Flying with Respiratory Disease

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Key Words

Air travel, respiratory diseases · Fitness for flight assessment · Hypobaric hypoxia · Hypoxia altitude simulation test

Abstract

Patients with respiratory diseases may be at risk during flight because at cruising altitude an important hypobaric hypoxia may occur. The only absolute contraindications to flying in these patients are pneumothorax, bronchogenic cyst and severe pulmonary hypertension. In order to evaluate the risks related to air travel in patients with respiratory diseases, an evaluation of their fitness to fly, including the hypoxia altitude simulation test, is required. The fitness to fly evaluation can identify patients requiring supplemental oxygen during flight which is provided by most airlines when prescribed by the passenger's physician. This review deals with the cardiorespiratory effects of flight, the risks associated with respiratory diseases during air travel and the procedures to follow in order to assess fitness to fly in patients with respiratory disorders.

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Introduction

More than a billion people travel by air each year around the world [1, 2]. Among them, the number of people affected by respiratory diseases is increasing [3]. Air travel may be risky in these patients because an important hypobaric hypoxia may occur at cruising level [4, 5]. In fact, respiratory as well as gastrointestinal and cardiac disorders are among the most frequent disorders reported during air travel, after neurological problems [6]. The aim of this review is to deal with the cardiorespiratory effects of flight, the risks associated with respiratory diseases during air travel and the procedures to follow in order to assess fitness to fly in patients with respiratory disorders.

Effects of Altitude on Cardiopulmonary Function

The percentage of oxygen in the air is 21% at sea level and barometric pressure ranges around 760 mm Hg. In the troposphere, which is up to 18,000 m above sea level (*osl*), as altitude increases, the percent of oxygen does not vary, whereas barometric pressure decreases gradually until it is halved at approximately 6,000 m *osl*. As barometric pressure decreases, partial inspiratory oxygen pressure (PiO_2) decreases consequently as well. Changes

Fig. 1. Schematic representation of changes in minute ventilation with progressive hypoxia in healthy subjects. Modified from Zhang and Robbins [11]. PETO₂ = End-tidal partial oxygen pressure; VE = minute ventilation.

in PiO₂ and in partial arterial oxygen pressure (PaO₂) in relation to altitude are listed in table 1. Notably, ordinary flights reach a cruising altitude between 25,000 and 45,000 ft *osl* (between 7,000 and 14,000 m *osl*).

Cabin pressurization during flight maintains the barometric pressure inside the airplane clearly higher than outside, even though cruising altitude is high. International laws stipulate that cabin pressure must not surpass that measured at 8,000 ft *osl* [7]. In a study conducted on 240 flights, barometric pressures measured in the aircraft cabins were similar to those obtained between 5,000 and 8,000 ft *osl* with a mean value of approximately 6,214 ft *osl* [8]. Higher levels of pressurization decrease the energy available for other aircraft systems, reduce the operational lifetime of aluminium airframes, and necessitate increased structural weight, resulting in decreased fuel efficiency. In cabins pressurized at 8,000 ft *osl*, the barometric pressure decreases from 760 mm Hg at sea level to 565 mm Hg, hence, the PiO₂ also undergoes a decrease of 40 mm Hg in comparison to the values measured at sea level (table 1). Consequently, there is a decrease in PaO₂ and in the percentage of oxygen saturated haemoglobin (SaO₂).

Table 1. Decrease of oxygen tensions with altitude and barometric pressure

Altitude		BP mm Hg	PiO ₂ mm Hg	PaO ₂ mm Hg
ft <i>osl</i>	m <i>osl</i>			
0	0	760	150	100
1,000	305	733	144	95
2,000	610	707	139	90
3,000	915	681	133	85
4,000	1,220	656	128	80
5,000	1,526	632	123	75
6,000	1,831	609	118	70
7,000	2,136	587	113	66
8,000	2,441	565	109	62
9,000	2,746	543	104	58
10,000	3,050	523	100	54

BP = Barometric pressure; PiO₂ = inspiratory oxygen partial pressure; PaO₂ = arterial oxygen partial pressure.

1 ft = 0.3048 m.

In practice, breathing at 8,000 or at 5,000 ft *osl* corresponds to breathing at sea level a hypoxic mixture with an oxygen percentage of 15.1 or 17.1%, respectively. In healthy subjects exposed to hypoxic mixtures with percentages of oxygen between 15.1 and 17.1%, the PaO₂ may vary between 53 and 64 mm Hg, with a SaO₂ between 85 and 91%, in relationship to age, basal PaO₂ values and minute ventilation [1]. Moreover, it has been shown that in healthy subjects moving from sea level to an altitude of 8,000 ft *osl* leads to an average fall in the SaO₂ of 4.4% [9]. The authors also found that 7.4% of subjects met criteria for acute mountain sickness and that cumulative prevalence of altitude-related malaise, muscular discomfort and fatigue increased at 8,000 ft exposure [9]. In this study, the effect of aircraft-cabin altitude on passenger discomfort and oxygen saturation was not evaluated in respiratory patients. Obviously, subjects with impaired gas exchange and a reduced baseline PaO₂ value may be likely heading towards severe oxygen desaturation, when exposed to a hypoxic environment. As a general rule, chronic respiratory patients with PaO₂ values <67 mm Hg at sea level can have a PaO₂ <50 mm Hg during an ordinary air flight [10].

The decrease in PiO₂ and the consequent decrease in PaO₂ lead to the stimulation of chemoreceptors and to the increase in minute ventilation as a reflex. Changes in minute ventilation in relation to oxygen tension in healthy subjects are shown in figure 1, modified from Zhang and Robbins [11]. In healthy subjects, the increase in minute

ventilation due to high-altitude hypoxia is mainly due to an increase in the tidal volume rather than the respiratory rate, even though individual variability should be considered [12]. Healthy subjects are characterized by a wide ventilatory reserve; therefore, the increased minute ventilation is generally well tolerated. On the other hand, respiratory patients may not tolerate exposure to even slightly hypoxic mixtures. In these patients, even a moderate increase in ventilation could exhaust the ventilatory reserve, which may already be reduced at rest. In turn, this can aggravate the reduced exercise tolerance and cause an increase in exertion dyspnoea. Additionally, in these patients, increased respiratory work leads to an increase in the blood flow to the respiratory muscles, which is subtracted from the cardiac output addressed to the limb muscles, thereby further limiting exercise capacity.

Besides the increase in minute ventilation, hypobaric hypoxia induces other cardiovascular compensatory answers such as an increase in heart rate and cardiac output and a vasoconstriction of the pulmonary circulation. There is a wide individual variability in both ventilatory response and hypoxic vasoconstriction of pulmonary vessels [13]. In healthy subjects, the hypoxic vasoconstriction redistributes pulmonary blood flow, causing an increased perfusion in the upper part of the lungs. This may reduce the mismatch in the perfusion/ventilation ratio, which may maintain the PaO_2 at an acceptable level during ordinary air travel [12]. Respiratory patients may have significant alterations of the perfusion/ventilation ratio, with poorly ventilated areas and the presence of pulmonary hypertension. The hypoxia-induced pulmonary vasoconstriction may further worsen the increase of the dead space and the pulmonary hypertension, which may further deteriorate the PaO_2 .

It is of note that there is a difference between what levels of hypoxia man can tolerate acutely and what can be tolerated after acclimatization. The incidence and severity of high-altitude illness increase with the altitude and ascent rate, because each factor influences the magnitude of hypobaric hypoxic stress. The incidence rate of acute mountain sickness in the general tourist population at about 8,202 ft (2,500 m) is reported at 20–25%, increasing to 40–50% in trekkers and climbers near 13,123 ft (4,000 m) [14]. When an ascent to about 4,000 m occurs over a number of hours rather than days, the incidence of acute mountain sickness increases to over 90% [14].

The time from takeoff to cruise altitude averages 20 min, thus the hypobaric hypoxic stress is acute for passengers whilst flying. In chronic respiratory patients, acute hypoxic challenge seems to be well tolerated both

in laboratory and flight settings, even when the PaO_2 falls to 50 mm Hg. Patients with chronic airway obstruction exposed to acute hypoxic challenge reported mild symptoms such as shortness of breath, dizziness or light-headedness, which did not correlate with the level of hypoxemia [15]. Other studies in COPD patients reported dyspnoea as a unique symptom [16, 17] or no symptoms [10, 18, 19]. It is of note that all these studies were conducted in COPD patients with mild to moderate severity of disease. Accordingly, no conclusions can be drawn about patients with more severe disease. Progressive exposure to mild hypoxic challenge does not appear to be affected by preexisting chronic respiratory disease. In mild to moderate COPD patients, Graham and Houston [20] reported that resting PaO_2 dropped to 51.5 mm Hg within 3 h of ascent to 6,300 ft (1,920 m). In this study, patients complained of mild symptoms of fatigue and insomnia after ascent [20]. By contrast, long-term residence at altitude was associated with increased mortality and a higher incidence of cor pulmonale in COPD patients [21, 22].

Respiratory Diseases and Air Travel

Asthma

Asthma is the most frequent respiratory disease reported by air travellers [2]. There are no contraindications to air travel for patients with stable and well-controlled asthma. It is important that patients do not interrupt their usual treatment on the occasion of the trip and that they carry along a short-acting β_2 -agonist, i.e. salbutamol, and a cycle of oral steroids in case of an emergency during the trip [2]. Patients with unstable asthma or those who have had a recent exacerbation of the disease should be dissuaded from air travel, until the illness is completely stabilized and controlled [2].

COPD

Patients affected by COPD are particularly susceptible to develop respiratory failure during flights [18, 19, 23–25]. In the study by Christensen et al. [18], at 8,000 ft 53 and 33% of COPD patients experienced PaO_2 levels below 55 and 50 mm Hg, respectively. In COPD patients, the ability to increase minute ventilation in response to the hypoxia is limited and the presence of an alteration in the perfusion/ventilation ratio makes it often difficult for them to maintain adequate oxygenation during the flight. Moreover, in these patients even modest physical activity during the flight at high altitude can worsen their gas exchange [16, 18, 19]. In COPD patients, the risk of develop-

ing respiratory insufficiency during air travel is generally proportionate to the severity of the disease. High-risk patients are those who report dyspnoea on exertion or tend to present hypercapnia or with PaO₂ values <70 mm Hg or SaO₂ values <92% at sea level and patients with maximal voluntary ventilation <40 l/min [26]. On the whole, patients with clinically unstable COPD should be dissuaded from undertaking air travel. The recommendations of the British Thoracic Society [1] and the guidelines of the Aerospace Medical Association [2] also suggest that all COPD patients should undergo a clinical and functional evaluation of fitness for flight before departure.

Chronic hypoxia in COPD is known to be associated with cognitive impairment [27]. Less well understood is the effect of acute hypoxia on cognitive function in COPD patients. Interestingly, a recent study [28] suggested that hypoxic COPD patients receiving supplemental oxygen, when placed on room air, did not have a deterioration in cognitive function. In this study, the cognitive function was assessed by 20-min simulated driving performance and psychomotor reaction times. It is to ascertain whether or not COPD patients exposed to acute hypoxia during air travel may have any deterioration in cognitive function.

COPD patients are at a high risk for venous thromboembolism, because of a variety of factors including limited mobility, inflammation, and comorbidities, and venous thromboembolism events can play a role in acute exacerbation of COPD [29]. Additionally, there is a relationship between airplane travel and venous thromboembolism. A recent meta-analysis showed that air travel is associated with a threefold higher risk for venous thromboembolism, with a dose-response relationship of 18% higher risk for each 2-hour increase in travel duration [30]. It is still unknown whether air travel can increase the risk of venous thromboembolism events in COPD patients.

Pneumothorax

Spontaneous pneumothorax or pneumomediastinum must be excluded before air travel. Boyle's law states that the volume of a gas is inversely proportionate to its pressure in a closed space. Thus, in an airplane cabin, as the barometric pressure decreases when the airplane reaches cruising altitude, so the air volume in closed body cavities increases. It has been calculated that the air volume of a closed cavity, such as a pneumothorax, can increase approximately 30% when moving from sea level to 8,000 ft *asl* [1]. Therefore, the presence of a pneumothorax is an

absolute contraindication to air travel [1, 2], since the pressure in the pneumothorax may critically increase during the trip [31].

Airline companies suggest waiting 6 weeks after recovering from a pneumothorax, before flying. This rule is based on the probability of a relapse, which is high during the 6 weeks immediately following a first episode of pneumothorax. However, this rule is arbitrary since the kind of pneumothorax, the presence of an underlying pulmonary disease and the kind of treatment are not considered. In fact, if a pneumothorax is treated with thoracotomy and surgical or talc pleurodesis, the probability of a relapse is extremely low and 6 weeks after recovery there are no more restrictions on air travel [1]. On the contrary, in case of other therapeutic options or in subjects with a concomitant respiratory disease or in smokers, the risk of relapse is considerable for at least 1 year after the first episode. Hence, these patients are urged to consider alternative forms of transportation for at least 1 year [1].

Few data are available regarding the prevalence of pneumothorax associated with air travelling in patients with cystic or bullous lung diseases. Recently, in a retrospective study of 449 patients affected by interstitial lung diseases with high prevalence of spontaneous pneumothorax, Taveira-Da Silva et al. [32] showed that there was a relatively low risk of pneumothorax following air travel. No patient with pulmonary fibrosis or sarcoidosis presented with pneumothorax after air travel. In patients with lymphangioleiomyomatosis, the authors reported a 2.9% frequency of a new pneumothorax in those who travelled by airplane and a 1.3% frequency in those who travelled by ground. However, since a new pneumothorax was more likely in patients with large cysts and more severe disease, the authors concluded that in patients with lymphangioleiomyomatosis the prevalence of pneumothorax associated with air travel may be related to the high incidence of pneumothorax and not to travel itself.

Although patients with extensive bullous emphysema may head for a bullae expansion as a consequence of decrease of ambient pressure, the available literature suggests that the real risk of pneumothorax is negligible [33]. Yanda and Herschensohn [34] took 4 COPD patients with air trapping to a simulated altitude of 18,000 ft (5,488 m) and did not find evidence of worsening pulmonary function or pneumothorax. Moreover, Tomashefski et al. [35] brought 6 COPD patients with blebs and bullae to a simulated altitude of 18,000 ft at a rate of 1,000 ft/min and found no radiographic evidence of bullae distention or pneumothoraces. The reason for

the absence of pneumothoraces in patients with bullous disease has not been elucidated. Bullae may likely communicate with the airways to a greater extent than expected, allowing for pressure equalization.

Bronchogenic Cyst

Bronchogenic cysts are the result of an abnormal bronchial development from the primitive ventral foregut, and are located either within the lung or in the mediastinum. They are often asymptomatic, however emergencies may be caused by a sudden increase in the size and rupture of the cyst following a rapid decompression. Rupture of the cyst wall may result in entrainment of air into adjacent pulmonary vessels whose walls have also been damaged during the rupture of the cyst. As a consequence, air embolism into the systemic circulation and cerebral ischemia may occur.

A few cases of cerebral air embolism have been reported in airplane passengers after bronchogenic cyst rupture [36–39]. In these case reports, patients collapsed during decompression and suffered brain injury; most of the cases were fatal [36, 37, 39]. Subjects with bronchogenic cyst should be advised against activities leading to rapid changes in ambient pressure, such as flying, diving or high-altitude climbing or consider elective surgical treatment.

Restrictive Pulmonary Diseases

A case of acute cor pulmonale, after intercontinental air travel, has been described in a patient with congenital kyphoscoliosis [40]. The episode of pulmonary hypertension and right heart insufficiency was attributed to the prolonged exposure to a hypoxic environment. Subsequently, three studies have demonstrated that patients with a restrictive defect due exclusively to interstitial lung diseases [19, 41, 42] or to other causes such as kyphoscoliosis [41], can develop a significant hypoxemia when exposed to hypoxic mixtures, simulating an air flight. In these patients, PaO_2 values under hypoxic stimulus were positively correlated with PaO_2 values at rest and with values for lung diffusion capacity for carbon monoxide (DLCO) and were negatively correlated with the partial pressure of carbon dioxide in the arterial blood (PaCO_2) [41]. Moreover, the decreases in PaO_2 and SaO_2 worsened when patients performed modest physical activity during the test [19].

Both in patients with a restrictive defect and in patients with COPD, the ability to increase the minute ventilation in response to hypoxia is limited, and the presence of an altered perfusion/ventilation ratio can deter-

mine a reduction of PaO_2 and SaO_2 values during air travel, down to particularly critical levels. Therefore, it is advisable that these patients undergo a clinical and functional evaluation of fitness for flight in anticipation of air travel or that they consider alternative forms of transport in case of instability or exacerbation of the disease [26].

Cystic Fibrosis

Patients affected by cystic fibrosis with lung damage are susceptible to the negative effects of hypobaric hypoxia at high altitude [43, 44] and the induced oxygen desaturation is predicted by resting spirometry data [44]. Moreover, in these patients the environment of the aircraft cabin can represent a further risk factor, due to a significant decrease in cabin air humidity. Comfortable humidity conditions are considered to be 40–70% relative humidity at sea level. The guidelines for humidity in aircraft cabin are between 12 and 22% relative humidity [45]. Cabin air humidity depends upon aircraft type, cruising altitude, ventilation rate and the number of people on board [45]. In-flight measurements have shown relative cabin humidity dropping from at least 47 to 11% within 30 min of ascent [46]. Humidity and temperature of inspired air can remarkably alter the function of airway mucosa [47]. Accordingly, in subjects with cystic fibrosis or bronchiectasis the low humidity rate could increase the risk of bronchospasm and mucus production, leading to mucus plugs and probably atelectasis. For these patients a clinical and functional evaluation of fitness for flight is advisable as well, when programming air travel.

Obstructive Sleep Apnoea Syndrome

Periodic breathing and central apnoeas may occur in normal subjects during sleep at high altitude [48]. Therefore, in patients affected by obstructive sleep apnoea syndrome the respiratory pattern may deteriorate significantly while sleeping during a flight, as may occur on long-distance flights. However, systematic studies of the effects of air travel on these patients are lacking. The case of an obese patient with respiratory sleep disorders who developed heart and respiratory insufficiency after two air flights and staying at high altitude, has been described [49]. Therefore, patients with obstructive sleep apnoea syndrome treated with mechanic ventilation in CPAP mode should be cautious and avoid long-distance air trips. In case they undertake air travel, they should inform the airline company of their problem and provide themselves with a ventilator and avoid alcohol before and during the flight [1]. According to the general prescription [50], patients affected by obstructive sleep apnoea

Table 2. Prediction equations of PaO₂ at high altitude

Equation	Authors	Used for
PaO ₂ ALT, mm Hg = 22.8 – (2.74 · Alt, ft) + 0.68 · PaO ₂ SL, mm Hg	Gong et al. [15]	COPD patients
PaO ₂ CAB, mm Hg = 0.519 · PaO ₂ SL, mm Hg + 11.855 · FEV ₁ , l – 1.76	Dillard et al. [23]	COPD patients
PaO ₂ CAB, kPa = 0.74 + (0.39 · PaO ₂ SL, kPa + (0.033 · DLco, % pred)	Christensen et al. [41]	Patients with restrictive defect

PaO₂ ALT = Predicted oxygen partial pressure at a certain altitude; Alt = expected altitude; PaO₂ SL = oxygen partial pressure measured at sea level; PaO₂ CAB = oxygen partial pressure expected at 8,000 ft (cruise altitude); FEV₁ = forced expiratory volume at 1 s; DLco = lung diffusion capacity for carbon monoxide. Conversion factors: 1 kPa = 7.5 mm Hg; 1 ft = 0.3048 m.

syndrome should also avoid sedatives before and during the flight.

Pulmonary Hypertension

Patients with both primitive and secondary pulmonary hypertension are at high risk of complications during air travel. Considering the important individual variability to pulmonary vasoconstriction induced by hypoxia, even a light worsening of hypoxemia during flight can induce a significant increase in pressure in the pulmonary artery leading to a serious right cardiac failure [12, 26]. Although there are no studies which specifically deal with this problem, it is prudent to consider severe (NYHA class III and IV) pulmonary hypertension as a contraindication to air travel [26].

Assessment of Fitness for Flight

Walking Test

The so-called 50-metre walking test [1, 2, 51, 52] is a very simple test and it is widely used in the medical departments of the airline companies. It consists in walking 50 m. The incapability to cover the distance or the onset of severe dyspnoea indicates that a clinical and functional assessment should be performed and that the patient may require oxygen supplementation during the flight. As with other tests based on walking capacity, the 50-metre walking test is considered a measure of the cardiopulmonary reserve to exercise. In particular, it is thought that assessing the ability to increase minute ventilation and cardiac output when walking is a simple, practical and reliable way to calculate the cardiopulmonary reserve that respiratory patients utilize when they face the physiological requests determined by the hypobaric hypoxia during flight [1].

The 50-metre walking test has not yet been standardized. Moreover, the potential travellers do not even perform the test, instead they are simply asked if they are able to walk 50 m [25]. Unlike the 50-metre walking test, the 6-min walking test (6MWT) has been standardized and validated [53, 54]. The 6MWT is widely used in lung function laboratories and the British Thoracic Society [1] recommends its use to evaluate the fitness to fly. We have recently demonstrated that in chronic respiratory patients, affected by COPD or interstitial lung disease, the desaturation observed during the hypoxia altitude simulation test (HAST) is strictly correlated and predicted by the 6MWT-induced desaturation [42].

Hypoxemia Prediction Equations

Equations have been published which predict the PaO₂ values at altitudes other than sea level. Gong et al. [15] provided the first equation in 1984, which refers to COPD patients (table 2). Subsequently, Dillard et al. [23] and Christensen et al. [41] proposed prediction equations for patients with COPD or restrictive pulmonary diseases (table 2).

The equations have been obtained by submitting the subjects to hypobaric rooms or to HASTs and provide PaO₂ and SaO₂ values with 90% confidence intervals equal to ± 7.5 mm Hg and to ± 2 –4%, respectively [1]. The equations are therefore sufficiently reliable to identify subjects who are not at risk of critical hypoxemia at high altitude (SaO₂ at sea level >95%) and those who are probably at risk (SaO₂ at sea level <92%). The subjects with SaO₂ values between 92 and 95% need to perform the HAST, given the margin of error of these equations [1].

Hypoxia Altitude Simulation Test

The ideal test which exposes the subject to hypoxia in a hypobaric room requires complex and expensive equip-

Fig. 2. Equipment necessary to perform the HAST.

ment which is not always available. The most frequently used test is the so-called HAST, proposed by Gong et al. [15]. This test consists in exposing the subject to a hypoxic mixture. In practice, the subject breathes a mixture of 15% oxygen and 85% nitrogen, from a Douglas bag, through a mouthpiece or a facial mask, connected to a two-way valve. Usually, during the test a pulse oximeter registers oxygen saturation (SpO_2) or, less commonly, the PaO_2 is measured; an ECG is also continuously monitored in order to find possible rhythm alterations. The equipment required to perform the test is illustrated in figure 2. The exposure to the hypoxic mixture lasts 20 min or until the pulse oximeter data reaches a stable condition. A subject is considered to be at risk of air travel-induced hypoxemia, a condition which would require oxygen supplementation, if a value of $SpO_2 < 85\%$ or of $PaO_2 < 50$ mm Hg is recorded during the test [1]. These cut-off values have been selected arbitrarily, even if they are considered to be quite reasonable by the experts [1]. In case a significant hypoxemia occurs, the test must be repeated with oxygen supplementation through nasal

cannula to titrate the necessary flow during the flight, starting with a flow of 2 l/min [26, 55]. In case of borderline results it can be useful to perform a second test while the patient performs modest exercise, such as walking on a treadmill [55].

It has been demonstrated that the HAST induces a decrease of the PaO_2 comparable to the one obtained after exposure in a hypobaric room, with an equivalent barometric pressure of 8,000 ft *asl*, both in COPD patients [51, 52] and in healthy subjects [56, 57]. This test is considered a reliable tool in predicting the hypoxemia measured during air travel both in healthy subjects [58] and in COPD patients [59]. Moreover, in patients affected by COPD, cystic fibrosis or interstitial lung disease the need of oxygen therapy during flight may be importantly overestimated if the hypoxemia-predicted equations are considered instead of the HAST [60]. Therefore, the HAST is considered the gold standard in the assessment of fitness for flight [1, 24, 55, 61, 62], even if at the moment it is not commonly used in clinical practice [63].

Fig. 3. Algorithm for the assessment of fitness to fly in respiratory patients.

Cramer et al. [64] proposed an interesting alternative to the HAST, as described by Gong et al. [15], which uses the plethysmographic box as a hermetically sealed environment, where the addition of nitrogen leads to a hypoxic condition. The test requires that the examined subject remains exposed to a hypoxic environment for 10 min.

Conclusions

In patients with respiratory disease there are no absolute contraindications to air travel, apart from pneumothorax, bronchogenic cyst and severe pulmonary hypertension. In respiratory patients, it is recommended to perform a clinical and functional assessment of fitness to fly in order to reduce the risk and identify patients which require oxygen supplementation during the flight. The

algorithm described in figure 3 is based on the current international literature [1, 2, 26, 55] and summarizes the approach to the respiratory patient before air travel.

Generally, the patients cannot carry onboard the aircraft any personal device for oxygen therapy, however most airline companies provide oxygen supplementation during the flight, after medical prescription. Obviously, this service has to be arranged in advance with the airline companies, which usually ask for at least a 48-hour notice before the departure, and it is generally free. However, the airline companies do not provide oxygen supplementation during the stay in the airports. Recently, in the USA the Federal Aviation Administration (FAA) has established that the airline companies can embark passengers who require personal portable oxygen concentrators approved by the FAA [26], in order to encourage travelling in respiratory patients.

References

- 1 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 Aerospace Medical Association, Air Transport Medicine Committee: Medical guidelines for air travel, ed 2. *Aviat Space Environ Med* 2003;74:A1–A19.
- 3 Gendreau MA, DeJohn C: Responding to medical events during commercial airline flights. *N Engl J Med* 2002;346:1067–1073.
- 4 Morgan MD: Air travel and respiratory disease. *BMJ* 2002;325:1186–1187.
- 5 DeHart RL: Health issue of air travel. *Annu Rev Public Health* 2003;24:133–151.

- 6 Gerencher K: Airlines get guidance on in-flight medical assistance from ground. April 27, 2007. Available at: www.marketwatch.com (accessed February 10, 2008).
- 7 Code of Federal Regulations: Title 14, Part 25.841. Washington, Government Printing Office, 1986.
- 8 Cottrell JJ: Altitude exposures during aircraft flight. *Chest* 1988;93:81–84.
- 9 Muhm JM, Rock PB, McMullin DL, Jones SP, Lu IL, Eilers KD, Space DR, McMullen A: Effect of aircraft-cabin altitude on passenger discomfort. *N Engl J Med* 2007;357:18–27.
- 10 Schwartz JS, Bencowitz HZ, Moser KM: Air travel hypoxemia with chronic obstructive pulmonary disease. *Ann Intern Med* 1984;100:473–477.
- 11 Zhang S, Robbins PA: Methodological and physiological variability within the ventilatory response to hypoxia in humans. *J Appl Physiol* 2000;88:1924–1932.
- 12 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.
- 13 Luks AM, Swenson ER: Travel to high altitude with pre-existing lung disease. *Eur Respir J* 2007;29:770–792.
- 14 Gallagher SA, Hackett PH: High-altitude illness. *Emerg Med Clin North Am* 2004;22:329–355.
- 15 Gong H, Tashkin DP, Lee EY, Simkons MS: Hypoxia-altitude simulation test. Evaluation of patients with chronic airway obstruction. *Am Rev Respir Dis* 1984;130:980–986.
- 16 Akero A, Christensen CC, Edvardsen A, Skjonsberg OH: Hypoxaemia in chronic obstructive pulmonary disease patients during a commercial flight. *Eur Respir J* 2005;25:725–730.
- 17 Dillard TA, Beninati WA, Berg BW: Air travel in patients with chronic obstructive pulmonary disease. *Arch Intern Med* 1991;151:1793–1795.
- 18 Christensen CC, Ryg M, Refvem OK, Skjonsberg OH: Development of severe hypoxaemia in chronic obstructive pulmonary disease patients at 2,438 m (8,000 ft) altitude. *Eur Respir J* 2000;15:635–639.
- 19 Seccombe LM, Kelly PT, Wong CK, Rogers PG, Lim S, Peters MJ: Effect of simulated commercial flight on oxygenation in patients with interstitial lung disease and chronic obstructive pulmonary disease. *Thorax* 2004;59:966–970.
- 20 Graham WG, Houston CS: Short-term adaptation to moderate altitude. Patients with chronic obstructive pulmonary disease. *JAMA* 1978;240:1491–1494.
- 21 Moore LG, Rohr AL, Maisenbach JK, Reeves JT: Emphysema mortality is increased in Colorado residents at high altitude. *Am Rev Respir Dis* 1982;126:225–228.
- 22 Cote TR, Stroup DF, Dwyer DM, Horan JM, Peterson DE: Chronic obstructive pulmonary disease mortality. A role for altitude. *Chest* 1993;103:1194–1197.
- 23 Dillard TA, Berg BW, Rajagopal KR, Dooley JW, Mehm WJ: Hypoxemia during air travel in patients with chronic obstructive pulmonary disease. *Ann Intern Med* 1989;111:362–367.
- 24 Shesser R: Medical aspects of commercial air travel. *Am J Emerg Med* 1989;7:216–226.
- 25 Johnson AO: Chronic obstructive pulmonary disease • 11: fitness to fly with COPD. *Thorax* 2003;58:729–732.
- 26 Mohr LC: Hypoxia during air travel in adults with pulmonary disease. *Am J Med Sci* 2008;335:71–79.
- 27 Incalzi RA, Gemma A, Marra C, Muzzolon R, Capparella O, Carbonin P: Chronic obstructive pulmonary disease. An original model of cognitive decline. *Am Rev Respir Dis* 1993;148:418–424.
- 28 Pretto JJ, McDonald CF: Acute oxygen therapy does not improve cognitive and driving performance in hypoxaemic COPD. *Respirology* 2008;13:1039–1044.
- 29 Rizkallah H, Man SF, Sin DD: Prevalence of pulmonary embolism in acute exacerbations of COPD: a systematic review and meta-analysis. *Chest* 2009;135:786–793.
- 30 Chandra D, Parisini E, Mozaffarian D: Meta-analysis: travel and risk for thromboembolism. *Ann Intern Med* 2009;151:180–190.
- 31 Fuchs HS: Idiopathic spontaneous pneumothorax and flying. With particular reference to the etiological role of decreased atmospheric pressure, pressure breathing, increased gravitational forces, and anti-G-suit action. *Aerosp Med* 1967;38:1283–1285.
- 32 Taveira-Da Silva AM, Burstein D, Hathaway OM, Fontana JR, Gochuico BR, Avila NA, Moss J: Pneumothorax after air travel in lymphangioleiomyomatosis, idiopathic pulmonary fibrosis, and sarcoidosis. *Chest* 2009;136:665–670.
- 33 Parker GW, Stonehill RB: Further considerations of the roentgenologic evaluation of flying personnel at simulated altitude. *Aeromed Acta* 1961;32:501–504.
- 34 Yanda RL, Herschensohn HL: Changes in lung volumes of emphysema patients upon short exposures to simulated altitude of 18,000 feet. *Aerosp Med* 1964;35:1201–1203.
- 35 Tomashefski JF, Feeley DR, Shillito FH: Effects of altitude on emphysematous blebs and bullae. *Aerosp Med* 1966;37:1158–1162.
- 36 Zaugg M, Kaplan V, Widmer U, Baumann PC, Russi EW: Fatal air embolism in an airplane passenger with a giant intrapulmonary bronchogenic cyst. *Am J Respir Crit Care Med* 1998;157:1686–1689.
- 37 Almeida FA, Desouza BX, Meyer T, Gregory S, Greenspon L: Intrapulmonary bronchogenic cyst and cerebral gas embolism in an aircraft flight passenger. *Chest* 2006;130:575–577.
- 38 Belcher E, Lawson MH, Nicholson AG, Davison A, Goldstraw P: Congenital cystic adenomatoid malformation presenting as in-flight systemic air embolisation. *Eur Respir J* 2007;30:801–804.
- 39 Edwardson M, Wurth D, Lacy JM, Fink J, Becker K: Cerebral air embolism resulting in fatal stroke in an airplane passenger with a pulmonary bronchogenic cyst. *Neurocrit Care* 2009;10:218–221.
- 40 Noble JS, Davidson JA: Cor pulmonale presenting in a patient with congenital kyphoscoliosis following intercontinental air travel. *Anaesthesia* 1999;54:361–363.
- 41 Christensen CC, Ryg MS, Refvem OK, Skjonsberg OH: Effect of hypobaric hypoxia on blood gases in patients with restrictive lung disease. *Eur Respir J* 2002;20:300–305.
- 42 Chetta A, Castagnetti C, Aiello M, Sergio F, Fabiano N, Tzani P, Marangio E, Olivieri D: Walking capacity and fitness to fly in patients with chronic respiratory disease. *Aviat Space Environ Med* 2007;78:789–792.
- 43 Oades PJ, Buchdahl RM, Bush A: Prediction of hypoxaemia at high altitude in children with cystic fibrosis. *BMJ* 1994;308:15–18.
- 44 Buchdahl RM, Babiker A, Bush A, Cramer D: Predicting hypoxaemia during flights in children with cystic fibrosis. *Thorax* 2001;56:877–879.
- 45 Hinninghofen H, Enck P: Passenger well-being in airplanes. *Auton Neurosci* 2006;129:80–85.
- 46 Eng W, Harada L, Jagerman L: The wearing of hydrophilic contact lenses aboard a commercial jet aircraft. *Aviat Space Environ Med* 1982;53:235–238.
- 47 Williams R, Rankin N, Smith T, Galler D, Seakins P: Relationship between the humidity and temperature of inspired gas and the function of the airway mucosa. *Crit Care Med* 1996;24:1920–1929.
- 48 Weil JV: Sleep at high altitudes; in Kryger MH, Roth T, Dement WC (eds): *Principles and Practice of Sleep Medicine*, ed 2. London, Saunders, 1989, pp 224–230.
- 49 Toff NJ: Hazards of air travel for the obese: Miss Pickwick and the Boeing 747. *J R Coll Physicians Lond* 1993;27:375–376.
- 50 Prisant LM, Dillard TA, Blanchard AR: Obstructive sleep apnea syndrome. *J Clin Hypertens* 2006;8:746–750.
- 51 Mills FJ, Harding RM: Fitness to travel by air. I. Physiological considerations. *BMJ* 1983;286:1269–1271.
- 52 Lyznicki JM, Williams MA, Deitchman SD, Howe JP 3rd: Council on Scientific Affairs, American Medical Association. Medical oxygen and air travel. *Aviat Space Environ Med* 2000;71:827–831.
- 53 American Thoracic Society Statement: Guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002;166:111–117.

- 54 Chetta A, Pisi G, Aiello M, Tzani P, Olivieri D: The walking capacity assessment in the respiratory patient. *Respiration* 2009;77: 361–367.
- 55 Dine CJ, Kreider ME: Hypoxia altitude simulation test. *Chest* 2008;133:1002–1005.
- 56 Dillard TA, Moores LK, Bilello KL, Phillips YY: The pre-flight evaluation. A comparison of the hypoxia inhalation test with hypobaric exposure. *Chest* 1995;107:352–357.
- 57 Naughton MT, Rochford PD, Pretto JJ, Pierce RJ, Cain NF, Irving LB: Is normobaric simulation of hypobaric hypoxia accurate in chronic airflow limitation? *Am J Respir Crit Care Med* 1995;152:1956–1960.
- 58 Kelly PT, Swanney MP, Frampton C, Secombe LM, Peters MJ, Beckert LE: Normobaric hypoxia inhalation test versus response to airline flight in healthy passengers. *Aviat Space Environ Med* 2006;77:1143–1147.
- 59 Kelly PT, Swanney MP, Secombe LM, Frampton C, Peters MJ, Beckert L: Air travel hypoxemia versus the hypoxia inhalation test in passengers with COPD. *Chest* 2008; 133:920–926.
- 60 Martin SE, Bradley JM, Buick JB, Bradbury I, Elborn JS: Flight assessment in patients with respiratory disease: hypoxic challenge testing vs. predictive equations. *QJM* 2007; 100:361–367.
- 61 Dillard TA, Bansal AK: Commentary: pulse oximetry during airline travel. *Aviat Space Environ Med* 2007;78:143–144.
- 62 Mohr LC: The hypoxia altitude simulation test: an increasingly performed test for the evaluation of patients prior to air travel. *Chest* 2008;133:839–842.
- 63 Coker RK, Partridge MR: Assessing the risk of hypoxia in flight: the need for more rational guidelines. *Eur Respir J* 2000;15:128–130.
- 64 Cramer D, Ward S, Geddes D: Assessment of oxygen supplementation during air travel. *Thorax* 1996;51:202–203.