Review Article

Fitness to Fly in Patients with Lung Disease
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Abstract

Background:
these cases may go unrecognized, and even among those who are known to be hypoxemic, some do not use supplemental oxygen. During air travel in a hypobaric hypoxic environment, compensatory pulmonary mechanisms may be inadequate in patients with lung disease despite normal sea-level oxygen requirements. In addition, compensatory cardiovascular mechanisms may be less effective in some patients who are unable to increase cardiac output. Air travel also presents an increased risk of venous thromboembolism. Each year worldwide, more than 2.75 billion passengers travel by air, 736 million in the United States alone¹. One study reports that over an approximately 3-year period, there were 11,920 In-flight medical emergency calls made by airlines to a medical communications Center; this was estimated to represent almost 1 medical emergency for every 600 flights². Respiratory symptoms accounted for 12% of this in-air emergencies. The development of respiratory symptoms during flight was associated with an increased risk of hospitalization after air travel (odds ratio [OR], 2.13), second only to possible stroke (OR, 3.36). A previous study reported an average of 72 in-flight deaths per year³, from a population representing approximately 50–60% of the total estimated number of worldwide passengers for that period. Of those deaths, 69% occurred in passengers with no known previous medical illness³. As such, a thorough assessment of patients with chronic lung disease and cardiac disease who are contemplating air travel should be performed.

Key words: Air travel complications; Hypoxia; Hypoxic challenge testing; Chronic lung disease

ALTITUDE AND HYPOXIA:
Commercial aircraft are pressurized during flight because passengers could not survive exposure to the low atmospheric pressure at the usual cruising altitude (10 000–13 500 m). For reasons of aircraft weight and fuel economy, it is impractical to maintain cabin pressure at sea level pressure but international regulations do not allow cabin pressure to fall below 74 kPa (the equivalent of atmospheric pressure at 2450 m (8000 ft)) except in emergencies. Cruising altitudes of commercial aircraft typically range from approximately 30,000 to 40,000 feet, but at times may reach altitudes of 60,000 feet⁴. However, the cabin altitude pressure equivalent is maintained at approximately 5,000–8,000 feet with cabin pressurization of approximately 520–570 mm Hg⁵. Pressurization of the aircraft cabin is achieved using exterior air that is compressed and mixed with filtered and recirculated cabin air. Up to 50% of the cabin air is not recirculated and is expelled, to be replaced with exterior air, with 20–30 complete air exchanges occurring per hour⁶. As the aircraft ascends, the decreasing cabin air pressure results in gas expansion, which can cause a “popping” sensation in the ears of passengers due to air escaping from the middle ear and the sinuses.

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EFFECTS ON PASSENGERS
In healthy passengers the hypobaric hypoxia of the aircraft cabin will result in only mild hypoxaemia; arterial oxygen tension (PaO₂) falls to about 8 kPa but the shape of the oxyhaemoglobin dissociation curve prevents any fall in oxygen saturation (SaO₂) below about 92%. However, some patients with chronic lung disease may not tolerate this mild degree of hypoxia and may become significantly hypoxaemic. Schwartz et al 7 studied 13 subjects with COPD exposed to an altitude of 2250 m whom arterial blood gas tensions were measured at sea level and at altitude. Mean PaO₂ fell from 9.0 kPa at sea level to 5.9 kPa, a level which most physicians would regard as undesirable although none of these subjects developed any symptoms. PaCO₂ fell from 5.4 kPa to 4.8 kPa. Individuals may be at increased risk of significant hypoxemia, even at altitudes within the normal operating range of the aircraft. Compensatory mechanisms in patients with pulmonary or cardiac disease may also be less effective, placing these patients at further risk of significant hypoxemia. In expiratory flow–limited patients, for example, an increase in minute ventilation may result in hyperinflation, and further exacerbate respiratory discomfort. In patients with restrictive lung disease (e.g., interstitial lung disease, kyphoscoliosis, and obesity), although an increase in minute ventilation may occur, this may also be limited as preexisting impairment of gas exchange may attenuate other compensatory mechanisms. Other conditions contributing to high-altitude hypoxemia and in-flight complications include obstructive sleep apnea, pulmonary hypertension, pneumothorax, and cystic fibrosis. In many of these conditions, even at rest, hypoxemia can result in respiratory symptoms, and critical end-organ dysfunction such as arrhythmia or syncope can occur. Furthermore, patients with cardiovascular disease may be unable to adequately increase cardiac output, which could further worsen hypoxemia and exacerbate end-organ hypoxia.

Assessment of Fitness to Fly
To date, assessment of fitness to fly in patients with pulmonary disease has largely been studied in patients with COPD, although patients with restrictive lung disease and cystic fibrosis have also been studied. The Centers for Disease Control and Prevention (CDC, Atlanta, GA) estimates that approximately 15 million people have a diagnosis of COPD in the United States alone, while globally, although precise data from outside Europe and North America are lacking. The prevalence of COPD within other populations may be even greater. However, within the COPD Gene cohort, for example, 7.7% of those with an FEV₁ less than 80% had resting hypoxemia (oxygen saturation as determined by pulse oximetry [SpO₂], 88%)13. Although this may be an overestimation, as many of these patients were recruited from the Denver study site (at an altitude of 5,280 ft)13, this study highlights the frequency of hypoxemia even at a modest altitude in a significant number of patients with mild COPD. Extrapolating these data to the CDC estimates, up to 288,750 patients with COPD in the United States may therefore be at increased risk of hypoxemia and in-flight complications. Even among those patients who are receiving supplemental oxygen, a significant number may be traveling with insufficient oxygen supplementation.

Preflight Screening:
History, Physical Examination, and Spirometry
As part of a preflight screening evaluation, medical history and physical examination should be performed. Co morbid conditions such as cardiovascular disease, cerebrovascular disease, other neurological disease, and anemia should be evaluated. Any previous flying history should therefore be explored, as this may yield important information as to symptoms or complications that may have occurred during or after air travel. In the absence of any contraindication, spirometry should be performed on patients with a history of acute or chronic lung disease or with symptoms suggestive of lung disease. Contraindications would include pneumothorax, massive hemoptysis, recent chest surgery, and tuberculosis. Pulse oximetry at rest should also be done, with arterial blood gas confirmation in addition to this if hypercapnia is suspected.
as a less reliable predictor of in-flight SpO2 (8). In the 2002 BTS guidelines, an SpO2 of 92–95% without risk factors or SpO2 greater than 95% was used to indicate that no further testing was warranted (14). Among 100 patients with COPD who were stratified on the basis of SpO2 thresholds from the 2002 BTS algorithm and then underwent pulse oximetry and normobaric hypoxic challenge testing, the sensitivity and specificity for these SpO2 thresholds were only 59 and 72%, respectively (15). Thus, a lower-normal SpO2 even without risk factors is no longer considered a sufficiently robust test by which to screen patients, and additional hypoxic challenge testing is recommended.

Normobaric hypoxic challenge testing is now the preferred method to assess risk of hypoxemia at altitude. It is becoming more widely available and correlates well with other means of assessment, and with air travel itself (16). It uses a decreased (normobaric) fraction of inspired oxygen (FIO2) to simulate the hypoxic conditions at altitude. Data from normobaric hypoxic challenge testing have been compared with actual in-flight data collated in the same individual patients with COPD (46). SpO2 decreased from 95% at sea level to 86% in-flight, which compared well with hypoxic challenge testing with a sea-level SpO2 of 96%, decreasing to 84% at simulated altitude. Hypoxic challenge testing correlated strongly with actual flight data (r = 0.84).

**Interpretation of Hypoxic Challenge Testing Results**

The BTS guidelines (2011) outline thresholds for prescribing supplemental oxygen for air travel. After the administration of a 15% fractional concentration of inspired oxygen for 20 minutes, a PaO2 greater than 50 mm Hg or a SpO2 of at least 85% could suggest that in-flight oxygen is not required. However, pulse oximeter or arterial blood gas values less than that require oxygen supplementation via nasal cannulas (17).

**Supplementary Oxygen**

After a positive hypoxic challenge test, titration of supplemental oxygen can be performed. However, this presents a number of challenges with normobaric testing. Compared with titration during hypobaric testing, there is an underestimation of supplemental oxygen requirements (18), which may reflect poorer accuracy in terms of the actual FIO2 administered during a normobaric test with supplemental oxygen. In addition, during a normobaric or hypobaric hypoxic challenge test, pulsed dose oxygen may result in a lower PaO2 than continuous flow oxygen (18).

Continuous flow oxygen may be delivered at rates of up to 6 L/minute depending on the portable concentrator used. Pulsed dose flow rates also vary depending on the portable oxygen concentrator used. For example, on a pulsed dose setting of 1, oxygen delivery may range from 9 to 16 ml/breath depending on the device, with rates of up to 192 ml/breath possible at higher settings on some devices. For this reason, if pulsed dosing rather than continuous flow is planned, it may be prudent to instruct the patient to bring his or her own particular portable oxygen concentrator to the hypoxic challenge test to assist in titration of oxygen using this specific setting.

**Arrangement of Supplemental Oxygen for Travel**

Since 2009, after the U.S. Department of Transport ruling “Nondiscrimination on the Basis of Disability in Air Travel,” all airlines traveling to and from the United States are required by law to permit passengers to carry their portable oxygen concentrators (POCs), provided they have been approved for use by the Federal Aviation Administration. The policy of individual airlines toward the specific concentrators that are permissible for use aboard the aircraft is, in turn, largely guided by the list of devices approved by the FAA. The list of portable concentrators currently approved for use by the FAA, and also those currently approved by the 10 largest airlines worldwide, based on annual passenger numbers, and information currently available from the relevant airline’s website.

Patients face a number of additional challenges with respect to arranging the use of portable concentrators. Patients typically must provide at least 48 hours’ notice of intent to travel, together with a physician statement for how and when the POC is to be used during flight. Many airlines do not guarantee a power outlet for use of the POC and instead recommend ensuring the machine is fully charged and those additional charged batteries are also carried. Finally, some airlines require patients to assume all risk by signing a waiver of liability before air travel. It is important therefore that physicians be well informed on such challenges faced by patients, to provide them with the best information available.
One speculates that a physician–patient discussion akin to informed consent might be appropriate under certain circumstances given the waiver of liability that the patient is expected to sign.

Respiratory Disease–Specific Recommendations

Patients with Interstitial or Restrictive Lung Diseases
• In patients with co morbidity, including PH and/ or cardiovascular disease, attention should also be paid to the impact of air travel on these conditions.
• Physicians may wish to consider HCT in those whom SpO2 falls to <95% on exercise, and/or in those in whom either Transfer Factor Carbon Monoxide (TLCO) ≤50% or PaO2 ≤9.42 kPa (if available).
• Patients with TLCO <50% of predicted or PaO2 ≤ 9.42 kPa are likely to need in-flight oxygen. If there are no concerns about hypercapnia it may be reasonable to recommend 2 L/min without recourse to HCT. In those in whom there are concerns about CO2 retention, titration HCT is advised to determine the oxygen flow rate.(BTS-2022)
• The patient should also bring a course of oral corticosteroids and antibiotics in the event of an acute exacerbation of their disease 14,17.

Patients with Neuromuscular Disease or Chest Wall Disease

All patients should undergo assessment as described previously as well as hypoxic challenge testing.

Patients with Cystic Lung Disease

In addition to hyperinflation within communicating airways, at an altitude of 8,000 feet, Boyle’s law predicts there will be a 38% increase in the size of closed air filled pockets within the body17. This gas expansion may be associated with an increased risk of pneumothorax in patients with bullous or cystic lung disease17.

However, from published data in patients with cystic lung disease, the incidence of pneumothorax related to air travel appears to be low19. Nonetheless, in patients with chronic lung disease who are already at risk of hypoxemia, the development of a pneumothorax in-flight could be devastating. A previous history of pneumothorax may be more relevant in patients with lung disease, as rapid changes in barometric pressure may precipitate recurrence.

Air Travel in Patients after Pneumothorax

Patients with a closed pneumothorax generally should not fly, with rare exceptions. It is currently recommended that patients not travel after a pneumothorax unless drainage has been performed and, in the case of recurrent pneumothoraces, when definitive surgical treatment has occurred17,20. Otherwise, provided chest imaging has determined the pneumothorax has resolved, patients should be safe to travel provided a further 7 days has elapsed17. However, it should be noted that patients with preexisting lung disease have a high risk of recurrence and that this risk remains increased for up to 1 year after a pneumothorax.

Air Travel after Chest Surgery

• The opinion of the surgeon or interventionalist should be obtained before the patient travels by air.
  Patients, professionals and their carers should be aware that this may result in a delay of 4 weeks for non-essential air travel and 2 weeks for essential air travel.
• Careful clinical assessment of the patient is required. This should include consideration of their baseline status including co morbidities, SpO2, postprocedure complications such as infection and/or pain, flight duration and destination.

Other interventional procedures

• The opinion of the interventionalist should be obtained before the patient travels by air.
• Careful clinical assessment of the patient is required. This should include consideration of baseline status including co-morbidities, SpO2, post procedure complications such as infection or pain, flight duration and destination.
• Patients with no pneumothorax seen on the post procedure chest X-ray should wait for 1week before air travel.
• Patients with a pneumothorax seen on the post-procedure chest X-ray should wait for one week after resolution on chest X-ray before air travel.

Similar to the advice pertaining to pneumothorax, in those who have undergone chest surgery, radiographic demonstration of lung reexpansion and resolution of pneumothorax after chest drain removal should be performed17. Signs or symptoms concerning for pneumothorax or postsurgical complications should prompt further investigation before air travel17.
**Bronchoscopic procedures**

- The opinion of the interventionalist should be obtained before the patient travels by air.
- Patients should be clinically stable before they travel.
- After interventional bronchoscopy including Transbronchial Needle Aspiration (TBNA), Transbronchial Lung Biopsy (TBB), Endobronchial Ultrasound Bronchoscopy (EBUS) and endobronchial valve insertion, those with no pneumothorax seen on the post procedure chest X-ray should wait for 1 week before air travel.
- After interventional bronchoscopy including TBNA, TBB and EBUS, those with a pneumothorax seen on the post-procedure chest X-ray should wait for 1 week after resolution on chest X-ray before air travel.

**Asthma**

- The patient’s condition should be optimised before travel, with attention paid to inhaler technique and smoking cessation referral as required.
- All medications and spacer devices should be carried in hand luggage to mitigate the risk of lost or missing hold baggage.
- Emergency medications, including salbutamol inhalers and spacers, must be immediately accessible.\(^{21}\)
- Individuals prescribed epinephrine auto-injectors should have them readily available.
- For acute exacerbations on board, the passenger’s own bronchodilator inhaler should be given, with a spacer if needed.
- The passenger should alert the cabin crew if symptoms do not respond rapidly to use of the inhaler, or if they recur after a short interval.
- If the passenger does not have their own inhaler with them, or if it is inaccessible, the airline may carry an inhaler in the emergency medical kit. Spacers are not commonly available.
- Those with severe asthma should consult their respiratory specialist beforehand and consider taking an emergency supply of oral corticosteroid in their hand luggage in addition to their usual medication.
- Most passengers with asthma will have relatively mild disease and do not require HCT. HCT should however be considered for those with severe asthma, regardless of baseline sea level oxygen saturation.
- Food allergy affects up to 8.5% of children and adults with asthma and asthma is a risk factor for severe or fatal anaphylaxis.\(^{22}\) Appropriate precautions for those affected include wiping tray tables and hands, informing the airline beforehand and the cabin crew of allergies, and not eating during flights or bringing known ‘safe’ foods from home.\(^{22}\)

**Chronic obstructive pulmonary disease**

- The patient’s condition should be optimized before travel, with attention paid to inhaler technique and smoking cessation referral where appropriate.
- All medications and spacer devices should be carried in hand luggage to mitigate the risk of missing hold baggage.
- Emergency medications, including salbutamol inhalers and spacers, must be immediately accessible.
- For acute exacerbations on board, the passenger’s own bronchodilator inhaler should be given, with a spacer if appropriate.
- Passengers with severe COPD are advised to carry a copy of their COPD management plan and/or relevant clinic letters. This information can be held securely as scanned copies on their mobile phone A history of previous pneumothorax or bullous lung disease necessitates assessment by a respiratory specialist to determine the potential risk of complications from reduced cabin pressure.
- Patients with COPD are at greater risk of VTE as a direct consequence of the underlying condition, as well as after an exacerbation. They should be advised accordingly, especially if planning longer flights when the risk is further enhance (23).
- Patients requiring long-term oxygen therapy should also plan for oxygen supplementation at their destination.
- Wherever possible, those who have had a recent exacerbation of their condition should not fly until their condition is stable and use of reliever therapy has returned to their usual baseline. If their condition deteriorates while overseas, medical advice should be sought before undertaking the return flight.

**Cystic fibrosis**

- All medications and spacer devices should be carried in hand luggage to mitigate the risk of missing hold baggage.
- Patients with CF under the age of 6 are likely to be well enough to fly at the pediatrician’s discretion.
- In those with CF who are old enough for spirometry and whose FEV1 is <50% predicted, HCT is recommended. If SpO2 falls below the 90% cut-off, as outlined above, in-flight oxygen is advised.
In children with chronic lung disease able to perform spirometry whose FEV1 is consistently <50% predicted, HCT should be considered. This includes children with CF and non-CF bronchiectasis. Children with chronic lung disease who are too young to reliably perform spirometry should have a clinical assessment of assess disease severity and their likely tolerance of hypoxia. For children with CF disease is rarely severe enough to severely compromise lung function at this age.

Non-CF bronchiectasis
- Regular airway clearance is essential for those dealing with overproduction of mucus.
- Advice from a respiratory physiotherapist on adapting airway clearance techniques should be sought for long-haul flights.
- Portable nebulizers and positive expiratory pressure (PEP) devices may be considered, but use of these devices in-flight must be approved by the airline before travel.
- Upper respiratory infection including otitis media and sinusitis
- In passengers who develop sinus barotrauma after flying, it may be helpful to consider topical and oral decongestants as well as appropriate analgesia. Prolonged use of decongestants is not advised owing to the risk of rebound congestion on withdrawal (25).
- If there is an allergic component, intranasal steroids used for a week prior to travel, and/or oral corticosteroids may be considered.
- Symptoms and signs of barotrauma should have resolved before flying again. This usually takes between 1 and 6 weeks.
- After an episode of acute otitis media, patients are usually advised not to fly for 2 weeks.

Viral infections
- Patients with highly contagious infections including measles, chickenpox, mumps, SARS, Middle East respiratory syndrome (MERS) or COVID-19 should not be allowed to travel until they are considered non-infectious.
- Passengers should familiarise themselves with current national and international regulations regarding air travel, which should always be observed.

Tuberculosis
- Smear positive patients must not fly until they have provided two smear negative. Those starting treatment for pulmonary tuberculosis (TB), where not all the information is yet available, should not travel by air for the first 2 weeks.
- For those who are smear negative and have a fully sensitive organism, treatment would be expected to render them non-infectious after 2 weeks.
- For patients with multidrug resistant/extensive drug resistant (MDR/XDR) TB, travel is prohibited until two negative culture samples have been produced and there is clinical evidence of improvement on treatment.
- Extrapulmonary TB does not usually warrant additional precautions before air travel.

Pneumonia
- All but essential travel should be postponed for 7 days in those who have reduced baseline sea level SpO2 (<94%).
- Obstructive Sleep Apnoea (OSAS) and Obesity Hypoventilation Syndrome (OHS)
- Daytime flights are advised wherever possible.
- The patient should be advised to carry their continuous positive airway pressure (CPAP) device as hand luggage, and a hospital letter to advise that the patient uses CPAP.
- Careful planning and preparation are required, and use of the patient’s own CPAP device is advised.
- Alcohol and sedatives should be avoided in the 12 hours before, and during, airline travel.
- Patients should use their CPAP device on board if they are travelling overnight, and avoid sleeping during daytime flights.
- Consideration should be given to device settings and whether adjustment is required for operation at altitude.
- Airline approval for carriage and use of device, including battery specification, must be gained before travel.
- Consideration should be given to the whole journey. If driving is required the following day, an overnight stay at destination may be advisable. Patients are advised to refrain from driving if tired and sleepy.

Prevention of VTE during air travel
- Limit the risk of dehydration with adequate fluid intake.
- Avoid alcohol.
- Keep mobile, if possible, by walking around or doing seat-based exercises once an hour.
- Consider graduated compression stockings (class 1 with 15–30 mm Hg).
• Low molecular weight heparin (LMWH) or a Direct Acting Oral Anticoagulant (DOAC) are advised for both outward and return long haul flights (long haul defined as flights of 6–12 hours) in high-risk patients including those with a history of VTE; local policy should be followed regarding liaison with primary care and/or haematology services to teach the patient how to administer the injection and dispose safely of the equipment. There is no formally recommended dose, but enoxaparin at a dose of 40 mg or weight based 1 mg/kg injected once 4–5 hours before the flight has been suggested.

• The prophylactic doses of the DOAC may also be used.

• All patients with a recent (<6 weeks) history of VTE, especially any who presented with significant right ventricular strain and decompensation should be reassessed before air travel.(28)

Air travel after VTE

• Air travel should be delayed for 2 weeks after a diagnosis of DVT or pulmonary embolism (PE).

Pulmonary hypertension

• Those in New York Heart Association (NYHA) WHO functional class 3 or 4 are usually advised to have in-flight oxygen. If there is no evidence of hypercapnia it seems reasonable to suggest 2 L/min by nasal cannulae. If there are concerns about hypercapnia, HCT should be considered if available(29)

• Those eligible for LTOT (sea level PaO2 <8 kPa at rest on air) should have in flight oxygen at double the flow rate recommended at sea level, provided there is no evidence of hypercapnia.

Continuous positive airway pressure

The 2011 BTS guidance (17) reported that a fixed-pressureCPAP machine without pressure compensation, set to deliver a pressure of 12 cm H2O at sea level, may deliver only 9 cm H2O at 8000 ft. The machine may therefore require adjustment to ensure a safe level of treatment throughout the flight.

The following are generally considered contraindications to air travel:

• Untreated respiratory failure.

• Untreated pneumothorax.

• Active infection representing a risk to others for example, TB, SARS, MERS, COVID-19.

• Bronchogenic cysts. Cerebral air embolism, in some cases fatal, has been reported in aircraft passengers after rupture of a bronchogenic cyst.30

• Patients with severe hypoxaemia requiring >4 L/min in-flight oxygen were previously advised against air travel, because 4 L/min was the maximum fixed flow rate routinely available on commercial aircraft. With the availability of flight approved POCs delivering a range of continuous and intermittent flow rates, this cut-off no longer applies. In-flight oxygen delivery is more varied, and maximum flow rate is determined by the equipment available. Pulse-dose delivery systems can however complicate determination of the flow delivered and may not be well tolerated. The effects of mouth-breathing, speech, snoring and/or sleeping should be considered. High-flow nasal oxygen (HFNO) cannot be delivered on board commercial aircraft.

In-flight oxygen may be contraindicated in adults and children with a history of type 2 respiratory failure.(31)Hypoxic challenge with arterial carbon dioxide tension (PaCO2) measurement was advised for this group in 1996 but there has been little research since. This document, therefore, follows the 2015 BTS Guideline for Home Oxygen Use in Adults (32) when making recommendations for managing patients with previously documented hypercapnia.

Clinical practice points

• All patients should undergo careful initial evaluation with history and physical examination by a clinician who is competent. The history should include:

• Review of symptoms, baseline exercise capacity, recent exacerbation history, treatments and previous experience of air travel.

• Consideration of the logistics of the intended journey, to include (if known):

• Number and duration of flights, including whether daytime or overnight.

• Location of stop-over(s) and destination: these determine air quality, altitude and available medical facilities.

• Time away from home.

• Return journey.

• Further assessment by a Respiratory Specialist is advised for those in whom screening raises concerns, and hypoxic challenge testing may be advised.

Additional Considerations When Evaluating Patients for Air Travel

It is important to highlight the following points in assessing
1. Even at 35,000 feet, different types of commercial aircraft will have widely differing cabin altitudes, ranging from an equivalent of approximately 5,400 to 8,000 feet. In addition, commercial aircraft may also vary their cruising altitude a number of times during the flight, which in turn can alter cabin pressure.

2. Respiratory symptoms may occur even despite having a preflight assessment. One study found 18% of patients with COPD developed respiratory symptoms despite having a preflight evaluation.

3. Flight duration is another important factor to consider. Longer flight durations are associated with increased symptoms, particularly when lasting over 3 hours.

4. The levels of activity of the patient during the flight should also be considered. Patients with COPD, restrictive lung disease, and cystic fibrosis demonstrate significant worsening of hypoxemia at simulated altitude with a workload equivalent to patients for air travel: that of walking around the aircraft cabin.

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References:


