

Key points

- ▶ Commercial aircraft have a hypoxic environment, equivalent to an altitude of 2,438 m (8,000 ft) above sea level.
- ▶ Normal subjects and the majority of respiratory patients can tolerate this without symptoms. In practice, medical diversions for respiratory problems are very rare.
- ▶ The tendency of individual patients to become hypoxic in these conditions cannot be predicted with accuracy from sea-level oxygen saturation or spirometry.
- ▶ Hypoxic challenge may be used to simulate the inflight environment, to predict hypoxaemia and to assess the effectiveness of inflight oxygen.
- ▶ Most airlines, with adequate warning, can provide oxygen at 2 or 4 litres per minute for respiratory patients.
- ▶ While it may be possible to predict hypoxia during flight, there are no means of predicting symptoms or actual risk of harm during air travel.



Problems of air travel for patients with lung disease: clinical criteria and regulations

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Educational aims

- ▶ To identify the potential problems that patients with chronic respiratory conditions may encounter during air travel.
- ▶ To recognise that guidelines have been developed from a number of sources to assist doctors involved in assessing a patient who is considering air travel.
- ▶ To make clinicians aware of the different methods of hypoxic challenge that have been developed to help with the clinical assessment of patients.
- ▶ To highlight that many patients with chronic lung disease are capable of air travel without developing significant hypoxia, but to raise awareness about which patients are likely to be at risk.
- ▶ To discuss the potential difficulties that may arise for the patient when they are arranging inflight oxygen.

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Summary

Doctors are frequently asked by patients with chronic lung disease if they are fit to fly. As commercial flights are not pressurised to sea level, there is a reduction in partial pressure of oxygen (PO_2), which may result in significant hypoxia in otherwise asymptomatic patients.

A number of different assessment methods have been developed to assess flight fitness and several professional organisations have developed guidelines to help doctors give informed advice.

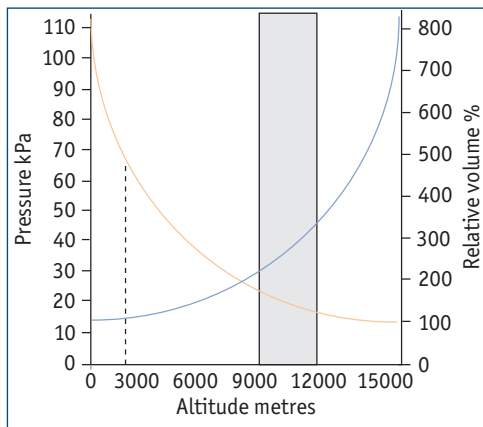
Patients who become significantly hypoxic during a flight assessment may still be able to travel with supplemental oxygen. However, the provision of supplemental oxygen is dependent on individual airline policy and considerable variations in policy have been recorded.

This review aims to give a brief overview of air travel for patients with lung disease, including physiology, guidelines, assessing fitness to fly and oxygen supplementation.



Figure 1

The relationship between altitude, and atmospheric pressure (orange line) and the relative volume of trapped gas (blue line). At normal commercial cruising altitudes (indicated by the shaded box), atmospheric pressure is ~25% of pressure at sea level, which will cause significant expansion of trapped gas. Within the partially pressurised cabin (indicated by the dotted line), the relative increase in gas volume is reduced.



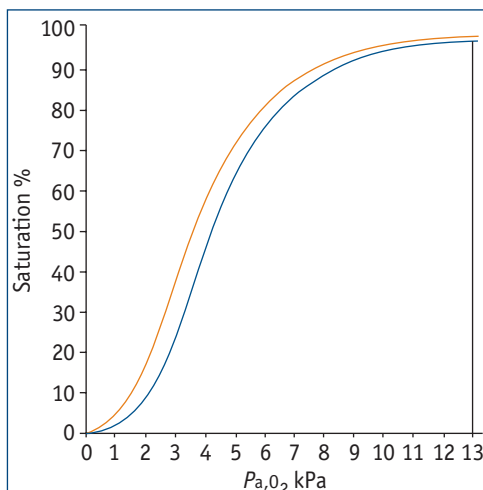
Air travel is a rapidly expanding mode of travel worldwide. Within the UK, Government forecasts for the increase in passenger numbers at UK airports between 2005 and 2010 range 16–25% [1], and by that analogy many more passengers with respiratory disease will be flying as a result of this increase. One direct consequence of this growth in travel has been that doctors are frequently asked by respiratory patients: "can I fly safely with my lung problems?".

At normal cruising altitudes (9,000–12,500 metres for commercial traffic), most aircraft are designed to maintain a reduced cabin pressure that is equivalent to an altitude of not greater than 2,438 metres (8,000 ft) above sea level (figure 1) [2]. At this altitude, the P_{O_2} is ~14.4 kPa and the inspired fraction of oxygen (F_{I,O_2}) is the equivalent of 15.1% at sea level. Most passengers can tolerate this reduction in P_{O_2} without experiencing any respiratory distress, but patients with chronic respiratory disease may develop hypoxia with or without an exacerbation of their symptoms.

Although the most significant effect of increasing altitude is a reduction in P_{O_2} , the

Figure 2

An oxygen dissociation curve. In healthy individuals (orange curve), sea-level arterial oxygen tension (P_{a,O_2}) is in the region of 13 kPa (solid black line). At 2,438 metres, P_{a,O_2} is ~9.7 kPa, which still gives an O_2 saturation of ~92%. Patients with chronic respiratory disease may have a rightward shift of the dissociation curve (blue curve) due to a reduction in arterial pH, placing them at greater risk of desaturation when exposed to a low-oxygen environment.



reduction in total atmospheric pressure may also affect lung function. Sudden reductions in pressure (hypobaria) during ascent to cruise can result in a temporary increase in the volume of any gas trapped within body cavities as the pressure slowly equalises with the cabin pressure. This may be of significance in patients with either cystic or bullous disease, where the increase in the volume of the trapped gas may have a detrimental effect on lung mechanics by the compression of adjacent healthy tissue.

The prediction of symptoms at altitude is not currently possible, so most studies have focused on attempts to predict hypoxia at altitude, and a number of different assessment protocols have been developed. These protocols either expose patients to the conditions they are likely to encounter during air travel or use sea-level arterial blood gas analysis to estimate altitude P_{O_2} . There are advantages and disadvantages to each method.

Fortunately for patients, airline surveys confirm that actual inflight medical emergencies are rare. For example, DELAUNE *et al.* [3] reported the incidence of inflight medical emergencies for one particular North American airline as one incident per 44,212 passengers carried. Of a total of 2,279 medical incidents reported, 251 (11%) were due to some respiratory condition. Only on nine occasions was a flight diverted as a result of a patient suffering an adverse respiratory event. From these data, it can be seen that commercial air travel is a safe proposition for most patients with chronic respiratory disease.

High-altitude physiology

The sigmoid shape of the oxygen dissociation curve (figure 2) allows healthy individuals to ascend to moderate altitude (~2,400 metres or 8,000 feet) without any appreciable hypoxaemia. Beyond this altitude, the fall in alveolar P_{O_2} is steep and significant hypoxia will quickly develop. Patients with respiratory disease may have a rightward shift in the oxygen dissociation curve due to chronic respiratory acidosis, which will result in a decreased affinity of haemoglobin for oxygen, increasing the possibility for the development of desaturation.

The normal response to an increase in altitude is an increase in cardiac output and minute volume, which will compensate for the reduced P_{O_2} . Passengers with either cardiac or respiratory limitations may experience difficulty in increasing

either of these parameters sufficiently to compensate for the increased altitude, resulting in alveolar and tissue hypoxia. In respiratory patients, desaturation may occur if there is a blunted ventilatory response to hypoxia, either due to chemoreceptor insensitivity, airway obstruction limiting an increase in ventilation or increased shunting in the lungs.

Existing guidelines

The current authors are aware of two comprehensive guides, published by the British Thoracic Society (BTS) and the Aerospace Medical Association (AsMA) [4, 5]. These publications aim to provide guidance for physicians who are involved in assessing patients considering commercial air travel. Both publications stress that they are not intended to provide inflexible rules for air travel, but should be used as a guide for advising each patient on an individual basis. The AsMA guidelines do not focus exclusively on respiratory disease, but include other aspects of travel medicine as it relates to air travel.

Some patient care guidelines for specific conditions (notably chronic obstructive pulmonary disease (COPD)) include some advice on patients considering air travel [6, 7].

Respiratory contraindications to travelling by air

Absolute contraindications to flight include infectious tuberculosis and unresolved pneumothorax, the latter because air trapped in the pleural space will expand at altitude. Following

thoracic surgery, some airlines will accept patients after 2 weeks of recovery, but individual assessment is required.

Predicting risk of flight in individuals: not a simple task

Ideally, it would be possible to predict risk of symptoms and of actual medical harm to lung disease patients if they are planning to fly. However, given the rarity of inflight emergencies, coupled with the diagnostic uncertainty about the cause of reported inflight respiratory incidents, it is not currently possible to predict actual risk. Most studies have therefore focused, not unreasonably, on efforts to predict hypoxia as a surrogate for flight-associated risk.

The link between hypoxia and actual clinical risk remains incompletely understood. However, recent work has highlighted mechanisms whereby hypoxia predisposes to a variety of clinical risks. Hypoxia of the magnitude encountered in flight appears to be thrombogenic in those with other risk factors [8], but not in healthy young subjects with no additional risk factors [9]. Pulmonary hypertension is a well-recognised consequence of hypoxia, and some of the cellular mechanisms are now being elucidated [10]. Chronic hypoxia (even mild levels) has detectable cognitive effects on children [11] and acute hypoxia at altitude affects the mental functioning of adult aircrew [12], even at altitudes <10,000 feet [13]. Thus it is not unreasonable to use hypoxia as a surrogate for clinical risk even though the individual risk of adverse effects from hypoxia remains uncertain.

Hypoxic challenge: a suggested protocol

The protocol described below has been used by the authors for a number of years and appears to be well tolerated by all patients. An interpretation algorithm of the results of hypoxia inhalation test carried out using this protocol can be found in [20].

1. Prepare the patient's earlobe by rubbing with a topical vasodilator cream.
2. Attach a pulse oximeter ear probe to the patient, and record resting S_{a,O_2} and heart rate every 30 seconds for 5 minutes with the patient breathing room air.
3. Fit the patient with nasal cannulae, which are connected to a supply of 100% O_2 . The cannulae are used to deliver supplemental O_2 if required.
4. Place a 40% Venturi mask over the patient's face, ensuring a good fit. The Venturi mask is supplied with 100% nitrogen at a flow of 10 litres per minute, which lowers the patient's F_{i,O_2} to 15.1%.
5. Record S_{a,O_2} and heart rate every 30 seconds for 20 minutes.
6. Patients on long-term oxygen therapy can be assessed using the same protocol, but with the patient receiving supplemental oxygen by nasal cannulae at a flow of 2 litres per minute during HIT.



Methods of predicting hypoxia

In order to assess a patient's risk of hypoxia, a number of different assessment protocols have been developed.

The easiest method is for the patient to breathe a hypoxic gas mixture (commonly referred to as a hypoxic challenge; see box on page 143), which will replicate the PO_2 experienced in a pressurised commercial airliner. Ideally, the sea level F_{I,O_2} should be 15.1%, as this replicates the PO_2 at 2,438 metres (8,000 feet). Most planes actually have a simulated cabin altitude lower than this figure (~2,000 metres), but it is prudent to assess a patient for the "worst case" scenario. If cabin altitude rises above 2,438 metres, emergency oxygen delivery systems are designed to deploy automatically.

Hypoxic challenge can be carried out using a specially prepared gas mixture either from a gas cylinder or by utilising a Douglas bag, which acts as a reservoir for the hypoxic gas mixture that a patient breathes from using a non-rebreathing valve [14]. A simplification of the hypoxic inhalation challenge method was described by VOHRA and KLOCKE [15] who used a 40% venturi-type oxygen mask driven by 100% N_2 , which lowers the F_{I,O_2} to 15.1%. This method has the advantage that very little specialist equipment is required to perform the challenge, and this method is being used in a number of respiratory function laboratories within the UK.

Hypobaric chambers have been used for research purposes [16], but they are not common and the current authors are not aware of

any chambers that are used for the routine clinical assessment of patients considering commercial air travel. Hypobaric chambers have a theoretical advantage over a hypoxic inhalation challenge, because they will also reproduce the reduction in atmospheric pressure likely to be experienced during the flight, which may affect distribution of ventilation. Hypobaric chambers have the disadvantage of being bulky and cumbersome, and many patients find being in them a claustrophobic experience.

DILLARD *et al.* [17] compared the results of hypoxic inhalation challenges with hypobaric chamber exposure and found no significant differences between the methods, both in healthy individuals and in patients with stable COPD.

CRAMER *et al.* [18] used a modified body plethysmograph as an exposure chamber, a method that has the advantage of eliminating the need for the patient to breathe through a mask, which some patients find uncomfortable or inhibiting. The F_{I,O_2} within the exposure chamber needs to be closely monitored to ensure that it remains within the desired range.

GONG *et al.* [14] developed a hypoxia-altitude simulation test, which involved the patient breathing a series of hypoxic gas mixtures with arterial blood gas analysis after patients had reached a steady state at each level of hypoxia. From their data, a nomogram was produced, which allowed the estimation of P_{a,O_2} at altitude from sea-level P_{a,O_2} .

DILLARD *et al.* [16] studied patients with stable COPD in a hypobaric chamber and found that including forced expiratory volume in one second (FEV₁) as a percentage of the predicted value improved the accuracy of the prediction equation they had developed. The same author also carried out a meta-analysis of available published data in 1993, which confirmed the need to include measurements of FEV₁ and ground-level P_{a,O_2} in prediction equations when assessing patients with stable COPD [19].

Most of the studies described above have used arterial blood gas analysis to directly measure P_{a,O_2} and thus directly determine the degree of hypoxia. Although arterial blood gas analysis remains the gold standard against which all other methods must be assessed, it is an invasive procedure, which can be uncomfortable for the patient, and is prone to measurement error unless samples are analysed immediately after collection. Measurement of oxygen saturation using a pulse oximeter is a simple, non-invasive method of assessing a

Hypobaric chamber at the Colorado Center for Altitude Medicine and Physiology. Picture from CNN (www.cnn.com).



patient's oxygenation, which can be used as a surrogate for arterial blood gas measurement. It should be stressed that, in some patients, measurement of arterial blood gas tensions will still need to be carried out when the results of O_2 saturation are unclear. Several studies of assessment of fitness to fly have been published, which utilise only measurements of O_2 saturation rather than arterial blood gas analysis [15, 17, 20].

Although the prediction equations described above will predict hypoxia in groups of patients, their accuracy in individual patients has been questioned. For example, CHRISTENSEN *et al.* [21] found that, despite adequate sea-level PO_2 , significant hypoxia occurred in simulated flight in one out of three patients at rest and two out of three during light exercise. These and other data support the view that the most precise way to predict hypoxia in individuals is by hypoxic challenge of the individual patient.

Are long flights more hazardous? Most hypoxic challenges used for the clinical assessment of a patient's fitness to fly are of 20–30 minutes' duration. The assumption has always been made that this is a sufficient time for any physiological changes to have taken place. AKERØ *et al.* [22] investigated hypoxia in a group of patients with COPD during a 6-hour commercial flight, and found that there was an initial fall in Pa,O_2 once the flight had reached cruising altitude, which was maintained throughout the flight. FISCHER *et al.* [23] have studied hypoxia in patients with cystic fibrosis at low altitude (530 metres) and after 7 hours at high altitude (2,650 metres). In this study, patients were hypoxic at altitude, but there was no trend to worsening with time and few reported any additional symptoms. Once again, there were no robust individual predictors of hypoxia.

Most published data have been concerned with investigating the response of patients with COPD. This is perhaps understandable as COPD is probably the most common relevant condition amongst airline passengers, although research in other patient groups has been published as well. OADES *et al.* [24] have assessed flight fitness in children with cystic fibrosis and found the hypoxic challenge to be a good predictor of which patients were at risk of significant desaturation during flight. CHRISTENSEN *et al.* [25] have studied patients with restrictive lung disease, from a variety of different causes, in a hypobaric chamber and have demonstrated that these patients may become hypoxic when exposed to 2,438 metres of simulated altitude.

Oxygen supplementation during air travel

Most of the studies described above have not only used hypoxic challenge or hypobaric chamber exposure to investigate the development of hypoxia, but have also explored the use of oxygen supplementation to reverse the hypoxia induced. In most cases, the use of supplemental oxygen at low flow rates (2–4 litres per minute) has proved effective in restoring Pa,O_2 to ground-level values.

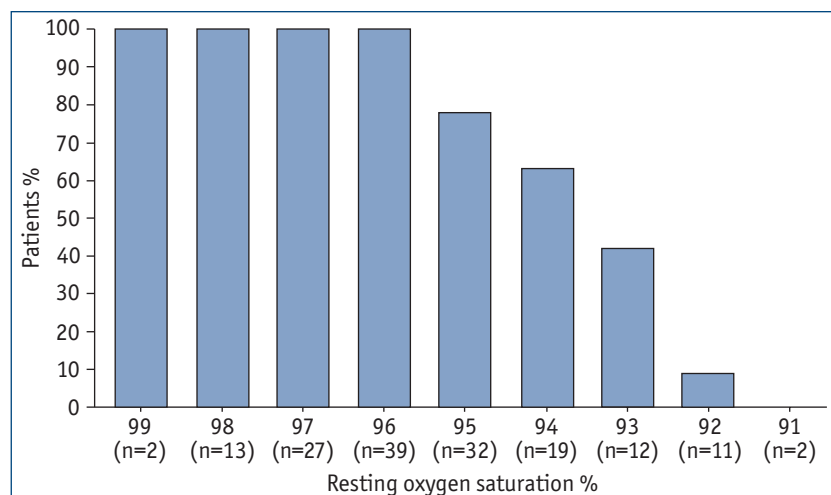
The BTS guidelines suggest that those with a resting sea-level O_2 saturation >95% will be able to fly without the risk of developing significant hypoxia. The BTS guidelines also recommend that anybody with a sea-level O_2 saturation <92% should not fly without supplemental O_2 . Patients already receiving supplemental O_2 (*i.e.* patients on long-term oxygen therapy) should have their usual flow rate increased by 2 litres per minute for the duration of the flight to compensate for the reduction in PO_2 .

In the current authors' experience of 157 patients undergoing assessment for flight fitness, it was found that those with a resting O_2 saturation >95% are unlikely to show significant desaturation (<90%) during hypoxic challenge (unpublished data, figure 3). These data come from patients with a number of different chronic respiratory conditions (mainly COPD, but including some with pulmonary fibrosis, cystic fibrosis and bronchiectasis) and reinforce the BTS criteria. For patients with a starting saturation of ≤95%, desaturation during hypoxic challenge cannot be predicted from the starting saturation nor from FEV₁ (either as an absolute value or as

Educational questions

1. How does the oxygen dissociation curve allow healthy individuals to ascend to a moderate altitude without developing significant hypoxaemia?
2. What F_{I,O_2} should be used for hypoxic challenge?
3. Are patients on long-term oxygen therapy able to travel on commercial flights?

Figure 3
The percentage of patients maintaining oxygen saturation >90% during hypoxic challenge, broken down by sea-level oxygen saturation.



Suggested further reading

Mortazavi A, Eisenberg MJ, Langleben D, Ernst P, Schiff RL. Altitude-related hypoxia: risk assessment and management for passengers on commercial aircraft. *Aviat Space Environ Med* 2003; 74: 922-927.

A good review of the problems associated with air travel.

Lumb AB. Nunn's Applied Respiratory Physiology. 5th Edn. Butterworth Heinemann, 2000. Chapter 16 of this excellent textbook gives a detailed description of high-altitude physiology.

a percentage of the patients' predicted value). For another example, see [20]. These results support the view that each patient should be assessed on an individual basis when they request an opinion on their fitness to fly.

The provision of supplemental oxygen on commercial flights is a difficult subject to tackle. International regulations prevent passengers from bringing pressurised cylinders into the cabin with them (empty cylinders may be accepted for transportation in the aircraft hold), which means that the oxygen-dependent patient will be reliant on the provision of oxygen by their chosen airline.

Oxygen can be supplied either in cylinders or by using the existing oxygen supply that is present in commercial aircraft [26]. The method of delivering supplemental oxygen to individual passengers will depend on the policy of each airline, but it is important to note that oxygen is unlikely to be available during take-off or landing for safety reasons.

Two portable oxygen concentrators weighing <5 kg are now approved by the Federal Aviation Administration for use during flight. Both can provide 1-5 litres per minute of 90% oxygen, but require external power for long flights. These devices offer the prospect of a convenient and inexhaustible supply of oxygen for patients but are not yet widely available.

Although nasal cannulae are preferred for oxygen delivery for patient comfort and convenience, some airlines still offer only facemasks and this will influence the actual concentration of oxygen received at a given flow rate. Oxygen flow rates of 2 and 4 litres per minute are usually available, patients requiring higher or lower flow rates (e.g. infants) will need to make special arrangements well in advance for appropriate provision.

Commercial airlines would, of course, prefer that the use of supplemental oxygen by a passenger is requested in advance so that appropriate arrangements can be made. STOLLER *et al.* [27] have investigated the arrangements that airlines have in place for the provision of supplemental oxygen. They found that 25 airlines out of 33 contacted (76%) were able to provide supplemental oxygen, with most carriers requiring some form of written notification from the passenger's clinician. Six of the carriers would provide supplemental oxygen free of charge and 18 would impose a charge, with a wide range of fees. Since this paper was published in 1999, it is possible that a number of airlines may have changed their policy on the provision of supplemental oxygen. Hence, patients should contact their prospective carrier before booking a flight

to ensure that their requirements can be met and to determine if a charge will be made for this service. The British Lung Foundation, a UK-based charity, keeps a list of up-to-date information on the provision of oxygen by the major airlines on their website (www.lung.org.uk).

Travel for technology-dependent patients

Patients with a need for either intermittent or permanent ventilation may also consult doctors about the possibility of air travel. The easiest group to manage are patients with obstructive sleep apnoea requiring treatment with continuous positive airway pressure (CPAP). No problems are anticipated on short-haul flights during the daytime, but difficulties may be encountered on long-haul flights where the patient may need to use CPAP. Patients will need to contact their chosen airline in advance to confirm that they will be able to use their device whilst on the plane, and may require a letter from their doctor outlining the need for the equipment in order to pass through airport security points.

For patients requiring other forms of non-invasive ventilation, a doctor's letter is normally required outlining the need for the equipment and should include a brief medical history and a note of the correct ventilator settings. Patients will need to contact their airline in advance to ensure that an electrical supply for the ventilator will be available and some form of battery back-up should also be taken in case of a failure in the electrical supply. Batteries should be sealed and of dry or gel cell type, as wet lead acid batteries are not permitted. They should be small enough to fit under the seat.

Patients requiring permanent ventilation will normally only be accepted for travel on a commercial flight if a medical escort accompanies them. Equipment should be taken so that the patient can be manually ventilated in the event of a power failure.

Conclusion

In response to the wishes of patients with lung disease undertaking air travel, doctors are faced with the complex challenge of assessing risk and the need for the provision of supplemental oxygen. Some progress has been made in the methods used to predict hypoxia, but the harder question of how to predict which patients will

develop symptoms or come to actual harm through hypoxia during flight requires further study. Fortunately for patients, it is clear from recent experience that air travel is safe for the

great majority of passengers and, with adequate planning for the provision of inflight oxygen, even more can now safely enjoy the benefits of air travel.

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Suggested answers

1. The sigmoid shape of the oxygen dissociation curve means that healthy individuals can increase ventilation sufficiently to maintain P_{O_2} near to sea level saturation.
2. Hypoxic challenge should use an F_{I,O_2} of 15.1%, as this equates to a simulated altitude of 2,438 metres. This is a slight underestimation of cabin altitude (normally ranging 1,900–2,200 metres), but equates to the highest cabin altitude that is likely to be encountered during flight.
3. Patients on long-term oxygen therapy are normally capable of commercial airline travel. According to both the BTS and AsMA guidelines, patients should have their normal oxygen flow increased by 2 litres per minute to compensate for the reduced F_{I,O_2} encountered at altitude. Patients should contact their chosen airline well in advance of travel in order to arrange for the supply of supplemental oxygen.