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?

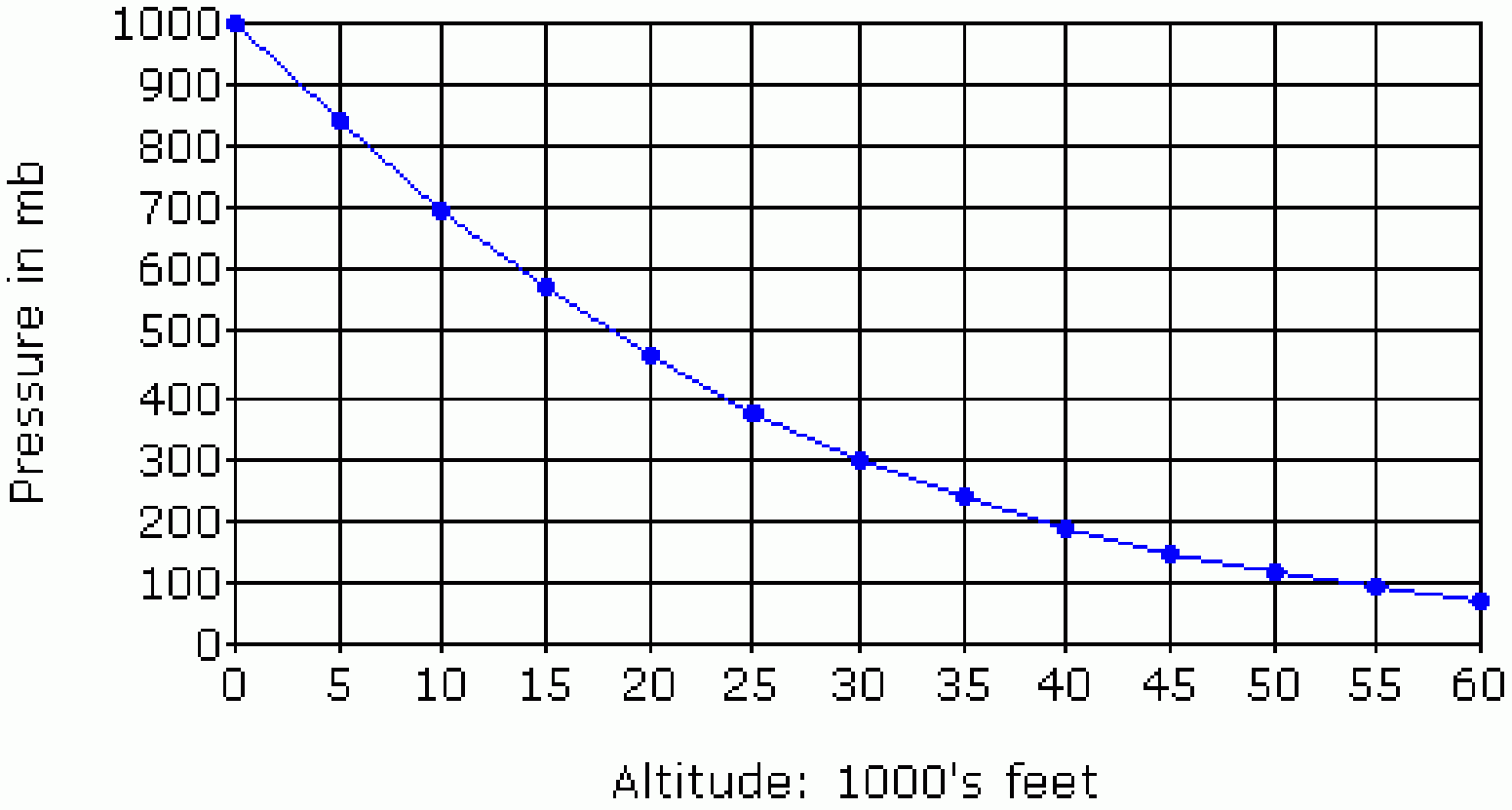
Air travel

- 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, CO_2)
- As altitude increases, % O_2 doesn't change; rather the partial pressure of O_2 (PaO_2) decreases, resulting in hypoxic environment.
  - PaO_2 decreases from 760mmHg (sea level) to 380mmHg (16,000ft.)

Pressure gradient graph



Air travel

- Commercial aircraft cruise at 30,000-40,000ft
  - reduced turbulence
  - fuel economy
- Without pressurisation of aircraft, insufficient O_2 to support life at such altitudes.
- Aircraft not pressurised to sea level, rather to 8,000ft.
  - Equivalent to FiO_2 14-15%.
  - PaO_2 likely to fall to 53-64mmHg
  - 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.
- [2] Lee et al. Pediatr Emerg Care 2002; 18(2):78-80.

- 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.

Specific guidelines for these pts

- ?? EX-PRETERM INFANTS??

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 ➡ 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% O_2 lead to desaturation, apnoeic pauses in 21 of 34 infants[3]
- BTS guidelines[4] 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.)

- [3]Parkins et al. BMJ 1998;316:887-894
- [4]British Thoracic Society recommendations. Thorax 2002;57:0-15

Hypoxia Challenge Test (HCT)

- Originally described by Gong[5].
- Assumes that breathing hypoxic gas mixture at sea level (normobaric hypoxia) equates to hypobaric hypoxia of altitude.
- Expose to 14-15% O_2 for 20 minutes.
- Failed test: SPO_2 falls below 85%; considered to need in-flight O_2.

- [5]Gong 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 O_2 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 SPO_2< 85%: failed test. Low-flow O_2 given, until 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 O_2.

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 O_2
  - 16 (34.7%) needed O_2 in-flight
  - O_2 administered at 20 (9-60) minutes
  - O_2 flow rate: 125 (32.5-500) ml/min

INFANTS NEEDING IN-FLIGHT OXYGEN

No.	GA (weeks)	BW (grams)	CGA at flight	Resp diagnosis	Resp support	Oxygen support
1	29.4	1180	37.5	HMD	CPAP & IPPV	Yes
2	33.6	2500	34.6	Nil	Nil	No
3	34.6	2420	36.4	HMD	CPAP & IPPV	Yes
4	24	655	43	HMD	CPAP & IPPV	Yes
5	32.2	2100	34.4	HMD	CPAP & IPPV	Yes
6	29.3	880	40.6	HMD	CPAP & IPPV	Yes
7	30.2	1680	37.2	HMD	CPAP & IPPV	Yes
8	30.2	1385	33.2	HMD	CPAP & IPPV	Yes
9	34.3	925	37.5	Non-specific respiratory distress	CPAP & IPPV	No
10	31.4	1735	33.1	Nil	Nil	No
11	32.3	2350	35.3	Nil	Nil	No
12	30.5	1480	33.5	Nil	Nil	No
13	32.2	1835	35.1	Non-specific respiratory distress	CPAP & IPPV	Yes
14	31.2	1615	34.4	HMD	IPPV	No
15	30.5	1710	33.4	HMD	IPPV	Yes
16	32.1	1740	34	Nil	Nil	No

Comparative demographics

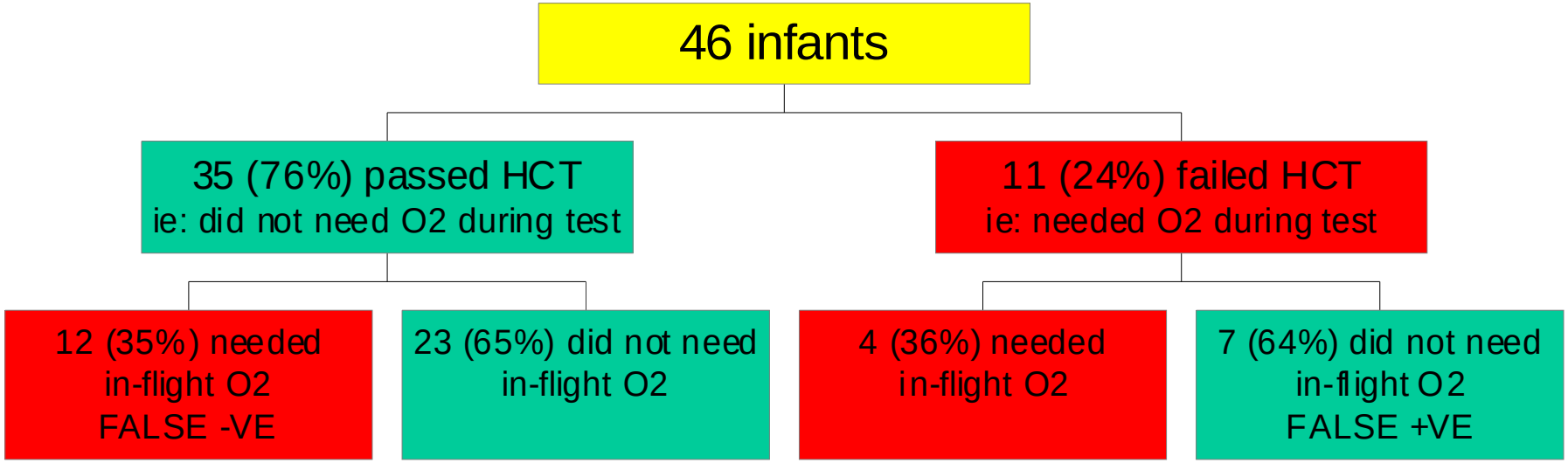
	No in-flight O2 n=30 Median (range)	*In-flight O2 n=16 Median (range)*	*p value*
GA (weeks)	33.2 (26.4-35.6)	31.3 (24-34.6)	0.066
BW (grams)	1647 (945-2815)	1695 (655-2500)	0.747
Sex (M:F)	10:20	10:6	0.057
CGA at time of HCT (weeks)	36.5 (33.4-38.4)	35.2 (33.1-43)	0.116
Flight Distance (km)	511 (417-2174)	593 (417-2174)	0.131
Flight duration (minutes)	65 (45-150)	60 (45-150)	0.264

Comparative demographics

	No in-flight O2 n=30 Median (range)	*In-flight O2 n=16 Median (range)*	*p value*
Duration CPAP (hours)	0 (0-686)	70.5 (0-747)	0.04
Duration IPPV (hours)	0 (0-68)	13.3 (0-1234)	0.004
Duration O2 (hours)	0 (0-308)	8 (0-2362)	0.028
Room-air SPO2	98.5 (1.3)	97.9 (1.14)	0.07
Time off O2 (days)	33 (6-61)	19 (7-33)	0.047
Time off resp support (days)	24 (6-57)	21 (7-52)	0.815

HCT RESULT

(SPO_2<85% =fail)



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 O_2 had **no nLD, no O_2 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 O_2.

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