The Hypoxia Challenge Test does not accurately predict hypoxia in-flight in ex-preterm neonates.

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IS AIR TRAVEL SAFE FOR PREMS?
Air travel

• Common, convenient form of travel.
• >1 billion passengers travel by air each year.
• For most, no hazard involved.
• Effects of flight environment on passengers with lung disease not well appreciated.
Flight environment

• Atmosphere has constant composition:
  – 21% Oxygen
  – 78% Nitrogen
  – 1% other gases (Argon, CO₂)

• As altitude increases, % O₂ doesn’t change; rather the partial pressure of O₂ (PaO₂) decreases, resulting in hypoxic environment.
  – PaO₂ decreases from 760mmHg (sea level) to 380mmHg (16,000ft.)
Air travel

• Commercial aircraft cruise at 30,000-40,000ft
  – reduced turbulence
  – fuel economy

• Without pressurisation of aircraft, insufficient \( \text{O}_2 \) to support life at such altitudes.

• Aircraft not pressurised to sea level, rather to 8,000ft.
  – Equivalent to \( \text{FiO}_2 \) 14-15%.
  – \( \text{PaO}_2 \) likely to fall to 53-64mmHg
  – \( \text{SPO}_2 \) likely to fall to 85-91%
Effects of altitude

- 84 passengers (aged 1-78) embarking on commercial flights\(^1\):
  - mean SPO\(_2\) declined from 97\% (sea level) to 93\% (cruising altitude)

- 80 healthy children (6 months - 14 years) travelling by air\(^2\):
  - desaturated from 98.5\% at sea level to 95.7\% (3 hours) & 94.4\% (7 hours.)

\(^1\) Humphreys et al. Anaesthesia 2006; 60(5):458-460.
• Effects of flight at high altitude not thought to be clinically important for most healthy adults & children.

• Altitude exposure may exacerbate hypoxaemia in patients with lung disease.
  – COPD
  – Cystic fibrosis
  – OSA.

• ?? EX-PRETERM INFANTS??

  Specific guidelines for these pts
Why the concern with ex-preterm infants??

• Increased risk of in-flight hypoxia:
  – Apnoeic/ hypoventilation response to hypoxia
  – Labile pulmonary vasculature
  – Increased airway reactivity
  – Smaller lung surface area \[ \Rightarrow \text{V:Q MISMATCH} \]
  – Fetal Hb (high affinity for \(O_2\))
  – Anatomical factors:
    • more compliant rib cage (less support of lung vol)
    • smaller airways (more likely to close)
Infants and air travel

• Paucity of data

• Exposure to 15% O₂ lead to desaturation, apnoeic pauses in 21 of 34 infants³

• BTS guidelines⁴ recommend:
  – Term infants: not fly <1 week of age
  – Ex-preterm infants with history of nLD: undergo 20-minute pre-flight Hypoxia Challenge Test (HCT.)

³Parkins et al. BMJ 1998;316:887-894
Hypoxia Challenge Test (HCT)

• Originally described by Gong⁵.
• Assumes that breathing hypoxic gas mixture at sea level (normobaric hypoxia) equates to hypobaric hypoxia of altitude.
• Expose to 14-15% O₂ for 20 minutes.
• Failed test: SPO₂ falls below 85%; considered to need in-flight O₂.

⁵Gong et al. Am Rev Respir Dis 1984;130:980-986
HCT in infants

- 47 ex-preterm infants, at median corrected age 1.4 months, with nLD, but not receiving supplemental O$_2$ studied.$^6$
- 81% desaturated below 85%, indicating need for in-flight O$_2$.
- The accuracy of HCT in infants not assessed.

- $^6$Udomittipong et al. Thorax 2006;61:343-347
Background

• WA largest state in Australia. All level 3 neonatal care in Perth.
• Premature babies born in Perth transferred by commercial aircraft to regional centre, at near-term corrected age.
• Previous practice: Infants without ongoing O₂ requirement assumed to be safe to fly. Not tested before flight, accompanied by nurse escort, but not monitored in-flight.
Hypothesis/ Aims

• Ex-preterm infants at risk of in-flight hypoxia, independent of presence of neonatal lung disease.
• The HCT accurately predicts which infants are at risk of hypoxia on commercial flights.
Methods

• Prospective observational study.
• Inclusion criteria:
  – ex-preterm (<35 completed weeks)
  – requiring air transfer to regional hospital
• Exclusion criteria:
  – Cyanotic CHD
  – Down Syndrome
Methods

- HCT performed prior to transfer.
- Infant exposed to 14% $O_2$ for 20 minutes.
- Sustained $\text{SPO}_2 < 85\%$: failed test. Low-flow $O_2$ given, until $\text{SPO}_2 > 94\%$: “Fly with $O_2$.”
- Remainder: “safe to fly.”
Methods

• Nurse accompanied all infants home, with lightweight O$_2$ cylinder, pulse oximeter.
• Nurse blinded to test result. During flight, if SPO$_2$ < 85%, opened sealed envelope, & commenced O$_2$ at recommended flow rate.
Results

- 46 infants
  - 14 male, 32 female
  - GA: 32.2 weeks (range 24-35.6)
  - BW: 1667g (range 655-2815g)

- 19 (41%) no history of nLD
- 27 (59%) with history nLD

- 2 with chronic lung disease, but none receiving supplemental O₂.
Results

- HCT at CGA 35.8 (33.1 - 43) weeks
- Flight distance: 593 (417-2174) km
- Flight duration: 62.5 (45-150) minutes
- 46 infants
  - 30 flew safely, without O₂
  - 16 (34.7%) needed O₂ in-flight
  - O₂ administered at 20 (9-60) minutes
  - O₂ flow rate: 125 (32.5-500) ml/min
### INFANTS NEEDING IN-FLIGHT OXYGEN

<table>
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<tr>
<th>No.</th>
<th>GA (weeks)</th>
<th>BW (grams)</th>
<th>CGA at flight</th>
<th>Resp diagnosis</th>
<th>Resp support</th>
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## Comparative demographics

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<th>No in-flight O2 n=30 Median (range)</th>
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<tr>
<td>GA (weeks)</td>
<td>33.2 (26.4-35.6)</td>
<td>31.3 (24-34.6)</td>
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<td>BW (grams)</td>
<td>1647 (945-2815)</td>
<td>1695 (655-2500)</td>
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<td>Sex (M:F)</td>
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<td>CGA at time of HCT (weeks)</td>
<td>36.5 (33.4-38.4)</td>
<td>35.2 (33.1-43)</td>
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<td>Flight Distance (km)</td>
<td>511 (417-2174)</td>
<td>593 (417-2174)</td>
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<td>Flight duration (minutes)</td>
<td>65 (45-150)</td>
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Comparative demographics

<table>
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<td>0 (0-308)</td>
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<td>Room-air SPO2</td>
<td>98.5 (1.3)</td>
<td>97.9 (1.14)</td>
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<td>Time off O2 (days)</td>
<td>33 (6-61)</td>
<td>19 (7-33)</td>
<td>0.047</td>
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<td>Time off resp support (days)</td>
<td>24 (6-57)</td>
<td>21 (7-52)</td>
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HCT RESULT
(SPO$_2$<85% = fail)

46 infants

35 (76%) passed HCT
ie: did not need O2 during test

12 (35%) needed in-flight O2
FALSE -VE

23 (65%) did not need in-flight O2

11 (24%) failed HCT
ie: needed O2 during test

4 (36%) needed in-flight O2

7 (64%) did not need in-flight O2
FALSE +VE

Accuracy: 61%
Sensitivity: 26.6%
Specificity: 77.4%
PPV: 36.4%
NPV: 65.7%
**Discussion**

- Ex-preterm infants with history of nLD more likely to be susceptible to effects of in-flight hypoxia.
- Significant % who needed in-flight O₂ had no nLD, no O₂ therapy, no resp support.
The Hypoxic Ventilatory Response (HVR)

- Adults exposed to hypoxic environment respond by hyperventilating.
- The HVR in newborns is biphasic:
  - Augmented phase: transient hyperventilation (1st 2 minutes)
  - Depressive phase: sustained decrease in MV
- HVR becomes similar to adults at 2-6 months corrected age.
Sleep & Hypoxia

• Arousal from sleep serves as a vital protective mechanism.
• Involves autonomic & behavioural components:
  – HR, BP, ventilation increase
  – Similar to “fight/flight” reaction
Sleep and Hypoxia

• Infants in quiet sleep often fail to arouse to hypoxia.
• The younger the infant, the less likely to be able to arouse in response to hypoxia\(^7\).

• Most infants studied were asleep when they desaturated in-flight.

\(^7\)Horne et al. Resp Physiol Neurobiol; 2005:257-271
Discussion

• HCT did not accurately predict need for in-flight $O_2$

• Limitations with HCT:
  – Not true simulation of flight
  – Not pressurised
  – Only expected $FiO_2$ simulated
  – Graded fall in $FiO_2$ doesn’t occur during HCT

• HCT could be improved:
  – ? Longer duration
  – ? Graded fall in $FiO_2$
Conclusions

• Ex-preterm infants at risk of in-flight hypoxia despite appearing healthy, with no ongoing $O_2$ requirement.
• The HCT is not accurate in predicting those at risk of hypoxia.
• Demographic data are of limited clinical significance in predicting who is safe to fly.
Conclusions

• Implications for air transfer:
  – COST vs SAFETY

• In absence of more accurate pre-flight test, & until we can better predict which infants are at risk of in-flight hypoxia, change in practice:
  – all ex-preterms fly with available O₂.
Unanswered questions

• Until what age are ex-prems unsafe to fly?

• If an ex-prem flies successfully without $O_2$, does that mean they are “in the clear”?
Thank you