Pre-flight hypoxic challenge in infants and young children with respiratory disease

Modern aircraft flying at high altitude are cabin pressurised to an atmospheric partial pressure of up to 8000 feet (2448 metres), equivalent to breathing approximately 15% oxygen. This may expose individuals with cardiorespiratory disease to the risk of developing hypoxia. In 2002 the British Thoracic Society (BTS) issued recommendations for passengers with respiratory diseases who are planning to fly.1 These recommendations included the use of a hypoxic challenge test in children with a history of respiratory disease too young to undergo conventional lung function tests. While pre-flight hypoxic challenge tests have been evaluated in older children2 and adults3 with respiratory disease, there are few data on hypoxic responses in infants and young children with respiratory disease although one study has observed profound desaturation in a small number of healthy infants while asleep.4

In the last 6 years we have tested 20 children under 5 years of age with a history of chronic pulmonary disease in early infancy (table 1). At our institution fitness to fly testing using 15% oxygen has been performed as a routine test in older children5 and adults6 with respiratory disease for some years, so formal ethical approval was not sought for this study. Children were exposed to a hypoxic challenge with 15% oxygen while sitting on the lap of a carer in a whole body box pressurised to an atmospheric partial pressure of up to 8000 feet (2348 metres), equivalent to breathing approximately 15% oxygen. This may expose individuals with respiratory disease for some years, so planning to fly.

We conclude that some children with a history of chronic pulmonary disease in early infancy may have normal oxygen saturations in room air but desaturate significantly below 90% when exposed to a 15% oxygen hypoxic challenge. These children may be at risk of hypoxia when flying at altitude. This uncontrolled observational series suggests that such infants should be advised to take supplementary oxygen during the flight. The hypoxic challenge test is a simple and practical test and may be performed in any lung function laboratory with a whole body plethysmograph, a source of nitrogen, and a means of measuring oxygen. As carbon dioxide concentrations do not reach clinically significant levels, oxygen concentrations in the body box could be measured with a conventional oxygen monitor. Further studies are required to evaluate fully the hypoxic challenge test in young children. SPO2 measurements during flight on subjects and healthy control children are needed. Measurements should be undertaken both in the awake and asleep states because there is evidence that Spo2 falls in some older children with cystic fibrosis while asleep during flight and in normal infants at sea level.7

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References

LETTERS TO THE EDITOR

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The editors will decide as before whether to also publish it in a future paper issue.
### Table 1: Hypoxic challenge test: subject details

<table>
<thead>
<tr>
<th>Case no</th>
<th>Sex</th>
<th>Age (months)</th>
<th>SpO&lt;sub&gt;2&lt;/sub&gt; in air</th>
<th>SpO&lt;sub&gt;2&lt;/sub&gt; in 15% O&lt;sub&gt;2&lt;/sub&gt;</th>
<th>Clinical</th>
<th>Destination</th>
<th>Advice given</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>2</td>
<td>98</td>
<td>88</td>
<td>100 (0.5 l/min)</td>
<td>Right hypoplastic lung</td>
<td>Malta</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
</tr>
<tr>
<td>1</td>
<td>M</td>
<td>14</td>
<td>98</td>
<td>90</td>
<td>100 (1.0 l/min)</td>
<td>Right hypoplastic lung Severe tracheobronchomalacia; Right pulmonary artery narrowing; gastro-oesophageal reflux; Ehlers Danlos syndrome; receiving O&lt;sub&gt;2&lt;/sub&gt; at night</td>
<td>Malta</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>11</td>
<td>97</td>
<td>71</td>
<td>100</td>
<td>Ex-preterm 27 w; CLD; receiving 0.1 l/min O&lt;sub&gt;2&lt;/sub&gt; at night Pakistan</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available 2 l/m because uncertain about sleep</td>
<td>Trip cancelled - non medical reasons</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>19</td>
<td>99</td>
<td>90</td>
<td>Ex-preterm 27 w; CLD; receiving 0.1 l/min O&lt;sub&gt;2&lt;/sub&gt; at night Pakistan</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available 2 l/m because uncertain about sleep</td>
<td>Trip cancelled because chest infection</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>4</td>
<td>97</td>
<td>88</td>
<td>97 (1.0 l/min)</td>
<td>Persistent tachypnoea at 4 m unknown aetiology - possible mild pulmonary hypoplasia</td>
<td>New York, USA</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>6</td>
<td>97</td>
<td>90</td>
<td>Persistent tachypnoea at 4 m unknown aetiology - possible mild pulmonary hypoplasia, bronchomalacia</td>
<td>New York, USA</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>45</td>
<td>92</td>
<td>86</td>
<td>92 (1.0 l/min)</td>
<td>Cyanotic episodes of unknown aetiology</td>
<td>Greece</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>54</td>
<td>98</td>
<td>92</td>
<td>Cyanotic episodes with colds; unknown aetiology</td>
<td>Greece</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available 2 l/m</td>
<td>Very tired at end of flight</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>20</td>
<td>97</td>
<td>87</td>
<td>Paraplegic with scoliosis on intermittent home O&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Malta</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available 2 l/m</td>
<td>Received O&lt;sub&gt;2&lt;/sub&gt; via nasal prongs onwards, mask return; no problems</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>9</td>
<td>97</td>
<td>92</td>
<td>Left upper lobe congenital lobar emphysema</td>
<td>Switzerland</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>2</td>
<td>100</td>
<td>94</td>
<td>Ex-preterm 25 w; CLD; on O&lt;sub&gt;2&lt;/sub&gt; 0.1 l/min at night Jamaica</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>7</td>
<td>98</td>
<td>90</td>
<td>Ex-preterm 26 w; CLD; off O&lt;sub&gt;2&lt;/sub&gt; Mauritius</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>6</td>
<td>99</td>
<td>92</td>
<td>Ex-preterm 28 w; intrauterine growth retardation; CLD; off O&lt;sub&gt;2&lt;/sub&gt; Pakistan</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>11</td>
<td>100</td>
<td>94</td>
<td>Ex-preterm 24 w; intrauterine growth retardation; CLD; off O&lt;sub&gt;2&lt;/sub&gt; UAE</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>6</td>
<td>100</td>
<td>94</td>
<td>Ex-preterm 34 w; CLD; VSD; off O&lt;sub&gt;2&lt;/sub&gt; Yugoslavia</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>2</td>
<td>100</td>
<td>95</td>
<td>Repaired neonatal diaphragmatic hernia Kuwait</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>3</td>
<td>99</td>
<td>92</td>
<td>Ex-preterm 34 w</td>
<td>Thailand</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>3</td>
<td>98</td>
<td>91</td>
<td>Ex-preterm 34 w; CLD; off O&lt;sub&gt;2&lt;/sub&gt; Thailand</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>42</td>
<td>96</td>
<td>89</td>
<td>Cystic fibrosis Majorca</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>49</td>
<td>100</td>
<td>94</td>
<td>Right middle lobe bronchus vascular ring Greece</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Uneventful flight</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>F</td>
<td>8</td>
<td>94</td>
<td>88</td>
<td>Pharyngomalacia Canary Isles</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available 2 l/m</td>
<td>Unventful flight</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>F</td>
<td>5</td>
<td>100</td>
<td>94</td>
<td>Ex-preterm 23 w; CLD; off O&lt;sub&gt;2&lt;/sub&gt; S Africa</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available 2 l/m</td>
<td>O&lt;sub&gt;2&lt;/sub&gt; was available but not administered</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>19</td>
<td>98</td>
<td>88</td>
<td>Spinal muscular atrophy + left lower lobe collapse Phoenix, AZ, USA</td>
<td>Have O&lt;sub&gt;2&lt;/sub&gt; available</td>
<td>Unventful flight</td>
<td></td>
</tr>
</tbody>
</table>

SpO<sub>2</sub>, oxygen saturation; CLD, chronic lung disease; VSD, ventricular septal defect; NA, data not available.
maintenance of regular physical activity at high altitude. NO improves the ventilation/perfusion ratio and lowers the alveolar to arterial oxygen tension difference by increasing oxygen saturation. The levels of aldosterone, one of the mechanisms of fluid retention, are increased during high-altitude exposure.

This finding is in agreement with the observation that antidiuretic hormone (ADH) is increased during high-altitude exposure.

The over-representation of wild-type alleles at the same locus are involved in HAPE and support the hypothesis that antidiuresis followed by increased levels of aldosterone observed in HAPE are eliminated in HLs whereas the levels of endogenous NO and aldosterone in the pathogenesis of HAPE, the over-representation of eNOS Asp and 4a alleles in patients with HAPE are consistently higher in the HLs (376.3 ± 239.0 pmol/l) whereas the levels of NO and aldosterone in the pathogenesis of HAPE are higher in patients with HAPE compared with HLs (p = 0.03) whereas the levels of endogenous NO and aldosterone in the pathogenesis of HAPE are lower in patients with HAPE compared with HLs (p = 0.03). The levels of aldosterone and NO are significantly higher in the HLs (376.3 ± 239.0 pmol/l) compared with LLs (155.5 ± 109.9 pmol/l; p = 0.05). Our results suggest a significant role for NO and aldosterone in the pathogenesis of HAPE. The over-representation of eNOS Asp and 4a alleles in patients with HAPE associates these alleles with the disorder, whereas over-representation of Glu and 4b alleles in HLs suggests that they have a role in adaptation to high altitudes. These findings suggest, for the first time, that allelic variants at the same locus are involved in HAPE and adaptation.

<table>
<thead>
<tr>
<th>Polymorphism</th>
<th>Frequency distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HLs (n = 136)</td>
</tr>
<tr>
<td>Glu298Asp</td>
<td></td>
</tr>
<tr>
<td>Glu298Glu</td>
<td>105 (78%)</td>
</tr>
<tr>
<td>Glu298Asp</td>
<td>29 (21%)</td>
</tr>
<tr>
<td>Glu</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Asp</td>
<td>23 (17%)</td>
</tr>
</tbody>
</table>

**Table 1: Genotype and allele frequencies of endothelial nitric oxide synthase (eNOS) polymorphisms in highland dwellers (HLs), lowland dwellers (LLs) and patients with high altitude pulmonary oedema (HAPE)**

Supported by grants from the Council of Scientific and Industrial Research.

**References**


**Prevalence of TB in healthcare workers in south west London**

In the UK, and London specifically, the rise in the incidence of tuberculosis (TB) has been ascribed to reactivation of latent disease and...
importation of infection from recent immi-
grants. The recent increase in the recruit-
ment of healthcare workers from countries
with a high prevalence of TB raises the possibil-
ity of healthcare workers being a
significant source of disease. Previous esti-
mates of TB infection among National Health
Service (NHS) employees were calculated
before the current levels of HIV infection
and the mass migration of healthcare work-
ers. Over two thirds had pulmonary TB and
the proportion of nurses among healthcare work-
ners which, in part, reflects the high
employment area (as of April 2003). Of these, 25
were healthcare workers (6.7%). Four were
men, five healthcare assistants, and three healthcare students. 22 (88%) were
diagnosis. Three were originally
from Africa, and one from the Caribbean. 18
patients had evidence of BCG vaccination
(14 had a scar, 13 born overseas) and 17 TB
patients had evidence of BCG vaccination. Nine patients (36%)
were diagnosed as being HIV antibody positive, although not all patients agreed to
being tested (table 1).
Healthcare workers contribute significantly
to the number of patients with TB. A large proportion (36%) were co-infected with HIV
and this is consistent with previous esti-
mates. The majority of patients identified
were nurses which, in part, reflects the high
proportion of nurses among healthcare work-
ers. Over two thirds had pulmonary TB and
would therefore be deemed a greater infec-
tion-risk.

Previous estimates of TB infection among
NHS workers were calculated more than a
decade ago. The total number of cases
reported annually ranged from 3 to 5 among
nearly 20 000 NHS staff monitored. The NHS
workforce in our sector was estimated at
25 273. In order to calculate a rate of
importation of infection from recent immi-
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