nasal Cannulae in Very Preterm Infants after Extubation

Manley BJ, Owen LS, Doyle LW, Andersen CC, Cartwright DW, Pritchard MA, Donath SM, Davis PG
NEJM 369;15 nejm.org october 10, 2013

303 infants <32 weeks were randomized at extubation to either:

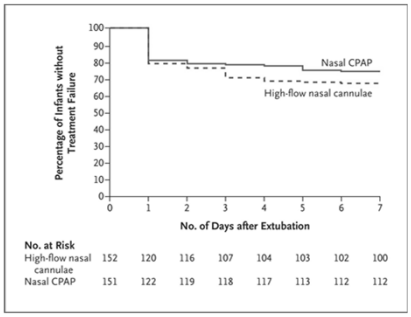
- HHHFNC 5-6 L/Min
- Nasal CPAP 7 cmH_2O

  Stratified to infants > or < 26 weeks GA
- Outcome- need for reintubation within the next 7 days

	HHHFNC	NCPAP
Birth weight	1041g	1044g
GA	27.7 weeks	27.5 weeks
Extubation Failure	52/152 (34.2%)	39/151 (25.8%)
Re-intubation	27/152 (17.8%)	38/151 (25.2%)

- Overall risk difference (95% CI) 8.4 (-1.9, 18.7)% - not significant but in favor of NCPAP
- Infants less than 26 weeks – risk reduction 20.0 (-1.9, 41.8)%

Conclusion: HFNC therapy <u>not inferior</u> to NCPAP as post-extubation respiratory support



Manley B NEJM October 2013

Box 1
Best practices for use of noninvasive respiratory support in preterm infants

Recommendations for the use of noninvasive respiratory support in preterm infants

- Nasal CPAP is recommended for primary support in preterm infants with respiratory distress
- For clinicians and units who wish to use nasal high flow as primary respiratory support, it is recommended that use is limited to infants born ≥30 weeks' gestation and with supplemental oxygen requirement less than 30% on admission
- Nasal high flow is noninferior to CPAP for postextubation support of preterm infants and is considered in infants ≥28 weeks' gestation
- CPAP should be available for back up in units using nasal high flow, to avoid intubation in a subset of patients
- Nasal high flow should be considered for use in infants with nasal trauma, depending on clinical stability

Hodgson KA, Manley BJ, Davis PG. Clin Perinatol. 2019 Sep

Conclusions

Continuous Positive Airway Pressure (CPAP)

- Can be successfully done in 60 to 70% of VLBW infant
- Small variations in surfactant pool size determine ability to be maintained on CPAP and the degree of injury from mechanical ventilation
- Some benefits may exist for BCPAP verses ventilator derived CPAP
- The nasal interface affects the amount of pressure transmitted

Heated, Humidified High-flow nasal cannula (HHHFNC)

- Generates unknown distending pressures in infants greater than 1500 grams or with leak at mouth
- Is not inferior to CPAP for VLBW infants extubated to HHHFNC (when CPAP is available for back up)
- Is inferior to CPAP as primary treatment of RDS

Questions?

