REVIEW

The effects of flight and altitude

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Increasing numbers of infants and children journey by aeroplane, or travel to high altitude destinations, for example, on holiday or as part of a population migration. Most are healthy, although increasingly children may be transported by aeroplane or helicopter specifically to obtain treatment for severe illness or injury. It is therefore useful to review the effects of altitude, and their relevance to children who undertake flights or travel to, or at high altitudes, particularly those with acute and chronic medical conditions.

The published literature on infants and children undergoing airline flights is sparse and limited to case reports and observational studies. There are no studies in the form of trials, for example, to test whether a specific action should be taken or not. This situation exists because firstly, problems in flight are considered rare occurrences; secondly, clinical researchers generally do not deal with large numbers of patients travelling by air; and thirdly, there are substantial logistical problems in undertaking studies involving airline companies and their flights. There is, however, a greater body of data regarding high altitude problems; this is predominantly observational, and has increased our understanding about the more extreme effects of altitude and in particular, hypoxia.¹ Nevertheless, there is little published guidance for the practitioner who is either offering a patient or parent advice, or having to deal with a medical problem in flight. The guidance that does exist is mostly directed towards adults and given against a small evidence base.^{2–3} Hence there is a need to learn more about what happens in flight or at altitude—as such knowledge is accrued, it will be possible to ensure that better guidance on management is provided.

There are a number of environmental changes that arise from altitude, including falls in humidity, irradiation (particularly over the polar areas) temperature, atmospheric pressure, and partial pressure of oxygen. Additional effects that occur as a result of flight include motion, vibration, noise, lack of space, and fatigue, for example, from “jet lag”. Of these physical effects, it is the fall in oxygen levels that is associated with the most potentially serious consequences. Table 1 gives details of the varying oxygen contents in the atmosphere at different altitudes. At sea level, barometric pressure is 760 mmHg (~100 kPa), and air has an atmospheric partial pressure of oxygen (pO₂) of 160 mmHg (~21 kPa)—that is, 21% of barometric pressure.

Airline flights usually cruise at altitudes of 9150–13 000 m (30–40 000 feet) above sea level, where the atmospheric pO₂ is usually ≤5 kPa, which would normally result in a lethal level of airway (alveolar) hypoxia. Aircraft cabins are therefore environmentally modified to atmospheric pressures of 1530–2440 m (5000–8000 feet) above sea level. At the maximum cabin altitude of 2440 m (8000 feet), the atmospheric pressure is 75 kPa (565 mm Hg), giving an atmospheric pO₂ of 15.7 kPa (118 mm Hg). This is equivalent to 15–16% of the ambient oxygen available at sea level.

Serious effects of altitude hypoxia do not usually arise until atmospheric pressure drops to that at about 3000–3500 m (10–12 000 feet), although there is considerable variability in the response to hypoxia between individuals. Air flight regulations require aircraft travel with maximum cabin altitudes of about 2440 m, although a study that measured in-flight cabin altitudes on 204 aircraft flights found the median altitude was 1894 m (6214 feet), with a maximum of 2717 m (8915 feet). It was noted that newer generation aircraft flew at higher altitudes than older aircraft, with a greater risk of altitude exposure to passengers.⁴ Thus there may be variable levels of airway hypoxia that occur on commercial airline flights. It is therefore useful to know and recognise the potential risks to infants and children from high altitudes.

SUSCEPTIBILITY OF INFANTS AND CHILDREN

Infants and children have a range of anatomical and physiological differences, which make their responses to illness and stresses, such as altitude exposure, different to adults. These apply particularly to newborns and infants in the first 12 months of life, and are summarised in table 2. Many of the factors listed may contribute to an increased tendency to ventilation-perfusion mismatch in early life, with the result that infants and young children are particularly susceptible to hypoxaemic episodes,¹⁵ particularly with illnesses and airway hypoxia. The adverse effects of chronic hypoxia are well documented, particularly in early infancy and those with chronic lung disease. These include:

- Poor weight gain
- Pulmonary hypertension
- Rise in airway resistance
- Apnoeic-cyanotic episodes
- Life threatening events.

The importance of these factors in the healthy infant, who sustains shorter periods of hypoxia,

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Table 1 Atmospheric and partial pressures of oxygen at different altitudes

Altitude		Barometric pressure		Atmospheric pO ₂		Inspired pO ₂ *	
Metres	feet	kPa	mm Hg	kPa	mm Hg	kPa	mm Hg
0	0	100	760	21	159	20	150
1000	3280	90	674	18.9	142	17.4	132
2000	6560	80	596	16.8	125	15.4	115
3000	9840	70	526	14.7	111	13.4	100
5000	16400	54	405	11.3	85	10.0	75
8000	26240	36	267	7.6	56	6.2	46
10000	32800	26	198	5.5	42	4.2	32

*Inspired oxygen pressure is calculated from: oxygen fraction in inspired air × [atmospheric pressure – saturation pressure of water at 37°C (6.28 kPa/47.1 mm Hg)].
The barometric pressure in kPa indicates the proportion (%) of inspired oxygen at that altitude compared to sea level; for example, at 3000 m, there is roughly 70% oxygen of that at sea level.
Aircraft cabin pressures are equivalent to those found at 1530–2440 m (5000–8000 feet), and serious altitude related problems usually occur >3000 m.

as occurs during airline flights, is unknown. Nevertheless, there are data on the short term effects of hypoxia in infancy, discussed below.

PHYSIOLOGICAL EFFECTS OF ALTITUDE

Numerous studies have examined the effects of altitude, both acute and long term; these are well reviewed^{16–20} and are summarised in table 3. Many of the effects of altitude have been learnt from the study of the physiology of travellers (usually adults) to high altitude regions, and comparing this with the physiology of high and low altitude residents. Studies in children in high altitude regions of the world (>3000 m) have shown them to have higher minute ventilation, tidal volume, expiratory duration,^{20–23} vital capacity,²⁴ lung compliance,²³ pulmonary diffusing capacity,²⁵ oxygen extraction,²³ haematocrits and haemoglobin levels,^{26–27} and pulmonary hypertension,²⁸ and to maintain pulmonary vascular reactivity.^{29–30}

Infants and children also have lower SaO₂ levels, dependent on altitude. The results of a number of studies looking at SaO₂ are summarised in table 4. Some of these studies set out

to determine the normal levels of oxygenation at their altitude, in order to help in decisions about when to prescribe oxygen therapy. At sea level, normal SaO₂ levels have been defined, but as with all such studies the results are highly dependent on the model of pulse oximeter used, the accuracy with which measurements during motion artefact are excluded, and the state of the infant. Using the Nellcor N-200 pulse oximeter, measurements in quiet sleep (when motion is minimal and a steady state is more reliably obtained) are 96–100% in healthy infants and children.^{31–38–9} These are similar to the values obtained by Reuland and colleagues,³² who used the Nellcor N10 in Lima, Peru (sea level), to collect controls for their measurements at altitude. It can be seen that up to an altitude of 3000 m, mean SaO₂ values are above 90%. In Tibet, Niermeyer *et al* found lower values in infants born to Chinese immigrant mothers, even though the pregnancy and birth occurred at altitude, compared to the indigenous Han infants.¹⁴ Even though newborn infants gestated and born at high altitude show an increased ability to extract a greater fraction of inspired oxygen compared to low altitude newborns,²³ the results from

Table 2 Factors increasing the susceptibility of infants and young children to hypoxaemia

Predisposition for paradoxical inhibition of respiratory drive (up to 1–2 months of age)
In early infancy, infections/hypoxia may present with apnoea/hypoventilation
More compliant rib cage
Negative intrathoracic (pleural) pressures less effective (i.e. less suck is generated)
Provides less support of lung volume, particularly during active sleep
Reduced surfactant (preterm newborns)
Increases tendency to atelectasis and hypoxia
<i>Preterm infants would not usually travel, except as part of a medical transfer</i>
Increased proportion of the pulmonary vascular bed with muscular arterioles (early infancy)
Airway or alveolar hypoxia* causes pulmonary vasoconstriction ⁵
Pulmonary vascular responses to inspired hypoxia are greater in older infants than in newborns, ⁶ and in those with perinatal vascular insults
Rise in pulmonary vascular resistance contributes to right to left shunting, ductal opening (in the early neonatal period), further ventilation-perfusion mismatch, and hypoxia
Increased airway reactivity in response to hypoxia (infancy)
Airway or alveolar hypoxia* in infants can cause bronchoconstriction ^{7–8}
Infants at 26 weeks of age show greater desaturation on histamine challenge than infants 4 weeks old ⁹
Lung volume at end expiration similar to closing volume ¹⁰ (early infancy)
Small airway closure, and hence non-ventilated units, occur more readily, e.g. during active sleep, feeding, and crying
Reduced upper and lower internal diameters of the airways
Airway conductance falls from birth to 2 months of age ¹¹
Reductions in diameter from e.g. respiratory infection, reduces airway patency sooner, ¹² increasing tendency to airway closure and ventilation-perfusion mismatch
Fewer alveoli (early childhood)
Growth in the alveolar region greater than that in the airways in early infancy ¹³
Increases the susceptibility to mismatch between ventilation and perfusion
Fetal haemoglobin present up until 4–6 months of age
Oxygen dissociation curve is shifted to the left, so oxygen is given up less readily to the tissues
At any given pO ₂ , the SaO ₂ is higher, consistent with the higher values reported at 3100 m in neonates compared to values at 4 months of age ¹⁴

*For example, arising from falls in inspired pO₂, respiratory infections, or chronic lung disease.

Table 3 The physiological effects of high altitude

	Acute effect	Found in indigenous
Respiratory		
Arterial pO ₂ and oxygen saturation	↓	↓
Minute ventilation	↑	↑
Carbon dioxide	↓	↓
Oxygen consumption/CO ₂ production	↓	→
Lung volumes (vital capacity, residual volume)	↑	↑
Lung compliance	↑	↑
Peak flow/forced expiratory volume in 1 s	↓	↑
Lung gas transfer (DLCO)	↓	↑
Nocturnal arousals/less active sleep	↑	↑
Periodic breathing	↑	↑
Cardiovascular		
Heart rate	↑	→
Cardiac output	↑	→
Pulmonary artery pressure	↑	↑
Pulmonary vascular resistance	↑	↑
Capillary leak	↑	↑
Erythropoietin and red blood cell production	↑	↑
Neurological		
Cerebral blood flow	↑	↑
Intracranial pressure	↑	↑
Body growth		
Birth weight		↓
Postnatal growth		↓*

Comparisons are related to sea level values: → no difference; ↑ increased; ↓ reduced.

Data relates to children where it exists (see text)

*May be accounted for by factors such as socioeconomic deprivation.

Tibet suggest that there are also genetically inherited factors that lend protection against hypoxaemia at high altitudes.

Hypoxaemia has been identified at altitude as a more useful predictor of illness severity, and was strongly associated with mortality in acute illness.^{32–34} Recognition has therefore been given to the value of pulse oximetry and a need for further exploration of its role in this clinical setting. More understanding of the effects of altitude related hypoxia

has come from experimental studies than from those in children living at high altitude.

EFFECTS OF HYPOXIA

Exposure to hypoxia is usually followed by increased minute ventilation, mainly as a result of increased tidal volume. Newborn infants, born at either full term or preterm, show a characteristic biphasic response, with a transient increase in ventilation followed by a decline by 3–5 minutes.⁴⁰ This decrease in ventilation may persist for some time after the reinstitution of normoxic breathing. This biphasic response is short lived, usually disappearing after a few weeks of age, but may persist longer in infants born preterm.⁴⁰ This may make them prone to greater degrees of hypoxaemia in relation to ambient hypoxia. The respiratory depressant effect appears to be related to a prolongation in expiratory time; this was found not to be due to alteration of the Hering-Breuer reflex, which involves vagal activity.⁴¹

In 34 healthy infants, exposure to 15% oxygen for six hours at sea level produced hypoxaemia, with a median fall in SaO₂ of 4.9%.⁴² The response was highly variable (range 9.3% to 0.7%), and not predicted from baseline variables of oxygenation, respiratory rate, or pattern. There was a decrease in regular breathing pattern (equated to quiet sleep), more time spent in periodic breathing, and interestingly a decrease in prolonged apnoeic pauses. The latter is opposite to the effect noted in preterm newborns, where increased apnoea occurred.⁴³ Episodic desaturation occurred much more frequently, and baseline levels below 80% stopped the exposure in four infants after 1.9–5.2 hours. None of the infants aroused to the hypoxaemia.

Another sea level study subjected thirty 5–7 year olds to 12% oxygen for 10 minutes; 7 of 10 whose SaO₂ fell ≤88% had histories of reactive airway disease.⁴⁴ Desaturation was a better predictor for reactive airway disease than spirometry (positive predictive values 70% and 30% respectively): desaturation had a sensitivity of 100% for reactive airway disease. This suggests that small airway disease contributes to the susceptibility to desaturate with exposure to hypoxia. This may be because airway/alveolar hypoxia induces bronchoconstriction.

It is not possible to predict on first exposure to hypoxia the degree of hypoxaemia and any systemic effect, without

Table 4 Normal SaO₂ levels at different altitudes

Altitude (m)	Location	n studied	Age	SpO ₂ (%)	Reference	Year
Sea level	UK	70	2–16 y, mean 8 y	Range 95.8–100 Median 99.5	31	1993
Sea level	Peru	189	2 mth–5 y	Range 96–100 Mean 98.7 ± 1.1	32	1991
1610	Colorado	150	<48 h	95% CI 88 to 97 Mean 93.0 ± 0.2	33	1991
			3 mth	95% CI 86 to 97 Mean 92.2 ± 0.4		
1670	Nairobi	87	7 days–36 mth	Range 89.3–99.3 Mean 95.7 ± 1.6	34	1993
2640	Bogota	189	5 days–24 mth	Range 84–100 Mean 93.3 ± 2.1	35	1992
2800	Colorado	72	3–670 days	Range 88–97 Mean 91.7 ± 0.2	36	1993
3100	Colorado	14	6 h–4 mth 1 wk 4 mth	Range 81–91 Mean 80.6 ± 5.3 Mean 86.1 ± 4.6	30	1993
3658	Tibet	15	6 h–4 mth	Immigrants * 76–90 Indigenous 86–94	14	1995
3750	Peru	153	2–60 mth	Range 81–97 Mean 88.9 ± 2.9	32	1991
4540	Peru		0.5–72 h	Range 57–75	37	1971

Values given are those in (quiet) sleep.

*Ranges for babies gestated and born to immigrant Chinese mothers, and babies whose families have lived at this altitude for innumerable generations.

undertaking some pre-exposure challenge test (see later in "Use of oxygen therapy"). Subsequently, individuals may have a repeatable response to hypoxia.⁴⁵ Although this knowledge is important for patients with already identified medical conditions, it is those who are healthy and travelling to high altitude destinations who would most benefit from knowledge of their individual response, in order to reduce the risk of serious or life threatening conditions, such as high altitude pulmonary or cerebral oedema.

HIGH ALTITUDE PROBLEMS

Acute mountain sickness, high altitude pulmonary oedema, and high altitude cerebral oedema usually occur over 2400 m (8000 feet) above sea level and represent the extreme effects of altitude related hypoxia. *Acute mountain sickness* is the mildest manifestation of altitude illness and is more readily reversible than pulmonary or cerebral oedema. Rapid ascent and previous episodes of acute mountain sickness are important risk factors. By symptom recognition, 28% of 558 children travelling from 1600 m to 2835 m developed acute mountain sickness.⁴⁶ However, 21% of 405 children developed similar symptoms on travel to sea level, suggesting the true incidence of this complication is 7%, and that travel itself imposes a significant stress on a child. Pre-verbal children are unable to cooperate with the self reporting needed to diagnose acute mountain sickness. To overcome this, there have been attempts to score such children with a "fussiness" score, and this estimated 21% of children 3–36 months old as suffering acute mountain sickness on travel from 1610 m to 3488 m. This compared well with an incidence of 20% in 45 adults, using a conventional scoring system.⁴⁷

Acute mountain sickness presents with headache, nausea, vomiting, anorexia, weakness, and insomnia. There may be peripheral oedema, and in a few cases inspiratory crackles on examination. Symptoms start 12–24 hours after arrival at altitude, and worsen over 2–3 days before resolving. Resolution usually occurs with rest and no further ascent. Dexamethasone helps relieve symptoms (in addition to simple analgesia), alone or in combination with acetazolamide. Although not formally evaluated in children, acetazolamide has also been used to prevent acute mountain sickness.

High altitude pulmonary oedema is more serious, but fortunately less common. In Leadville, Colorado (3100 m), high altitude pulmonary oedema occurred in 50/100 000 of the population, but for 140/100 000 when limiting the analysis to 1–14 year olds.⁴⁸ Most episodes began 1–3 days after return from a 2–7 day visit to a low altitude, but "lowlanders" visiting at high altitude were also affected. Rapid ascent, exertion, cold exposure, and previous episodes of high altitude pulmonary oedema are risk factors. Symptoms include shortness of breath, cough, and chest pain, and are accompanied by increased heart and respiratory rates, cyanosis, crackles, mild fever, and a loud second heart sound. Chest x ray examination shows bilateral pulmonary infiltrates, and with mild leucocytosis and fever can give a presentation initially indistinguishable from pneumonia. The oedema may progress to produce respiratory failure, coma, and death. Treatment includes oxygen therapy, rest, and in the more severe case, descent to lower altitude. Other effective therapies include nifedipine (0.5 mg/kg/dose 8 hourly), positive airway pressure, and phentolamine.

High altitude cerebral oedema is a rarer and more severe manifestation of acute mountain sickness, which has the same clinical features, but in addition visual disturbance, dizziness, impaired memory, hallucinations, ataxia, disorientation, and retinal changes (for example, haemorrhages and papilloedema). Such cases can rapidly progress to coma and

death. Treatment includes oxygen, descent, and dexamethasone (0.15 mg/kg/dose 4 hourly).

Chronic mountain illness refers to the situation where many of the above features develop more slowly. It is seen predominantly in the older population who have lived in high altitude regions of the world, rather than children, and responds to descent to a lower altitude. However, there is evidence that newborns may develop chronic hypoxia related problems. Of 15 Han (Chinese) infants gestated and born in Tibet at 3658 m above sea level, 14 repeatedly had cyanotic episodes during sleep, with feeding, and with minor respiratory illnesses, compared to only 1/15 infants born to indigenous Tibetan mothers. The Han infants had lower SaO₂ levels, and three developed evidence of a circulatory disorder (murmur and gallop, central cyanosis, pedal oedema).¹⁴ It is probable that these infants had early or developing stages of *subacute infantile mountain sickness*, which can cause death from pulmonary hypertension and right heart failure.⁴⁹

Awareness of the manifestations of altitude related illness and the factors that make infants and young children susceptible helps in making recommendations about altitude exposure.

SUSCEPTIBILITY TO ALTITUDE PROBLEMS

Two important factors contributing to acute mountain sickness includes a poor hypoxic ventilatory response and a loss of the normal diuresis seen at altitude. The hypoxic ventilatory response is the increase in minute ventilation mediated by hypoxia on the carotid body, leading to stimulation of the brain stem respiratory centre. If this does not occur, then there is not the increased exhalation of carbon dioxide, the development of a respiratory alkalosis, and a resultant (protective) cerebral vasoconstriction. This, in conjunction with increased blood volume, probably contributes to increased cerebral blood flow and the development of mild cerebral oedema in the form of acute mountain sickness.

High altitude pulmonary oedema is linked to an individual's tendency to respond to hypoxia with an abnormally increased pulmonary artery pressure.⁵⁰ As the pulmonary hypertension arises from vasoconstriction of pre-capillary arterioles, it is unclear how raised pulmonary artery pressures lead to pulmonary oedema. It may occur as a result of capillary leak from increased hydrostatic pressures, in areas not protected by the hypoxia induced vasoconstriction. Alternatively, the integrity of the alveolar capillary membrane may be damaged itself by hypoxia, or from inflammatory mediators.

That inflammatory mediators might be involved in altering the integrity of the capillary-alveolar membrane is supported by the finding that 79% of children in whom high altitude pulmonary oedema developed had a respiratory infection in the two weeks before arrival at altitude, compared to only 13% of adults (child controls were not used).⁵¹ As a marker of inflammatory response, eight patients with asthma and a mean age of 14 years who returned to an altitude of 1560 m after a 14 day break at sea level, showed increases in airway reactivity and inflammatory mediators, compared to controls who stayed at altitude.⁵²

More recently, it has been shown that genetic factors may play an important role in protection against the effects of altitude. The presence of a specific angiotensin converting enzyme (ACE) genotype (I allele), resulting in low ACE activity, is associated with protection of SaO₂ levels in climbers who ascend rapidly to over 5000 m.⁵³ In addition, climbers susceptible to high altitude pulmonary oedema were more likely to have certain genetic markers associated with low levels of nitric oxide production in the lung.⁵⁴

These data are useful in helping understand the reasons for some individuals' susceptibility to the effects of altitude related hypoxia.

HYPOXIA AND THE SUDDEN INFANT DEATH SYNDROME

There is dispute as to whether the effects of high altitude hypoxia are related to sudden and unexpected infant death.⁵⁵ However, there is epidemiological, pathological, and clinical evidence that links hypoxia to sudden death. That severe hypoxaemic episodes can lead to sudden death supports such an association.⁵⁶ There is also a high prevalence of hypoxaemia in preterm infants who have suffered near death events.⁵⁷ In addition, epidemiological studies have identified that the groups of infants who are at risk of subclinical hypoxaemia—preterm infants, those with respiratory infections, and those who have suffered apparent life threatening events—are also groups with an increased risk of sudden infant death. Other epidemiological studies have shown a link between mortality and altitude.

Getts and Hill examined the number of infants dying of sudden infant death syndrome (SIDS) and birth rates in the state of Nebraska for the period 1973 to 1978, and categorised the counties into 13 different bands of altitude.⁵⁸ There was a strong correlation between altitude and SIDS rates, which did not apply to other post-neonatal deaths. At 300 m, SIDS accounted for 25% of all post-neonatal deaths, and increased as a proportion with altitude, until at 1500 m, SIDS accounted for 55% of deaths. SIDS infants died at a mean of 9 weeks of age at 1200 m, compared to 17 weeks of age at 300 m, suggesting that hypoxia from higher altitudes might accelerate any susceptibility to sudden death. Although social class was not controlled for, SIDS infants at altitude had higher levels of prenatal care.

In Colorado, the mortality rate in preterm infants at altitude (>2740 m) was 73% higher than at <2130 m.⁵⁹ This difference was attributable to respiratory deaths, and did not exist for non-respiratory deaths. Because birth weights were lower at higher altitudes (and this applied at all gestations), it was postulated that intra-uterine hypoxia might affect fetal lung development and increase the risk for preterm mortality.⁵⁹ This could include a greater tendency to suffer hypoxaemia, which has been linked to increased respiratory mortality.³⁴ A subsequent review of deaths in Colorado found no effect of altitude on the absolute numbers of SIDS or non-SIDS deaths;⁶⁰ however, this was not related to population mortality rates.

In Austria, the risk of SIDS increased gradually at higher altitudes in a dose-response fashion (odds ratio 1.12/100 m; 95% confidence intervals 1.02 to 1.24).⁶¹ This relation was even stronger for infants lying prone, a known risk factor for SIDS (odds ratio for >1000 m compared to ≤600 m, 4.4). In this study, socioeconomic variables were controlled for. The authors concluded that the higher rate of SIDS with increasing altitude may be accounted for by the relative environmental hypoxia for the infant, the effects of maternal hypoxia on fetal growth, or colder outdoor temperatures, with resultant increased thermal environment indoors (also postulated as a potential risk mechanism for SIDS).

It has previously been discussed that an abnormal hypoxic ventilatory response increases the risk for high altitude illness. Similarly, infants who have suffered apparent life threatening events, often considered a living model for SIDS, have been described as having smaller increases in tidal volume,⁶² and poorer arousal responses⁶³ in response to hypoxia or hypercarbia, compared to controls.

There is pathological support for the association between hypoxia and SIDS: Naeye found pathological markers for hypoxia in infants who died of SIDS,⁶⁴ and increased muscle

in the pulmonary arterioles has been reported in SIDS infants.⁶⁵

Nevertheless, despite the above evidence linking altitude related hypoxia and sudden death, the altitude in aircraft cabins is probably not sufficiently high to cause major problems. In the UK's Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI, 1995–96), questions on the use of air travel were made to parents of 130 cases of sudden infant death syndrome (SIDS) and 528 controls.⁶⁶ None of the infants who died had flown, compared with two controls. However, the sample size may have been too small to discount a relation between air travel and sudden infant death.

Despite case reports,⁴² the evidence that suggests there is an increased chance of infants dying during and in the first few days after a long haul airline flight is not strong enough to make recommendations that infants should not fly. Milner concluded in an associated editorial that flying appears to be safe for healthy children in the first year of life.⁶⁷ It has also been suggested that care is taken in the use of sedatives and undertaking flights with current respiratory infections, particularly in infants under 1 year of age.⁶⁸ Further study is warranted to examine these risks.

USE OF OXYGEN THERAPY

In the normative studies undertaken in children at altitude, a key question for researchers was when oxygen therapy should be administered. For example, should a healthy child who has SaO₂ levels below the normal range at any given altitude receive additional inspired oxygen? Clinicians have given additional oxygen to infants without pulmonary disease to maintain SaO₂ ≥90% at 1610 m,³³ and ≥88% at 2800 m.³⁶ It has already been described that infants at high altitude have lower levels of SaO₂ compared to sea level (see table 4), and a proportion at higher altitudes will develop pulmonary hypertension, right heart failure, and death. In the presence of respiratory problems, it would seem prudent to use oxygen therapy to maintain levels of SaO₂ in the higher end of the relevant normal range.

Relevant to sea level, cardiac catheterisation in infants with bronchopulmonary dysplasia, has shown that pulmonary hypertension develops when SaO₂ falls from 96–98% to 93–94%, with the greatest changes occurring when SaO₂ was below 90%.⁶⁹

In an attempt to determine whether patients with underlying medical problems should receive additional inspired oxygen when flying by aeroplane, methods have been devised to challenge the patient with a hypoxic environment similar to that in the flight cabin. The hypoxia altitude simulation test (HAST) involved 22 adult patients with chronic obstructive lung disease who were given 20.9%, 17.1%, 15.1%, and 13.9% inspired oxygen to determine the effects of hypoxia at 1524 m, 2438 m, and 3048 m (5000, 8000 and 10 000 feet) above sea level. This study involved extensive monitoring, including the use of arterial blood samples. The sea level arterial pO₂ was found to be the best predictor of altitude arterial pO₂;⁷⁰ poor predictors were lung function studies, respiratory acidosis, and exercise tolerance.

In another study, 30 adults were put into a body plethysmograph with 15% oxygen, SaO₂ levels were monitored and then the flow of additional inspired oxygen determined to restore SaO₂ levels to 90% or baseline levels in 21% oxygen.⁷¹ When patients were given 2 litres/minute oxygen by nasal cannulae while still in 15% ambient oxygen, SaO₂ levels were restored in all but one patient, who needed 3 litres/minute. The authors concluded that provided SaO₂ levels were not raised above the patients' usual level, no significant change in arterial carbon dioxide levels should occur.

A study in 22 children aged 11–16 years with cystic fibrosis measured responses to 15% oxygen before a flight to a high altitude destination (1800 m).⁷² The laboratory test was 100% sensitive and highly specific in identifying those at risk of showing desaturation below 90%. Even though in adults, there is some reproducibility in individual response to exposure to high altitude,⁴⁵ individual tolerance to hypoxaemia is extremely variable. The authors therefore concluded that the test could identify only a *group* among whom clinical problems are more likely to arise. Patients with cystic fibrosis have previously been identified as being at risk of high altitude.^{73–74} More recently, patients with other chronic lung conditions have been assessed by placing the patient in a body box filled with 15% O₂ and then titrating the flow needed to raise SaO₂ levels to normal. For infants, this can be done by placing them on the parent's lap (Buchdahl R and Bush A, personal communication).

None of these tests subjected patients to exposures of oxygen for durations that may occur on transcontinental flights. Parkin *et al* found that desaturation to $\leq 80\%$ for ≥ 1 minute occurred on exposure to 15% oxygen in 4/34 healthy infants, but after variable periods of time: 1.9–5.2 hours (median exposure time to 15% oxygen was 6.3 hours).⁴² Only more prolonged studies undertaken in infants exposed to hypoxic environments, such as during long haul flights or at high altitude destinations, will answer the question as to whether duration of exposure affects the degree of response.

AIR TRANSPORT OF SICK CHILDREN

Transport of sick neonates and children to specialised units can occur by aeroplane or helicopter to allow large distances to be covered quickly. In this setting, it is important to consider other effects of the transport, as well as those of hypoxia. These include expansion of trapped gases, stress from noise, vibration, and motion, and decreased temperature.

If the patient is receiving additional inspired oxygen, the fractional inspired oxygen concentration may be increased to account for the hypoxia at altitude. This is best titrated during the journey by continuous pulse oximetry, as was done, for example, in the 4907 mile transfer from Vancouver, Canada to London, England of a 6 year old boy for heart-lung transplantation.⁷⁵ In this case, the aircraft (Lear 35) travelled at low altitude (maximum cabin pressure of 3700 feet) to ensure SaO₂ levels of at least 80%. In patients who are ventilated, it would also be possible to increase the positive end expiratory pressure to help oxygenation.

Positive gravity (G) forces during take off and landing can result in pooling of blood, for example, in the lower extremities on take off if the head is placed towards the front of the aircraft. Such effects may be harmful in shock, as can the pooling of blood to the head in cases of raised intracranial pressure. Positive airway pressure respiratory support may enhance the effects of gravity forces, while patient placement perpendicular to the direction of travel reduces these effects.

Gases expand at altitude (100 ml at sea level becomes 130 ml at 1830 m (6000 feet) and 400 ml at 10 000 m). This may have adverse effects on gases trapped in body cavities, such as the pleural space, gut, and middle ear. Without anticipation and management of these problems, severe discomfort, pain, and clinical instability may occur. These may result from pneumothorax, pneumomediastinum, pulmonary interstitial emphysema, and subcutaneous emphysema. Abnormal air collections, such as might occur in the pleural space, should be drained before transport by air. Intrapulmonary cysts invariably seem to equilibrate on ascent

and do not rupture. Pressurised cabins will reduce the likelihood of gas expansion problems.

Helicopters produce more stress from vibration and noise than do fixed wing aircraft, which is mostly not preventable. However, the stress from these may particularly disturb the sick neonate, producing hypoxaemia, apnoea, or bradycardia.⁷⁶ Temperature regulation should be maintained, as hypothermia and shivering increase oxygen consumption, and may aggravate metabolic acidosis and hypoglycaemia in sick patients. As the humidity drops with altitude, additional means should be used to provide this, for example, in inspired gases. This will help temperature control, fluid balance, and the tenacity of secretions.

OTHER MEDICAL CONDITIONS

There is little published advice on the suitability of flying or travel to high altitude for medical conditions other than those where hypoxia is a risk factor. For example, advice on the timing of travel after surgery, particularly when air has entered a body cavity, is predominantly down to the views of individual practitioners. British Thoracic Society Guidelines recommend waiting two weeks after uncomplicated thoracic surgery, and six weeks after resolution of a pneumothorax.² Surprisingly, these guidelines do not mention avoidance of flying during acute asthma exacerbations.

There has been discussion of the risks of flying with *serous otitis media* (glue ear): the danger is of either air in the middle ear not escaping as expansion occurs on ascent, or of air not entering the middle ear on descent, because of Eustachian tube dysfunction. This failure to equilibrate pressures in the middle ear is more likely in children with adenoidal hypertrophy, and recurrent otitis media. Middle ears that are filled entirely with fluid are probably less likely to cause problems, than those where there is a fluid-air interface.⁷⁷ Because air travels more easily from the ear to nasopharynx, descent is potentially more of a problem. If the Eustachian tube does not vent, the tube may block because of the higher atmospheric pressures.⁷⁸ Simple manoeuvres, such as swallowing, drinking liquids, and Valsalvas during ascent and descent may help avoid such problems. Alternatively, nasal decongestants have been used 1–2 hours before take off, and 30 minutes before descent.

Patients with *sickle cell disease* are at risk from sickling crises during flight. This particularly applies to patients with splenomegaly and relatively higher blood viscosity (for example, from near normal haemoglobin levels). Thus patients with HbSC and sickle cell thalassaemia are more at risk, such that oxygen therapy has been recommended at altitudes over 2135 m (7000 feet).⁷⁹ These recommendations suggested that for classical sickle cell disease, where the spleen was known to have previously auto-infarcted, travel in pressurised aircraft should not pose a problem.

ADVICE FOR TRIPS TO HIGH ALTITUDE

With increasing numbers of families and children travelling to high altitude locations for holidays, information needs to be provided about the risks of high altitude illness so that informed decisions can be made. Factors previously discussed that lead to an increased risk of acute illness include:

- Young age
- Exercise
- Genetic susceptibility
- Recent infection
- Rapid ascent
- High altitude
- State of hydration
- Underlying illness.

The importance of gradual ascent is stressed, but is not always possible with increasing accessibility of high altitude locations. Rest on arrival, maintenance of good hydration, and the early recognition of new symptoms as being possibly due to high altitude illness are recommended. In pre-verbal children, non-specific symptoms such as irritability, clinginess, excessive crying, poor appetite, lethargy, and vomiting should be assessed with altitude related problems borne in mind.

Recent recommendations for children included advice to start descent immediately in any child who becomes unwell above 2500 m.⁸⁰ Because of the risks of subacute infantile mountain sickness, it was also recommended that children under 2 should sleep no higher than 2000 m, and children 2–10 years, no higher than 3000 m. In addition, travellers should be aware of the underlying illnesses that increase susceptibility to hypoxia related problems, shown in table 5.

ADVICE FOR FLYING

Any uncertainty about whether or not an infant or child will suffer health related consequences during or after an airline flight should involve a medical consultation to ensure that the child is healthy. In young infants, some reassurance may be gained by normal SaO₂ levels at sea level, although this does not predict the response to altitude related hypoxia, particularly in those with a complicated perinatal course (Buchdahl R, Bush A, personal communication). If there is a respiratory problem, which is known to or might involve hypoxaemia (see table 5), further assessment should be undertaken to assess whether additional oxygen should be used in flight. This would ideally involve some form of hypoxia challenge to simulate flight, but this is not universally available. An opinion that oxygen might be needed on flight should be accompanied by a request to the airline to provide oxygen, as this needs to be arranged in advance. Pre-flight assessment of the flow of oxygen needed to maintain adequate SaO₂ and ensuring that supplies of oxygen (if needed) are available before and after the flight helps minimise the stress of flight for the patient and carers. In-flight monitoring of SaO₂ might be reassuring if the patient is receiving additional inspired oxygen; if oxygen is not being used, it is unknown what levels of oxygen should be considered as “normal”.

Table 5 Medical conditions with increased risk for hypoxia related problems

Chronic lung disease
Of prematurity
Cystic fibrosis
Sleep related upper airway obstruction
? reactive airway disease
Chest wall conditions
Muscle weakness, e.g. muscular dystrophy
Restrictive lung disease, e.g. scoliosis and other rib cage disorders
Infections
Respiratory: upper and lower
Haematological
Sickle cell diseases, e.g. SC, trait
Cardiac conditions
Increased pulmonary blood flow, e.g. ventricular septal defect, patent arterial duct
Pulmonary hypertension
Heart failure
Cardiomyopathy
Arrhythmias
Neurological
Seizure disorder with respiratory effects
Brain stem disorder (with bulbar effects or sleep disordered breathing)
Raised intracranial pressure

MANAGEMENT OF COMMON MEDICAL EMERGENCIES

Medical emergencies in infants and children in flight are fortunately uncommon. If a child has a known medical condition, then it is important that the parents/carers are clear about how to deal with potential problems. These are usually no different from those that may occur everyday, although the stress of long distance travel, and the changes in physical environment in an aircraft cabin and of time zone, increase the likelihood of a deterioration in most physical conditions. Consultation with the physician who usually manages the child's medical condition is advised prior to long flights, particularly where the stability of the child's condition is less than optimal, or where clinical deterioration has potentially serious or life threatening consequences.

Although the passenger lists on many flights include one or more health professionals who might provide emergency care, it would be preferable for all parents/carers to be trained in basic life support. Basic information on how to treat medical emergencies in infants and young children is well covered in a number of standard texts, such as *Advanced paediatric life support*.⁸¹ However, the presence and standard of drug kits and medical equipment varies enormously between different airlines, making precise guidance on management in an aircraft difficult.

REFERENCES

- 1 Barry PW, Pollard AJ. Altitude illness. *BMJ* 2003;**326**:915–19.
- 2 Air Travel Working Party of the British Thoracic Society Standards of Care Committee. Managing passengers with respiratory disease planning air travel. *Thorax* 2002;**57**:289–304.
- 3 Cummin ARC, Nicholson AN, eds. *Aviation medicine and the airline passenger*. London: Arnold Press, 2002:66–78.
- 4 Cottrell JJ. Altitude exposures during aircraft flight. Flying higher. *Chest* 1988;**93**:81–3.
- 5 Voelkel NF. Mechanisms of hypoxic pulmonary vasoconstriction. *Am Rev Respir Dis* 1986;**133**:1186–95.
- 6 James LS, Rowe RD. The pattern of response of pulmonary and systemic arterial pressures in newborn and older infants to short periods of hypoxia. *J Pediatr* 1957;**51**:5–11.
- 7 Teague WG, Pian MS, Heldt GP, et al. An acute reduction in the fraction of inspired oxygen increases airway constriction in infants with chronic lung disease. *Am Rev Respir Dis* 1988;**137**:861–5.
- 8 Tay-Uybo JC, Kwiatkowski K, Cates DB, et al. Hypoxic airway constriction in infants of very low birth weight recovering from moderate to severe bronchopulmonary dysplasia. *J Pediatr* 1989;**115**:456–9.
- 9 Young S, Geelhoed GC, Stick SM, et al. The effect of age on oxygen desaturation during histamine inhalation challenge in normal infants. *Pediatr Pulmonol* 1993;**16**:158–62.
- 10 Mortola JP, Fisher JT, Smith B, et al. Dynamics of breathing in infants. *J Appl Physiol Respir Environ Exercise Physiol* 1982;**52**:1209–15.
- 11 Martinez FD. Sudden infant death syndrome and small airway occlusion: facts and a hypothesis. *Pediatrics* 1991;**87**:190–8.
- 12 Martinez FD, Taussig LM, Morgan WJ. Infants with upper respiratory illnesses have significant reductions in maximal expiratory flow. *Pediatr Pulmonol* 1990;**9**:91–5.
- 13 Hislop AA, Haworth SG. Airway size and structure in the normal fetal and infant lung and the effect of premature delivery and artificial ventilation. *Am Rev Respir Dis* 1989;**140**:1717–26.
- 14 Niermeyer S, Yang P, Shanmina, et al. Arterial oxygen saturation in Tibetan and Han infants born in Lhasa, Tibet. *N Engl J Med* 1995;**333**:1248–52.
- 15 Poets CF, Samuels MP, Southall DP. Potential role of intrapulmonary shunting in the genesis of hypoxicemic episodes in infants and young children. *Pediatrics* 1992;**90**:385–91.
- 16 Lenfant G, Sullivan K. Adaptation to high altitude. *N Engl J Med* 1971;**284**:1298–309.
- 17 Lockhart A, Saiaq B. Altitude and the human pulmonary circulation. *Clin Sci* 1981;**60**:599–605.
- 18 De Meer K, Heymans HS, Zijlstra WG. Physical adaptation of children to life at high altitude. *Eur J Pediatr* 1995;**154**:263–72.
- 19 Carpenter TC, Niermeyer S, Durmowicz AG. Altitude-related illness in children. *Curr Probl Pediatr* 1998;**28**:177–98.
- 20 Lahiri S, Brody JS, Motoyama EK, et al. Regulation of breathing in newborns at high altitude. *J Appl Physiol Respir Environ Exercise Physiol* 1978;**44**:673–8.
- 21 Cotton EK, Grunstein MM. Effects of hypoxia on respiratory control in neonates at high altitude. *J Appl Physiol Respir Environ Exercise Physiol* 1980;**48**:587–95.
- 22 Mortola JP, Rezzonico R, Fisher JT, et al. Compliance of the respiratory system in infants born at high altitude. *Am Rev Respir Dis* 1990;**142**:43–8.

- 23 **Mortola JP**, Frappell PB, Frappell DE, *et al*. Ventilation and gaseous metabolism in infants born at high altitude, and their responses to hyperoxia. *Am Rev Respir Dis* 1992;**146**:1206–9.
- 24 **Lahiri S**, DeLaney RG, Brody JS, *et al*. Relative role of environmental and genetic factors in respiratory adaptation to high altitude. *Nature* 1976;**261**:133–5.
- 25 **Vargas E**, Beard J, Haas J, *et al*. Pulmonary diffusing capacity in young Andean highland children. *Respiration* 1982;**43**:330–5.
- 26 **Balieu C**, Haas JD. Hematologic evidence of fetal hypoxia among newborn infants at high altitude in Bolivia. *Am J Obstet Gynecol* 1986;**155**:166–9.
- 27 **Moore LG**, Rounds SS, Jahnigen D, *et al*. Infant birth weight is related to maternal arterial oxygenation at high altitude. *J Appl Physiol* 1982;**52**:695–9.
- 28 **Peñaloza D**, Arias-Stella J, Sime F, *et al*. The heart and pulmonary circulation in children at high altitudes. *Pediatrics* 1964;**34**:568–82.
- 29 **Sime F**, Bancharo N, Penaloza D, *et al*. Pulmonary hypertension in children born and living at high altitudes. *Am J Cardiol* 1963;**11**:143–9.
- 30 **Niermeyer S**, Shaffer EM, Thilo E, *et al*. Arterial oxygenation and pulmonary arterial pressure in healthy neonates and infants at high altitude. *J Pediatr* 1993;**123**:767–72.
- 31 **Poets CF**, Stebbens VA, Samuels MP, *et al*. Oxygen saturation and breathing patterns in children. *Pediatrics* 1993;**92**:686–90.
- 32 **Reuland DS**, Steinhoff MC, Gilman RH, *et al*. Prevalence and prediction of hypoxemia in children with respiratory infections in the Peruvian Andes. *J Pediatr* 1991;**119**:900–6.
- 33 **Thilo EH**, Park-Moore B, Berman ER, *et al*. Oxygen saturation by pulse oximetry in healthy infants at an altitude of 1610 m (5280ft). What is normal? *Am J Dis Child* 1991;**145**:1137–40.
- 34 **Onyango FE**, Steinhoff MC, Wafula EM, *et al*. Hypoxaemia in young Kenyan children with acute lower respiratory infection. *BMJ* 1993;**306**:612–15.
- 35 **Lozano JM**, Duque OR, Buitrago T, *et al*. Pulse oximetry reference values at high altitude. *Arch Dis Child* 1992;**67**:299–301.
- 36 **Nicholas R**, Yaron M, Reeves J. Oxygen saturation in children living at moderate altitude. *J Am Board Fam Pract* 1993;**6**:452–6.
- 37 **Gamboa R**, Marticorena E. Presión arterial pulmonar en el recién nacido en las grandes alturas. *Ach Inst Biol Andina* 1971;**4**:55–66.
- 38 **Poets CF**, Stebbens VA, Southall DP. Arterial oxygen saturation and breathing movements during the first year of life. *J Dev Physiol* 1991;**15**:341–5.
- 39 **Poets CF**, Stebbens VA, Alexander JR, *et al*. Arterial oxygen saturation in preterm infants at discharge from the hospital and six weeks later. *J Pediatr* 1992;**120**:447–54.
- 40 **Martin RJ**, DiFiore JM, Jana L, *et al*. Persistence of the biphasic ventilatory response to hypoxia in preterm infants. *J Pediatr* 1998;**132**:960–4.
- 41 **Mortola JP**, Trippenbach T, Rezzonico R, *et al*. Hering-Breuer reflexes in high-altitude infants. *Clin Sci* 1995;**88**:345–50.
- 42 **Parkin KJ**, Poets CF, O'Brien LM, *et al*. Effect of exposure to 15% oxygen on breathing patterns and oxygen saturation in infants: interventional study. *BMJ* 1998;**316**:887–94.
- 43 **Rigatto H**, Brady JP. Periodic breathing and apnea in preterm infants. II. Hypoxia as a primary event. *Pediatrics* 1972;**50**:219–28.
- 44 **Wagner C**, Brooks JG, Richter SE, *et al*. The “88% saturation test”: a simple lung function test for young children. *Pediatrics* 1994;**93**:63–7.
- 45 **Forster P**. Reproducibility of individual response to exposure to high altitude. *BMJ* 1984;**289**:1269.
- 46 **Theis MK**, Honigman B, Yip R, *et al*. Acute mountain sickness in children at 2835 meters. *Am J Dis Child* 1993;**147**:143–5.
- 47 **Yaron M**, Waldman N, Niermeyer S, *et al*. The diagnosis of acute mountain sickness in preverbal children. *Arch Pediatr Adolesc Med* 1998;**152**:683–7.
- 48 **Scoggin CH**, Hyers TM, Reeves JT, *et al*. High-altitude pulmonary edema in the children and young adults of Leadville, Colorado. *N Engl J Med* 1977;**297**:1269–72.
- 49 **Sui GJ**, Liu YH, Cheng XS, *et al*. Subacute infantile mountain sickness. *J Pathol* 1988;**155**:161–70.
- 50 **Fasules JW**, Wiggins JW, Wolfe RR. Increased lung vasoreactivity in children from Leadville, Colorado, after recovery from high-altitude pulmonary oedema. *Circulation* 1985;**72**:957–62.
- 51 **Durmowicz AG**, Noordewier E, Nicholas R, *et al*. Inflammatory processes may predispose children to high-altitude pulmonary oedema. *J Pediatr* 1997;**130**:838–40.
- 52 **Christie PE**, Yntema JL, Tagari P, *et al*. Effect of altitude on urinary leukotriene (LT) E4 excretion and airway responsiveness to histamine in children with atopic asthma. *Eur Respir J* 1995;**8**:357–63.
- 53 **Woods DR**, Pollard AJ, Collier DJ, *et al*. Insertion/deletion polymorphism of the angiotensin I-converting enzyme gene and arterial oxygen saturation at high altitude. *Am J Respir Crit Care Med* 2002;**166**:362–6.
- 54 **Drama Y**, Hanaoka M, Ota M, *et al*. Positive association of the endothelial nitric oxide synthase gene polymorphisms with high-altitude pulmonary edema. *Circulation* 2002;**106**:826–30.
- 55 **Niermeyer S**, Moore LG. No known mechanism links hypoxia and sudden infant death syndrome. *BMJ* 1998;**317**:675–6.
- 56 **Southall DP**, Samuels MP, Talbert DG. Recurrent cyanotic episodes with severe arterial hypoxaemia and intrapulmonary shunting: a mechanism for sudden death. *Arch Dis Child* 1990;**65**:953–61.
- 57 **Samuels MP**, Poets CF, Stebbens VA, *et al*. Oxygen saturation and breathing patterns in preterm infants with cyanotic episodes. *Acta Paediatr* 1992;**81**:875–80.
- 58 **Getts AG**, Hill HF. Sudden infant death syndrome: incidence at various altitudes. *Dev Med Child Neurol* 1982;**24**:61–8.
- 59 **McCullough RE**, Reeves JT. Fetal growth retardation and increased infant mortality at high altitude. *Arch Environ Health* 1977;**32**:36–9.
- 60 **Barkin RM**, Hartley MR, Brooks JG. Influence of high altitude on sudden infant death syndrome. *Pediatrics* 1981;**68**:891–2.
- 61 **Kohlendorfer U**, Kiechl S, Sperl W. Living at high altitude and risk of sudden infant death syndrome. *Arch Dis Child* 1998;**79**:506–9.
- 62 **Hunt CE**, McCulloch K, Brouillette RT. Diminished hypoxic ventilatory responses in near-miss sudden infant death syndrome. *J Appl Physiol Respir Environ Exercise Physiol* 1981;**50**:1313–17.
- 63 **McCulloch K**, Brouillette RT, Guzzetta AJ, *et al*. Arousal responses in near-miss sudden infant death syndrome and in normal infants. *J Pediatr* 1982;**101**:911–17.
- 64 **Naeye RL**. Pulmonary arterioles and arteries in sudden infant death syndrome. *J Clin Pathol* 1978;**31**:198–9.
- 65 **Williams A**, Vawter G, Reid L. Increased muscularity of the pulmonary circulation in victims of sudden infant death syndrome. *Pediatrics* 1979;**63**:18–23.
- 66 **Platt M**, Fleming PJ, Blair PS, *et al*. Hypoxic responses in infants. Danger to babies from air travel must be small. *BMJ* 1998;**317**:676.
- 67 **Milner AD**. Effects of 15% oxygen on breathing patterns and oxygenation in infants. *BMJ* 1998;**316**:873–4.
- 68 **Savulescu J**. Hypoxic responses in infants. Public must be warned of weak evidence for risk of serious harm. *BMJ* 1998;**317**:677.
- 69 **Abman SH**, Wolfe RR, Accurso FJ, *et al*. Pulmonary vascular responses to oxygen in infants with severe bronchopulmonary dysplasia. *Pediatrics* 1985;**75**:80–4.
- 70 **Gong H**, Tashkin DP, Lee EY, *et al*. Hypoxia-altitude simulation test. Evaluation of patients with chronic airway obstruction. *Am Rev Respir Dis* 1984;**130**:980–6.
- 71 **Cramer D**, Ward S, Geddes D. Assessment of oxygen supplementation during air travel. *Thorax* 1996;**51**:202–3.
- 72 **Oades PJ**, Buchdahl RM, Bush A. Prediction of hypoxaemia at high altitude in children with cystic fibrosis. *BMJ* 1994;**308**:15–18.
- 73 **Speechly-Dick ME**, Rimmer SJ, Hodson ME. Exacerbations of cystic fibrosis after holidays at high altitude—a cautionary tale. *Respir Med* 1992;**86**:55–6.
- 74 **Buchdahl RM**, Babiker A, Bush A, *et al*. Predicting hypoxaemia during flights in children with cystic fibrosis. *Thorax* 2001;**56**:877–8.
- 75 **Macnab AJ**, Vachon J, Susak LE, *et al*. In-flight stabilization of oxygen saturation by control of altitude for severe respiratory insufficiency. *Aviat Space Environ Med* 1990;**61**:829–32.
- 76 **Miller C**. The physiologic effects of air transport on the neonate. *Neonatal Network—J Neonatal Nursing* 1994;**13**:7–10.
- 77 **Weiss MH**, Frost JO. May children with otitis media with effusion safely fly? *Clin Pediatr* 1987;**26**:567–8.
- 78 **Brown TP**. Middle ear symptoms while flying. Ways to prevent a severe outcome. *Postgrad Med* 1994;**96**:135–42.
- 79 **Green RL**, Huntsman RG, Serjeant GR. The sickle-cell and altitude. *BMJ* 1971;**4**:593–5.
- 80 **Pollard AJ**, Murdoch DR, Bärtsch P. Children in the mountains. *BMJ* 1998;**316**:874–5.
- 81 **Mackway-Jones K**, Molyneux E, Phillips B, Wieteska S, eds. *Advanced paediatric life support. The practical approach*, 3rd edn. London: BMJ Books, 2001.