Fitness to fly and altitude physiology in young infants

This article summaries current guidelines and the important physiological implications of altitude physiology in a baby or young infant. It provides a framework for clinicians who may be required to advise families about commercial air travel.

Charlotte Bennett
MBBS, FRCPCH, MD, PGCertAeroRT
Neonatal Consultant,
John Radcliffe Hospital, Oxford
charlotte.bennett@ouh.nhs.uk

Keywords

commercial air travel; safety; infancy

Key points

Bennett C. Fitness to fly and altitude physiology in young infants. *Infant* 2012; 8(2): 38-42.

1. It is advisable to wait 7-14 days after birth before flying with a well term baby.
2. Infants with a history of neonatal respiratory problems should be assessed carefully before a decision to fly in the first year.

Air travel is so popular that it is estimated that over four million passengers travel on commercial fights every day. Parents who wish to travel with their babies seek advice about whether this is safe and how old the baby must be before they can fly.

The reduction in cabin pressure of a commercial aircraft in flight is equivalent to 1530-3440 metres altitude. As the altitude increases the partial pressure of oxygen in the atmosphere falls, so that passengers at the cruising altitude are breathing the equivalent of 15-16% of fractional inspired oxygen at sea level.

Traditional advice suggests that babies born after a 'normal' full term delivery should not fly until at least one week of age[1]. However, it seems that there is little access to straightforward information to explain the physiological basis for these recommendations in order for parents to make sound decisions about the relative risks of flight. Media attention raising concerns about the potential risk of sudden unexpected death in infancy (cot death) following air travel[2] or a risk of 'smothering'[3] during flight add to understandable concerns for both parents and professionals with respect to air travel in the early months. The 'fitness to fly' decision-making process with respect to babies who have required special attention at birth including those born prematurely adds a further level of complexity.

This article focuses on the flight stresses incurred by the effects of hypoxic hypoxia and changes in barometric pressures in flight in babies and young infants and aims to provide some clarity with respect to:

- Rationale for fitness to fly decisions
- Guidance for aeromedical considerations for healthcare professionals and parents when making decisions about relative risks of commercial air travel for young infants.

It is not intended to provide guidance regarding the inter-hospital transportation of sick babies by air.

Effects of altitude hypoxia on young infants

In 1998, a paediatrics group in Stafford led by Professor Southall published a study recording the effect of breathing 15% oxygen in healthy babies aged one to six months old[4]. Their interest in airway hypoxia on respiratory control in infants had arisen after two families reported that their infants had died of sudden infant death syndrome (cot death) 14-19 hours and between 40-41 hours respectively after an intercontinental flight. Earlier work had shown that babies exhibited unpredictable apnoeic responses in the presence of hypoxia and the researchers were concerned that the effects of altitude-induced hypoxia might in some way be linked to these unexpected deaths. They recruited 34 well babies (20 males and 14 females) born at term, with no history of respiratory illness at birth, at a mean age of 3.1 months. Thirteen of these infants were siblings of babies who had died unexpectedly in infancy.

The infants were recorded in room air during overnight monitoring at home (mean 7.7 hours) and during a supervised

challenge period of overnight monitoring (mean 6.3 hours) in hospital breathing 15% oxygen in an oxygen tent. The infants were monitored for a further period after the challenge (mean 4.5 hours). The study recorded oxygen saturations, breathing movements, heart rate and respiratory rates during the baseline, challenge and post challenge periods. The researchers defined 'apnoeic pauses' if there was no respiratory effort for over four seconds and 'desaturations' as SpO_2 less than 80% for over 60 seconds. Periodic apnoea was reported if there were three or more apnoeic pauses each separated by less than 20 breaths.

The study showed that the baseline saturations fell from a median of 97.6% in room air to 92.8% in 15% oxygen. The extent of the fall was highly variable (range -9.3% to 0.7%) and there was no correlation between baseline oxygen saturation and the extent of fall during the challenge. The respiratory rate did not change, but heart rate increased by eight beats per minute. Although the frequency of isolated apnoeic pauses did not change, there was a 3.5 fold increase in the proportion of time spent in periodic apnoea ($p<0.001$). In addition there was a significant increase in the number of desaturation episodes ($p<0.001$), the majority of which were associated with apnoeic pauses. In four infants, the challenge was discontinued on the basis of predefined criteria, when the saturations fell below 80% for over 60 seconds. Withdrawal from the challenge occurred after 1.9-5.2 (median 3.1) hours and interestingly none of the babies woke spontaneously during the index desaturation episode. One infant received low flow oxygen to maintain saturation over 94% for one hour after the challenge was discontinued. There was no observed difference in any variable between infants recruited from the postnatal wards and those from families in which an infant had previously died of sudden infant death syndrome.

The editorial article by Professor Milner published in the same edition of the *British Medical Journal* attempted to ameliorate the potential public concern relating to these findings on the assumption that very few cases of cot death were reported to the aviation authorities[5]. He concluded therefore that "all epidemiological evidence indicates that whatever the effect of relative hypoxia on breathing patterns, flying appears to be safe for healthy children during the first year of life".

The publication of this work generated a flurry of correspondence for some weeks[6]. Themes focused on the ethical approval granted in non-therapeutic research, the risks to study participants and potentially inadequate post challenge recording period in view of the index cases.

A further observational study conducted by Lee in 2002 recorded oxygen saturations and heart rate changes during a commercial flight between Honolulu, Hawaii and Taipei, Taiwan in a group of 80 healthy children (43 males)[7]. Baseline measurements were taken before departure followed by subsequent recordings after three and seven hours in flight.

They found that the oxygen saturation declined and heart rate increased after three hours (95.7%, 105 beats per minute [bpm]) and seven hours (94.4%, 108 bpm) of flight compared with preflight levels at sea level (98.5%, 100 bpm). The fall in saturations was statistically lower ($p<0.001$) at both three and seven hours in those children who were asleep rather than awake during the recording. The drop in oxygen saturation was associated with the decreased cabin partial pressure of oxygen (PO_2); PO_2 was 159mmHg at sea level, 126mmHg after three hours and 124mmHg after seven hours. The three and seven hour difference suggests that there was poor acclimatisation and that flight duration may also worsen oxygen desaturation.

The British Thoracic Society guidelines

The British Thoracic Society published guidelines in 2002 for professionals on the management of passengers with respiratory disease planning air travel. These were subsequently updated in 2004 (**TABLE 1**).

Recommendation 1: Wait one week to fly after birth

The 'expert opinion' resulting in the recommendation to defer air travel in a well term baby until at least one week of age appears to be multi-factorial. These include concerns about respiratory pauses and the risk of pulmonary hypertension triggered by hypoxia, the decreased oxygen offloading, characterising fetal haemoglobin, as well as a risk of undiagnosed congenital abnormality or silent spontaneous pneumothorax. These issues are explored in more depth in the following bullet points:

- The physiological effects of breathing hypoxic gases mixtures in newborn infants are less predictable than in adults or older children and may involve an initial period of stimulation followed by suppression[8]. However, this suppression is only seen in the first 10-14 days in term infants, though it may persist longer in preterm babies and may re-emerge in the presence of intercurrent viral infection. Hypoxia in newborn infants can also trigger bronchospasm

The recommendations for children included the following:

1 It is prudent to wait for one week after birth before allowing infants to fly to ensure that the infant is healthy [C].
{This guidance is similar to the Aerospace Medical Association which suggests waiting one to two weeks after birth.}
2 If the infant has had any neonatal respiratory problems, the proposed journey should be discussed with a paediatrician and a hypoxic challenge test considered [B].
3 For oxygen dependent children, including ex-premature infants with neonatal chronic lung disease (bronchopulmonary dysplasia) where flying is imperative, oxygen requirements should be titrated in a body box [B]: "The infant, receiving oxygen via nasal cannulae, is placed in the body box in the company of a parent or carer, and the SpO_2 monitored. The air in the box is diluted to 15% oxygen with nitrogen. Any fall in SpO_2 can be restored to the original value by titration of the flow of oxygen through the nasal cannulae. This flow of oxygen should be supplied during the flight".

Evidence grading

(B) requires availability of well conducted clinical studies but there are no randomised clinical trials on the topic of recommendation. (C) is based on expert committee reports, opinions and clinical experience of respected authorities.

NB A hypoxia challenge testing in adults was recommended if the patient's saturation when resting at sea level was less than 95%.

TABLE 1 British Thoracic Society guidelines, 2004.

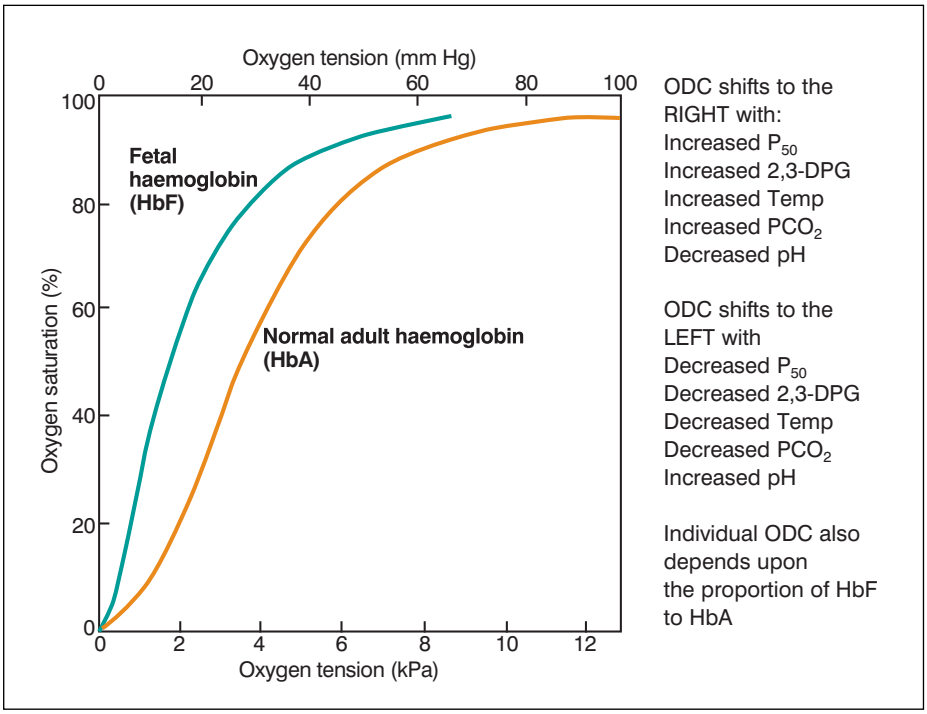

FIGURE 1 Oxygenn dissociation curves for fetal and adult haemoglobin.

which has more of an effect on ventilation than in older children given the increased chest wall compliance and already narrower airways.

- Hypoxia acts as a profound pulmonary vasoconstrictor. In an estimated 10% of term infants, the pulmonary vascular tone remains very labile with a persistent right to left pulmonary shunt detectable in otherwise healthy babies in the first week. These changes can trigger a significant increase in both extra pulmonary shunt and intrapulmonary ventilation to perfusion (V/Q) mismatch in susceptible infants with a spiralling worsening of hypoxia.
- Fetal haemoglobin (fHb) is present in variable but none the less significant amounts until three months of age. The characteristics of fHb result in a left shift of the oxygen dissociation curve (**FIGURE 1**). Although this enhances loading of oxygen in a hypoxic environment, the greater affinity to oxygen leads to decreased unloading in peripheral tissues.
- Modern day obstetric care providing access to high resolution antenatal ultrasound scanning with experience operators enables a high detection rate of congenital anomalies. However, this sophisticated screening is not universal and even when it is available there is always a margin for error. This is particularly true if the anomaly does not result in a structurally detectable change in appearance antenatally or if the anomaly arises after the conventionally timed 'anomaly scanning' has taken place. These include late onset congenital diaphragmatic hernia, duct-dependent complex congenital heart disease such as transposition of the great vessels or co-arcation of the aorta or arterio-venous malformations such as vein of Galen anomalies. These conditions may not necessarily be symptomatic or readily detectable in the first few days after birth but could undergo a precipitous deterioration in the presence of the flight stresses such as hypoxic hypoxia and reduced barometric pressure at altitude.
- It is well recognised that healthy term babies not uncommonly undergo a spontaneous pneumothorax at birth as a result of the significant pressures generated during initial lung inflation. Studies have suggested that as many as 2% of otherwise healthy term babies have an asymptomatic air leak detectable on plain chest X-ray. These resolve spontaneously during the first week and rarely come to the attention of the healthcare professionals. These infants might well be expected to become more symptomatic with an increase in the volume of free air occurring at altitude.

Summary

All of these issues make good clinical sense and it would seem prudent to heed this advice, bearing in mind that as in so many medically-led decisions there should be a carefully appraised judgement of the perceived risks and benefits depending on the clinical and logistical circumstances. If the need for air transport is considered imperative it is possible to mitigate against some of these factors by careful postnatal assessment, however one has to acknowledge a certain degree of unpredictability in how an individual, otherwise healthy baby might behave in flight.

Recommendation 2: A hypoxia challenge test should be considered in any baby who has had any neonatal respiratory problems

In 2004, Buchdahl et al[9] subjected 20 young children with previous respiratory disease and saturations over 95% in room air, to the hypoxia test. Six of these children (30%) experienced desaturation below 90% during the test.

Dr Hall and co-workers in Perth, Australia set out to determine which neonatal factors might be predictive of the requirement of in-flight oxygen among a group of 47 infants and young children with a history of neonatal respiratory problems. The infants were studied between January 2000 and December 2003 and the results published in 2006[10]. The infants were referred for assessment of fitness to fly prior to planned air travel. The hypoxia challenge test was delivered by applying high flow (15L/min) 14% oxygen in nitrogen via a non-rebreathing mask incorporating a one way valve assembly. Studies had shown that the high flow surrounding the face combined with a small leak from the mask maintained a FiO_2 of 14-15% measured at the nares for the duration of the study[11]. The children were fitted with nasal cannulae to allow oxygen administration if required.

All the infants studied had saturations over 95% (range 95-100%) in room air and were tested at a median corrected age of 1.4 months (range-0.7 to 17.0). They were considered to have failed the 20 minute hypoxia challenge test if the saturations fell below 85%. If this occurred, oxygen was delivered via the nasal cannulae at incremental doses commencing at 0.125L/min until SpO_2 was restored above 94% and for a further five minutes at the oxygen delivery to ensure that saturations remained stable.

Thirty eight of the 47 (81%) children tested failed the hypoxia challenge test. The most powerful predicating factors for

failing the test were age and weight at the time of testing, although weight was subsequently excluded because of significant co-linearity with age. Neither the duration of oxygen requirement nor time since oxygen administration contributed to the ability to predict the result of the hypoxia test. The median age for those infants who passed the test was 12 months. All those with a corrected age of less than three months failed the hypoxia test and required in-flight oxygen. This included babies who met criteria for 'neonatal chronic lung disease' (nCLD) defined as, 'oxygen dependence at a corrected age of 36 weeks' gestational age', as well as a babies who did not meet criteria for nCLD who had had early respiratory problems.

The study demonstrated that a normal SpO_2 in room air in infants and young children with a history of neonatal respiratory disorders was a poor predicator of the safety of this patient group in the low oxygen environment encountered during flight. In addition, they found that infants of less than 12 months corrected age were significantly more likely to fail the test suggesting that a pre-flight hypoxia test would be indicated in these infants. The authors concluded that children under one year of age with a history of neonatal lung disease should not undergo air travel without adequate monitoring and access to supplemental oxygen until a successful pre-flight hypoxia challenge test had been completed.

In 2004 the BTS changed their recommendation by 'arbitrary consensus' that desaturation below 90% during a 'fitness to fly' test should be used as a criteria to define the need for supplemental oxygen. A study in 2008 examined the impact of this change in threshold in an attempt to provide a better evidence base for this guidance[12]. Martin and co-workers tested a group of under five-year-olds who were planning to fly in the near future, 34 healthy children and 35 children with a history nCLD. The study design and hypoxia testing were similar to that described in the earlier work by Hall et al. All children had saturations in room air recorded above 94%. The median corrected age at testing was 38 weeks (13-221 weeks) in the healthy children and 53 weeks (25-255 weeks) in the nCLD group with matched body weights at the time of testing in the region of 8.5kg.

All children over two years passed the hypoxia challenge test. Regarding those children under two years of age at testing and applying the threshold SpO_2 of <90%, 12/24 'healthy' children and 14/23 'nCLD' children failed the test, whereas using <85% as a cut off only 1/24 'healthy' children and 6/23 children with nCLD failed. Interestingly the one healthy child who failed the test had fallen asleep during testing and her saturations returned to normal when she spontaneously awoke. It seemed unrealistic that half of otherwise well children would need oxygen during air travel. The authors therefore recommended that the threshold of 85% better discriminated those children who might benefit from supplemental oxygen, although they acknowledged that the relative implication of saturations between 85-90% during the period of the flight was relatively unclear. While they felt that they could safely recommend that hypoxia challenge testing was not indicated in children with nCLD who were over two years' corrected age, similarly to earlier studies, there were few clinical parameters which predicted the likelihood of failing the test in the under two-year-olds, other than length of oxygen supplemental use.

All children studied were in good health at the time of testing and the authors expressed caution that in reality, children might well fly during intercurrent infections placing them at increased risk of hypoxaemia during flight. The BTS 2004 guidelines have incorporated these concerns into their guidelines suggesting that ex-preterm babies with respiratory infection should not fly under the corrected age of six months due to an increased risk of apnoeic episodes.

A study published in 2011 has examined two further clinical questions[13]. Bossley et al set out to determine whether ex-preterm infants who did not meet criteria for nCLD would also be at risk of failing a hypoxia challenge test *after* three months of age as this was not altogether clear from the earlier work by Hall et al. They compared a group of ex-preterm babies without nCLD with term babies at three and six months corrected age. In addition, they also planned to test the effect of feeding babies during hypoxia challenge testing. The work was undertaken during 2007-9 at the Brompton Hospital in London and Sydney Children's Hospital using an identical protocol involving monitoring the infants in a sealed body plethysmograph as recommended within the BTS guidelines.

A failed test was defined as a SpO_2 less than 90% for a minimum of two minutes as defined by the BTS 2004 guidelines, current at the time. Twenty four of the 41 (59%) term infants and 24 of the 30 (80%) preterm infants were tested at three months corrected and the remainder at six months corrected age.

There was a significant drop in SpO_2 during the test with a median change of -6% and a range from -12% to -1% in the term and -13% to -3% in the preterm infants. Two infants in each group (term and preterm) failed the hypoxia testing undertaken at either three or six months based on the <90% criteria although none fell below the <85% criteria.

During feeding the saturations fell further with a median change of -4% in term infants and -2% in ex-preterm babies. Only one baby in each group, tested at three months, recorded saturations below 85% during a feed. All feed-related desaturation resolved spontaneously within a minute of discontinuing the feed.

Summary

The authors concluded that based on the cut-off of SpO_2 <85% none of the babies in the study would have deemed to have failed when tested at a corrected age of three or six months. They recommend that routine pre-flight testing of ex-preterm babies *without* nCLD, otherwise termed bronchopulmonary dysplasia (BPD), was not warranted if the baby was over three months corrected age at the time air travel was planned. However they still recommended caution if an ex-preterm infant, still younger than six months corrected age, had an intercurrent infection at the time of flying. Continuing from Dr Hall's earlier work, it was recommended that babies *with* a history of nCLD should undergo a hypoxic challenge test if under a corrected age of 12 months at the time of the planned flight, even if they are out of oxygen and saturating above 95% in air.

Recommendation 3: Oxygen dependent infant should undergo a pre-flight 'hypoxic assessment' to determine likely oxygen requirement in flight

Twenty-five to 30% of babies born less than 29 weeks' gestational age or with a birthweight of less than 1500g develop nCLD or BPD, as defined by an oxygen dependency at 36 weeks' corrected age. A fifth of these (5%) will go home in oxygen. This decision is made in close

collaboration with the family and in part is dependent on the availability of community-based support.

Once home, the babies are progressively weaned out of oxygen over a variable period which can extend over some weeks, months and occasionally several years. The gradual improvement arises as a result of new lung growth and a progressive decline of the inflammatory lung responses triggered in the early neonatal period. The greatest threat to these graduates is the risk of intercurrent infection. This is particularly challenging in the winter months when respiratory syncytical virus (RSV) and other similar respiratory viruses causing bronchiolitis are most prevalent.

Bronchiolitis in an oxygen-dependent ex-preterm infant can be a devastating and potentially life-threatening disease. Babies not uncommonly require re-ventilation on a paediatric intensive care unit and in some cases, critical care support on an extra-corporeal membrane oxygenation circuit (ECMO). Neonatal chronic lung disease with oxygen dependency is the only category of babies for whom a true cost benefit can be demonstrated for passive vaccination using a monoclonal antibody directed against RSV. This is given by monthly intramuscular injections over the winter months and reduces the risk of hospitalisation with RSV infection by 45-55%. It would be the author's practice to recommend RSV vaccination (palivizumab) to all babies with an ongoing oxygen dependency in their first winter, but this is not universal due to the cost considerations. Should an oxygen-dependent baby need to undertake a flight on a commercial aircraft, the potential risk of exposure to intercurrent infections would seem an extremely important factor to consider when balancing the potential 'need to travel' and 'risk associated with the flight environment'. Vaccination can help to mitigate against these risks but does not completely protect the infant from harm.

Jones et el have published their experiences undertaking pre-flight assessment of adult patients with lung disease who are oxygen dependent. They also found that the pre-flight saturation was a poor predictor for the response at hypoxia equivalent altitude[14]. They found that profound hypoxaemia was more likely to occur if the underlying pathophysiology is predominately due to a reduced ventilation-perfusion ratio (V_A/Q) rather than increased shunt.

They suggested a simple modification to the hypoxia altitude simulation test whereby arterial saturation percentage by pulse oximetry (SpO_2) is plotted against partial pressure of inspired oxygen (PIO_2) during a stepwise reduction in inspired oxygen. A reduction in V/Q produces a curve whose shape reflects the dissociation curve but is shifted to the right along the (PIO_2) axis but has little effect on the plateau. This is in comparison to an increasing shunt which does lower the position of the upper part of the curve. This method has also been used to assess disease severity in babies with bronchopulmonary dysplasia[15]. It has been suggested that this is also a more sophisticated tool to determine the likely effects of altutude-induced hypoxia in pre-flight testing of babies who are oxygen dependent[16] and in more accurately assessing likely inflight oxygen requirements.

Most babies who are receiving oxygen at home are provided with a non portable oxygen concentrator in the home and small lightweight cylinders as a portable supply and for backup in the home. When making arrangements for a flight, medical clearance would be required in advance of the flight to either provide additional supplies of cylinder oxygen or for the use of a continuous flow portable oxygen concentrator.

Summary

Given the option one would probably not chose to fly with an oxygen-dependent infant. Although not insurmountable, the challenges and risks of flying need to be carefully weighed against the need to fly. Comprehensive vaccination cover would be highly recommended. Travel with inflight saturation monitoring and even a specialty-trained nurse escort may be a safer option, but cannot completely protect the infant from other risks such as exposure to infection.

Conclusion

Air travel is such a commonplace part of our modern lives it is easy to overlook the physiological stresses that occur at cabin altitude. This article provides a framework to advise families to ensure the optimal safety of their infants during commercial air travel.

Footnote

Dr Charlotte Bennett is Neonatal Medical Director of AirMed Ltd an international fixed-wing air ambulance service. She is currently undertaking a 'Diploma in Aeromedical Transfer and Retrieval' with the University of Otago, NZ.

References

1. **Ahmedzai S., Balfour-Lynn I.M., Berwick T., et al. British Thoracic Society Standards of Care Committee.** Managing passengers with respiratory disease planning air travel: British Thoracic Society recommendations. *Thorax* 2002;57:289-304.
2. **Parkins K.J., Poets C.F., O'Brien L.M., Southall D.P.** Effects of exposure to 15% oxygen on breathing patterns and oxygen saturations in infants: interventional study. *BMJ* 1998;316:887-94.
3. www.dailymail.co.uk/news/article-1232265.
4. **Parkins J., Poets C.F., O'Brien L.M., Stebbens V.A., Southall D.P.** Effects of 15% oxygen on breathing patterns and oxygen saturation in infants: interventional study. *BMJ* 1998;316:887-94.
5. **Milner A.D.** Effects of 15% oxygen on breathing patterns and oxygenation in infants, editorial. *BMJ* 1998;316:873.
6. **Letters** Hypoxic responses in infants. *BMJ* 1998;317:675-78.
7. **Lee A., Yamamoto L., Relles N.** Commercial airline travel decreases oxygen saturation in children. *Ped Emerg Care* 2002;18,2:78-80.
8. **Cross K.W., Oppe T.E.** The effect of inhalation of high and low concentrations of oxygen on the perspiration of the premature infant. *J Physiol (Lond)* 1952;117:38-55.
9. **Buchdahl R., Bush A., Ward S., et al.** Pre-flight hypoxia challenge in infants and young children with respiratory disease. *Thorax* 2004;59:1000.
10. **Udomittipong K., Stick S.M., Verheggen M., Oostryck, Sly P.D., Hall G.L.** Preflight testing of preterm babies with neonatal lung disease: a retrospective review. *Thorax* 2006;61:343-47.
11. **Hall G., Verheggen M., Stick S.** Assessing fitness to fly in young infants and children. *Thorax* 2007;62:278.
12. **Martin A., Verheggen M., Stick S., et al.** Definition of cutoff values for hypoxia test used for preflight testing in young children with neonatal chronic lung disease. *Chest* 2008;133:914-19.
13. **Bossley C.J., Cramer D., Mason B., et al.** *Arch Dis Child Fetal Neonatal ed* 2011; doi:10.1136/adc.2011.212001.
14. **Jones J.G., Bakewell S.E., Heneghan C.P.H., Jones S., Snape S.** Profound hypoxia in pulmonary patients in airline equivalent hypoxia: Roles of V_A/Q and shunt. *Aviation Space Environ Med* 2008;79:81-86.
15. **Quine D., Wong C.M., Boyle E.M., Jones J.G., Stenson B.J.** Non-invasive measurement of reduced ventilation: perfusion ratio and shunt in infants with bronchopulmonary dysplasia. *Arch Dis Child Fetal Neonatal Ed* 2006;91:F409-F414.
16. **Gupta A., Stocks J., Jones G.** Evaluation of patients prior to air travel *Chest* 2009:135:882-83.

Additional reading

Samuels M.P. The effects of flight and altitude *Arch Dis Child* 2004;89:448-55.

Bossley C., Balfour-Lynn I.M. Is this baby fit to fly? Hypoxia in aeroplanes. *Early Human Dev* 2007;83:755-59.

Community Paediatric Committee, Canadian Paediatric Society. Air travel and children's health issues. *Paediatr Child Health* 2007;12:45-50.