NICHOLAS S. HILL, MD, is Chief of the Division of Pulmonary, Critical Care and Sleep Medicine at Tufts Medical Center in Boston and Professor of Medicine at Tufts University School of Medicine. He received his M.D. from Dartmouth Medical School in 1975. He did his internship and residency in Medicine at Tufts-New England Medical Center. He did a fellowship in Cardiovascular Medicine at the University of Massachusetts Medical Center and in Pulmonary Medicine at Boston University School of Medicine. He is Board Certified in Internal Medicine, Pulmonary Diseases, and Critical Care Medicine. He has done extensive research and writing in the fields of noninvasive ventilation and pulmonary hypertension dating back over 30 years. He has edited several books related to these topics. He established the Pulmonary Hypertension Center at Tufts Medical Center. He is a Past President of the American Thoracic Society and has received a Distinguished Scholar Award in Critical Care from the Chest Foundation of the American College of Chest Physicians as well an Award for Excellence in Pulmonary Hypertension Care from the Pulmonary Hypertension Association. He has served on the Board of Directors of NAMDRC in the past and is an avid triathlete.

OBJECTIVES:
Participants should be better able to:
Walter O’Donohue Lecture –
Humidified High Flow Nasal
Cannulae Oxygen Therapy

Nicholas S Hill MD
Tufts Medical Center
Boston, MA

Disclosures

• Research Grants
  – Fisher Paykel
• Advisory Board
  – Alung technologies
  – Fisher Paykel
• Consultant
  – Respironincs
  – ResMed
  – Vapotherm
Walter J O’Donohue MD (1934-2002)

- Charter member and Past President of NAMDRC
- Chair of Medicine, Creighton U Sch of Med
- Expert on Home Oxygen Therapy
- Indefatigable advocate for removal of barriers to care

Outline

- Technical Considerations
- Physiologic effects
- Compare and contrast with Standard Oxygen and NIV
- Clinical Applications
- Practical Considerations
- Knowledge gaps
What’s in a name?

- HHFNCOT - Humidified High Flow Nasal Cannulae Oxygen Therapy
- HFNO – High Flow Nasal Oxygen
- HFNC – “ ” Nasal Cannula
- HFNT - “ ” Nasal Therapy
- HFN – High Flow Nasal
- NHF – Nasal High Flow

Technical Aspects

<table>
<thead>
<tr>
<th></th>
<th>NIV</th>
<th>NHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat</td>
<td>Variable</td>
<td>31-34°C</td>
</tr>
<tr>
<td>Humidity</td>
<td>Variable</td>
<td>Saturated</td>
</tr>
<tr>
<td>Pressure</td>
<td>Pre-set insp and Exp</td>
<td>Variable</td>
</tr>
<tr>
<td>Flow</td>
<td>Variable</td>
<td>Continuous (20-60 L/min)</td>
</tr>
<tr>
<td>Circuit</td>
<td>Single or Double</td>
<td>Single-heated</td>
</tr>
<tr>
<td>Oxygen</td>
<td>Bled-in or blender</td>
<td>Blender (0.21-1)</td>
</tr>
</tbody>
</table>
Favorable aspects of NHF compared to Standard O2 and NIV include all except:

- Secretion mobilization
- Oxygenation
- Comfort and Tolerability
- Decreased nasal resistance
- None of the above

NHF: Heat and Humidification

- Dry gas at high flow cools, dessicates, causes constriction and is uncomfortable
- High flow gas conditioned to body temperature and saturation
- Enhances comfort and tolerability
- Reduces metabolic cost of breathing
HF: Heat and Humidification

- Loose-fitting comfortable interface
- Permits unimpeded speaking and eating
- Enhances tolerance

Comfort with NHF

20 pts with O2sat < 96% on FIO2 50%, 2 30 min periods

<table>
<thead>
<tr>
<th></th>
<th>Face Mask</th>
<th>NHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>6.8</td>
<td>3.8*</td>
</tr>
<tr>
<td>Mouth dryness</td>
<td>9.5</td>
<td>5.0*</td>
</tr>
<tr>
<td>Overall Comfort</td>
<td>5.0</td>
<td>9.0*</td>
</tr>
</tbody>
</table>

Roca O et al, Respir Care 2010
Secretion Mobilization

- One of first favorable effects posited
- Humidifies and loosens secretions
- Avoids dessication of airway
- Avoids bronchoconstriction caused by airway cooling
- Preserves mucociliary function
- Possible reduction in respiratory infections

Removal of Radioaerosolized Secretions

10 pts with bronchiectasis, 3 hrs daily for a week

Hasani A et al, Chronic Respir Dis 2008
Effective Oxygenation

- Peak inspiratory flow rate (PIFR) high in dyspneic patients with respiratory failure
- Standard oxygen systems provide flows of 10-15 l/min
- Leads to entrainment of room air and dilution of inhaled oxygen
- Using high inspiratory flow rates, NHF reduces entrainment of room air and maintains FIO2 closer to target
Effective Oxygenation

• Oxygenation also enhanced by washout of dead space in upper airway – first portion of inhaled gas is mixture at target FIO2, not exhaled gas with lower FIO2

Oxygenation with HF

20 pts with O2sat < 96% on FIO2 50%, 2 X 30 min periods

<table>
<thead>
<tr>
<th></th>
<th>Face Mask</th>
<th>HF*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIO2 (%)</td>
<td>100 (?)</td>
<td>100</td>
</tr>
<tr>
<td>PaO2 (mm Hg)</td>
<td>77</td>
<td>127*</td>
</tr>
<tr>
<td>SpO2 (%)</td>
<td>95</td>
<td>98</td>
</tr>
</tbody>
</table>

Roca O et al, Respir Care 2010
These mechanisms contribute to ↓ work of breathing with NHF except:

• Reduced dead space
• Positive end-expiratory pressure
• Increased end expiratory lung volume (EELV)
• Reduced respiratory rate

Physiologic Study on NHF for Acute Hypoxemic Failure*

In 15 pts c/w standard O2 mask NHF:

• Lowered RR, minute volume, no change VT
• Decreased esophageal pressure swings
• Lowered pressure time product (PTP)
• No change in PaCO2
• Increased end expiratory lung volume (EIT**)
• Better homogeneity of V/Q

** Electrical impedance tomography  *Mauri T, AJRCCM 2017
Enhancing Efficiency of Ventilation

• Washes out expired CO2 from upper airway before next inhalation
• Reduces dead space ventilation and VD/VT

Spence CJ et al Exp Fluids 2011
Reduced Work of Breathing:

\[ WOB = RR \times (Pr \times Vol)/breath \]

Roca O et al, Respir Care 2010

Less Breathing for Same Alveolar Ventilation = More Efficient

\[ \downarrow V_E = \downarrow RR \times V_T = \downarrow V_D + V_A \]
Positive End Expiratory Pressure with NHF

Corley A et al, Brit J Anaesth 2011

Positive End Expiratory Pressure with NHF – Effect of open mouth

Groves N, Tobin A. Austral Crit Care 2007
Physiologic Effects of NIV

• Expiratory pressure (or continuous) –
  – Increases FRC, improves oxygenation
  – Counterbalances auto-PEEP

• Inspiratory pressure support
  – Reduces inspiratory effort
  – Augments Tidal Volume

• Reduced WOB, improved gas exchange, reduced dyspnea and reversal of resp failure
Summary: HFNT Physiologic Effects

- Heated, humidified oxygenated gas with loose fitting nasal prongs renders HFNT more comfortable, tolerable
- Unimpeded speech and eating with HFNT
- HFNT enhances mucociliary clearance
- HFNT effective oxygenator – high insp flow, ↓ dead space
- HFNT clears dead space in upper airway; ↑ vent efficiency
- Reduces WOB/min largely by virtue of decreasing resp rate

Applications of NHF that are supported by evidence include:

- Hypoxemic respiratory failure
- Hypercapnic respiratory failure
- Post-extubation respiratory insufficiency
- Post-cardiac surgery respiratory insufficiency
- All of the above
Clinical Applications of NHF
Supported by evidence (no guidelines)

– Hypoxemic Respiratory Failure
– Post-operative
– Post extubation
– Do not intubate
– Humidify secretions
– Endoscopy
– Acute Pulmonary Edema?
– Hypercapnic Respiratory Failure?

The Case of Mr B

• 74 yo former professional hockey goalie visiting family from his horse farm in TN.
• History of radical neck surgery, XRT for squamous cell CA of tongue; chronic aspiration
• Now presents with fever, cough, SOB.
• In ED, RR 38, O2 sat 51%, using access muscles, diffuse crackles posterior, Rt > Lt
• On 100% NRB, RR lo 30s, O2 sat 84%
You Would:

- Add standard nasal prongs at 6 l/min to 100% NRB
- Place on CPAP
- Place on BPAP (NIV)
- Place on NHF
- Intubate
- Transfer to another institution in a hurry
**CPAP for Hypoxemic RF**

123 pts with ALI (PaO2/FIO2 < 300) 21 cardiac

<table>
<thead>
<tr>
<th>CPAP (10 cm H2O)</th>
<th>STD</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>62</td>
</tr>
<tr>
<td>1h P/F</td>
<td>203</td>
</tr>
<tr>
<td>Intubated</td>
<td>34%</td>
</tr>
<tr>
<td>ICU LOS (d)</td>
<td>6.5</td>
</tr>
<tr>
<td>Died</td>
<td>31%</td>
</tr>
<tr>
<td>Adverse events</td>
<td>18</td>
</tr>
</tbody>
</table>

Delclaux C et al, JAMA 2000; 284:2352

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**Acute Hypoxemic Respiratory Failure**

- Italian multicenter study of 354 NIV cases, 30% failures; 50% ARDS or CAP, 10% cardiogenic pulmonary edema
- ARDS/pneumonia 3.75 times likelier to fail NIV than acute cardiogenic pulmonary edema

Antonelli et al, Int Care Med 2001 27:1718
NIV as “First Line” Therapy in ARDS

- 147 pts eligible of 479 (332 intubated), had dyspnea, RR > 30 and ≤ 2 new organ failures
- 54% avoided intubation – VAP rate 2 vs 20%, mortality 6 vs 53%
- Success more likely if SAPS II ≤ 34 and PaO2/FIO2 > 175 p 1st hr of NIV therapy

Antonelli et al, CCM, 2006

Observations on NIV Use in the LUNG SAFE study on ARDS

- International prospective study involving 459 ICUs in 50 countries
- Collected data on 2813 ARDS pts (P/F < 300) and new bilat infiltrates
- 507 (18%) managed with NIV
- Rate of use same in mild, mod, severe, but mortality 22%, 42% and 47%, respectively
- Propensity analysis showed in subgroup with P/F<150 mortality 36% v 25% in NIV v INV

Bellani G et al, JAMA 2016
Why is NIV so challenging for ARDS/Severe Hypoxemic RF?

- Severe O2 defect – more PEEP, more leak, desaturation if mask “falls off”
- Stiff lungs – Higher insp pressure, more leak, less comfort
- High minute volumes, tachypnea – harder to meet demands, synchronize
- Hard to tolerate
- Sick patients – sepsis, secretions, MODS, deteriorating

What about HFNO for AHRF?

RCT of NHF v NIV v SO

- P/F ≤ 300, RR > 25, No PaCO2 > 45, no CRF
- 2506 pts with AHRF – 525 eligible - 313 enrolled
- Baseline RR 33/min, P/F 155, 75-80% PNA
- NRB ≥ 10 l/min, NHF 50 l/min, FIO2 1.0 (actual 82 %), NIV VT 7-10 ml/kg (actual PS 8, PEEP 5, FIO2 67%, VT 9.2 ml/kg), 8 hrs daily X 2d

Frat J-P et al, NEJM 2015
## RCT of NHF v NIV v SO in AHRF

### Patients

<table>
<thead>
<tr>
<th></th>
<th>HFNO</th>
<th>SO</th>
<th>NIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>106</td>
<td>94</td>
<td>110</td>
</tr>
</tbody>
</table>

### Outcomes

- **Intubation (%):**
  - NHF: 38%
  - SO: 47%
  - NIV: 50%
  - *P* < 0.05

- **Intub P/F < 200:**
  - NHF: 35%
  - SO: 53%
  - NIV: 58%
  - *P* < 0.05

- **Vent free days:**
  - NHF: 24 days
  - SO: 21 days
  - NIV: 18 days
  - *P* < 0.05

- **Death ICU (%):**
  - NHF: 11%
  - SO: 19%
  - NIV: 25%
  - *P* < 0.05

- **Death 90d (%):**
  - NHF: 30%
  - SO: 45%
  - NIV: 49%
  - *P* < 0.05

### References


### Post-hoc Analysis

Outcomes for NIV even worse in a post-hoc subgroup analysis of immunocompromised patients with hypoxic ARF

Concerns re Frat Study

• NIV was actually 16hrs NHF, 8 hrs NIV for 1st 2 days
• Explanation for mortality difference?
  – Average VT 9.2 ml/kg during NIV (targeted)
  – More refractory shock in NIV group (6% v 17%)
• Impossible to blind

What about Mr B?

• Placed on CPAP 10 in ED, O2 sats 92%, RR 30s
• Switched to NHF, 50l/min 100% FIO2, O2 sat to 96%, RR hi 20s
• Weaned to 80%, 70% and 60% FIO2 next 4d
• Very comfortable and tolerated without difficulty
• Expectorated and cleared secretions well
• On day 5 FIO2 50%, 20l/min and converted to nasal prongs 6l/min
What about Mr B?

RCT Post Cardiac Surgery

- Hi Flow 50 l/min, O2 sat 50% v BiPAP 8 cm H20 IPAP, 4 EPAP at least 4 hrs daily
- 414 v 416 pts with failed SBT (P/F < 150) or failed extubation (P/F < 300, RR > 25, Access muscle use), BMI > 30 or LVEF < 40%
- Treatment failure 1st outcome (reintubation or early discontinuation)
- BL RR 33, P/F 200, pH 7.39, PaCO2 39 mm Hg

Stephan F et al, JAMA 2015
### RCT Post Cardiac Surgery

<table>
<thead>
<tr>
<th></th>
<th>NHF</th>
<th>BiPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>414</td>
<td>416</td>
</tr>
<tr>
<td>Settings (l/min; cm H2O)</td>
<td>46.7</td>
<td>9.3/4.2(VT 7.2)</td>
</tr>
<tr>
<td>RR</td>
<td>26.7</td>
<td>29.7</td>
</tr>
<tr>
<td>Reintub (%)</td>
<td>14.0</td>
<td>13.7</td>
</tr>
<tr>
<td>Crossovers (%)</td>
<td>10.8</td>
<td>7.9</td>
</tr>
<tr>
<td>PaO2/FIO2</td>
<td>157</td>
<td>187*</td>
</tr>
<tr>
<td>Hrs /day</td>
<td>20</td>
<td>6.5*</td>
</tr>
</tbody>
</table>

Stephan F et al, JAMA 2015

### RCT Post Cardiac Surgery

Pts without Treatment Failure

![Graph](image)

No diff Comfort or Dyspnea, Mortality (6.8 v 4.8%), Focal erythema (9.4 v 2.5%) Stephan JAMA 2015
HNFO for Post-extubation

- 105 pts passed SBT with P/F ≤ 300, 3/4 with pneumonia, trauma or atelectasis
- Randomized to HFNO (50 l/min) or venturi mask adjusted to maintain SaO2 ≥ 92%
- 1ary outcome P/F ratio at 24 hrs
- BL RR 23 PaO2 91, P/F 241
- Reintubations 4% (HFNO) vs 21% (venturi)*

Maggiore SM et al, AJRCCM 2014

NHF for Post-extubation

- Maggiore SM et al, AJRCCM 2014
  - 105 pts, Reintubations 4% (HFNT) vs 21%* (Venturi)
- Hernandez G et al, JAMA 2016 (Low risk)
  - 440 pts, Reintubations 14% (HFNT) vs 37%* (SO)
- Hernandez G et al, JAMA 2016 (High risk)
  - 604 pts, Reintubations 19% (NIV), 23% (HFNT)
RCT of HFNO v SO in “low-risk” Post Extubations Pts

- 440 pts (<65 yrs; APACHE II <12; BMI <30; secretions manageable; ≤1 comorbidity
- Baseline P/F 230, ¾ postop or neurological
- Reintubation within 72 hrs; 4.9% v 12.2%*
- Reasons for reintub: inability to clear secretions: 3 (14%) v 14 (37%)*
  — Hernandez G et al, JAMA 2016

NHF for Do-not Intubate pts

- Greater comfort than standard high flow oxygen
- Allows speaking and eating po
- Among 183 pts with CA, 85% tolerated and improved or remained stable

Epstein AS et al, J Pall Medicine 2011
HFNO for Cardiogenic Pulm Edema

- Cohort series - inconclusive
- Personal observation
- PS and PEEP may be important – is it enough with HFNT?

A Role for HFNO in Hypercapnic Respiratory Failure (COPD)?

- Flushes dead space, improves ventilatory efficiency
- Enhances secretion mobilization
- Extrinsic PEEP to counterbalance auto-PEEP
- Decreases resp rate, more time for exhalation, lower WOB/min*; may avoid resp muscle fatigue
- Sequential use of NIV and NHF

*Pisani L et al, Thorax 2017
High Velocity Nasal Insufflation v NIV in the ED (noninferiority)

5 EDs, > 18 yrs, need for NIV, excl drug OD, cardiovasc, secretions, uncoop; COPD 25%, CPE 21%, AHRF/PNA 30%
Settings: HVNI: 30 l/min, FIO2 62%, temp 35
NIV: IPAP 13, EPAP 5 cm H2O

<table>
<thead>
<tr>
<th>Group</th>
<th>HVNI</th>
<th>NIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>104</td>
<td>100</td>
</tr>
<tr>
<td>RR/min</td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td>SaO2 (%)</td>
<td>93</td>
<td>94</td>
</tr>
<tr>
<td>PaCO2 (mm Hg)</td>
<td>53</td>
<td>59</td>
</tr>
<tr>
<td>Therapy Failure (%)</td>
<td>26</td>
<td>17</td>
</tr>
</tbody>
</table>


High Velocity Nasal Insufflation v NIV in the ED (Arm Failure)

<table>
<thead>
<tr>
<th>Failure to:</th>
<th>HVNI</th>
<th>NIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygenate</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Ventilate</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Distress</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>

Doshi et al, Ann Emerg Med 2017
When to start HFNT?

Hypoxemic Resp Failure
• When standard O2 (NC 6l/min) is incapable of maintaining desired oxygenation (O2sat ≥ 90%)

Secretion retention, postextubation, postoperative
• Inspissated secretions, risk factors

HFNT: Practical Considerations
• What flow? Take advantage of high flow – dead space washout, greater effect on rate, higher PEEP
  • Start with 50l/min, adjust to comfort

• What heat? Some find 37°C too hot, 34°C may be preferable in those
  • Start with 37°C, adjust to comfort

• What FIO2? Make sure flow is adequate first, then adjust FIO2.
  • Start at 100% if very hypoxic, lower if not

• How to wean?
  • Lower FIO2, then flow. Transition to NC at 20-30l/min, 50% FIO2
Summary: HFNT for ARF

- HFNT preferred to NIV in mild to moderate Hypoxemic RF – severe not tested
- May be helpful postop for humidification, secretion mobilization, not inferior to NIV in post-cardiac surg, ED pts
- Role in post-extubation, do-not intubate pts
- ? Other applications; cardiogenic pulm edema, trauma – results from RCTs are awaited – COPD not yet tested in RCT

What role for HFNT?

Hypoxemic Respiratory Failure

SO₂  HFNO and/or NIV?  Intubation  ECMO

Hypercapnic Respiratory Failure

SO₂  HFNO?  NIV  ECCO₂R?  Intubation

Mild  Severe