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RECOMMENDATIONS OF THE SPANISH SOCIETY OF PULMONOLOGY AND THORACIC SURGERY (SEPAR)

Air Travel and Respiratory Disease

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Rationale

In recent years there has been a progressive rise in the number of people who travel by air. According to data from the International Civil Aviation Organization, 1647 million people traveled by air in 2000 and, despite problems related to security restrictions and severe acute respiratory syndrome (SARS), it is anticipated that the number of passengers will increase annually by 4.4% until 2015.[1] More than 2 million air traffic operations were handled during 2005 in airports managed by the Spanish aviation authority (Aeropuertos Españoles y Navegación Aérea, AENA), representing travel by 179 million passengers.[2] Those figures correspond to a 29% increase in the number of passengers since 2000, with an annual increase of 6%.[2]

In addition, advances in the monitoring and treatment of many chronic respiratory diseases have allowed changes in the lifestyle of patients. Thus, patients are now able to consider leisure and professional activities that were not possible some years ago.

Although adverse respiratory events as a result of air travel are not common, this form of transport does present potential risks.[3] Data from 120 airline companies forming part of the International Air Transport Association (IATA) show that between 1977 and 1984 there were 577 deaths in flight, corresponding to 0.31 deaths per million passengers or 25.1 deaths per million takeoffs.[4] Respiratory complications represented the third highest known cause of death (7%) after cardiac causes (65%) and deaths due to cancer (9%).[4] In addition, it was noteworthy that while there was prior knowledge of the presence of heart disease in only 22% of deaths due to cardiac events, there was prior knowledge in 46% of those due to respiratory disease, suggesting that there are problems in the assessment of patients prior to the flight or in their in-flight care.[4]

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Aside from fatal events, respiratory symptoms are responsible for a good proportion of the emergencies that occur on board aircraft. Analysis of all 2322 cases in which the first-aid kit was used on commercial aircraft belonging to the IATA between August 1984 and July 1988 showed that chest pain and dyspnea were 2 of the 3 most common causes, along with loss of consciousness.[5,6] Likewise, 62% of passengers who required medical assistance had a known medical condition associated with the episode that occurred on board the aircraft,[6] further indicating the importance of careful assessment prior to flight. Along similar lines, a service offering the assistance of experts by radio during in-flight emergencies received 8450 calls in 2001, of which 11% corresponded to respiratory problems.[7,8] Thus, respiratory problems may represent up to 11% of in-flight emergencies.

In response to this situation, various guidelines and recommendations have been prepared by scientific societies or the airline companies themselves.[7,9-17] However, little scientific information supported by a high level of evidence is available in this field, meaning that the majority of the recommendations are based solely upon expert consensus. In fact, in recent years, conflicting results have been reported using the regimens recommended in previous guidelines. Furthermore, there is a local problem generated by differences in the legislation and the wide range of criteria, resources, and attitudes of the different airline companies.

The aim of these guidelines is to define assessment protocols for patients with chronic respiratory disease intending to travel by plane that are adapted to the situation in Spain and the most recent available data. In addition, the guidelines aim to establish specific recommendations for the most common respiratory diseases.

Environmental Conditions on Commercial Flights

Extensive information is available on respiratory physiology during air travel in both healthy individuals and patients.[9,14-16,18-21] Some of those detailed reviews of

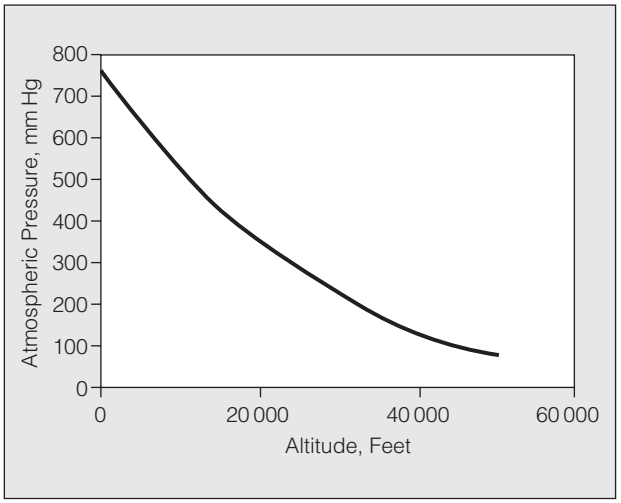

Figure 1. Relationship between altitude and atmospheric pressure

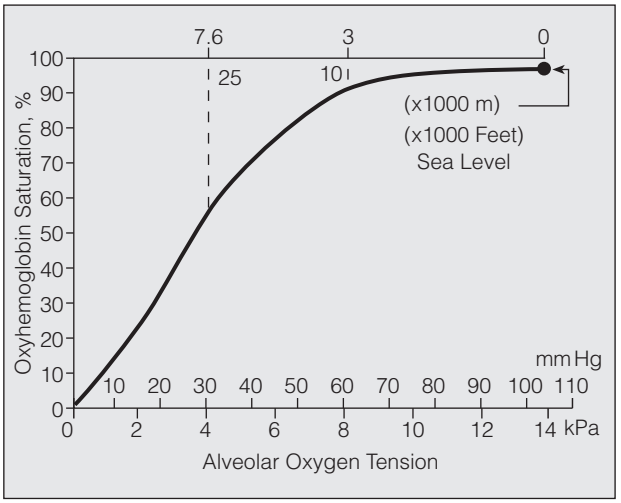

Figure 2. Effect of altitude on alveolar oxygen tension and oxyhemoglobin saturation.

environmental conditions and their control are published by the airlines themselves and are available on the Internet.[22,23]

It is worth remembering that the atmosphere surrounding the Earth's crust is made up of different layers or strata: the troposphere, the stratosphere, the mesosphere, the thermosphere, and the exosphere. The layer closest to the Earth is the troposphere, which extends from sea level to 9144 m (30 000 feet) at the poles and to 18 288 m (60 000 feet) at the equator (Appendix 1). Today's commercial aircraft fly within this zone. Atmospheric pressure depends on the column of air above the measurement point; consequently, the higher the altitude, the lower the pressure. Since the reduction in atmospheric pressure is logarithmic (Figure 1), at lower levels small changes in altitude produce substantial changes in pressure. Thus, at 6096 m (20 000 feet) the atmospheric pressure is less than half that at sea level.

The composition of the troposphere is constant and contains approximately 78% nitrogen and 21% oxygen. Since the partial pressure of a gas is a function of its concentration and the total pressure, oxygen tension is directly dependent upon altitude and drops exponentially as altitude increases (Figure 2). This hypoxia is the cause of the limitations and risks faced by mountaineers and also of acclimatization problems in high-altitude populations. In addition, adaptation to this type of environment is affected by the amount of exercise that is performed.

In terms of the physiologic response of the human body, the atmosphere can be divided into 3 zones: the physiologic zone, the physiologically deficient zone, and the zone equivalent to space. The physiologic zone is where the human body is well adapted and where the oxygen level is sufficient to maintain normal processes. This zone extends from sea level to an altitude of 3000 m. Nevertheless, rapid changes in altitude within this zone can cause minor problems due to the expansion of gases trapped within the body. The physiologically deficient zone extends from 3000 to 15 200 m. In that zone, the reduction in barometric pressure causes a critical environmental hypoxia, necessitating the use of supplementary oxygen at higher altitudes. From a physiologic point of view, space begins at an altitude of 15 000 m. In this zone, the low ambient pressure means that humans are unable to survive even with supplementary oxygen and they require pressurized suits. Above 19 355 m the barometric pressure is lower than the vapor pressure of water at 37ºC and body fluids evaporate.

Commercial aircraft generally fly at an altitude of around 11 000 to 12 200 m (36 000-40 000 feet).[1,24,25] If the internal pressure of the aircraft were to be directly dependent upon the external atmospheric pressure the environment would be incompatible with life. Consequently, aircraft must be pressurized, that is, have elevated pressure compared with that of the external environment. To achieve this, they take ambient air and compress it. Since the gas heats up in this process, it must subsequently be cooled.[26] The pressure is controlled according to the quantity of air injected and through the use of escape valves set to the desired pressure. To support the pressure difference, the structure of the aircraft must be reinforced and that increases its weight. As a result of both the increased weight and the additional energy required to compress the air, cabin pressurization increases aircraft fuel consumption and thereby decreases their independence. The pressurization system used by commercial aircraft is known as isobaric.[27] Initially, as the aircraft climbs in altitude, it maintains the same ambient pressure as its environment, and then, from a certain altitude, it maintains a constant (isobaric) pressure, irrespective of changes in altitude. Many military aircraft employ a different system known as differential-isobaric pressurization, which imposes fewer structural requirements and thereby saves weight.[27]

Due to the technical limitations mentioned and the cost, aircraft pressure is not maintained at that of sea level but rather at an intermediate pressure; that pressure depends on the type of aircraft but is usually approximately equivalent to that of an altitude of 2400 m.[1,24,25,28-33] At that

altitude, the atmospheric oxygen tension is equivalent to breathing 15.1% oxygen at sea level. Although international legislation establishes that minimum cabin pressure should correspond to an altitude of 2438 m (8000 feet),[34] the pressure does not remain constant throughout a flight. In a large series of measurements performed during commercial flights, it was determined that the conditions within aircraft cabins usually correspond to an altitude of 1800 to 2400 m (6000-8000 feet) above sea level.[29,30,35] Survival in the event of a sudden reduction in cabin pressure necessitates the use of oxygen masks (obligatory equipment on commercial flights). It is also important to note that at an altitude of 10 600 m a person will lose consciousness in 30 to 45 seconds.

The degree of pressurization also depends on the type of plane. The old Concorde was pressurized at a comfortable level corresponding to an altitude of 1829 m (6000 feet). The current tendency for new models of aircraft, whether manufactured by Boeing or Airbus, is to pressurize at this more comfortable, safer pressure.[36] However, the new Airbus 380 is expected to carry around 600 passengers with a cabin pressure equivalent to an altitude of more then 2438 m (8000 feet) for up to 20 hours.[24]

In addition to the difficulties caused by changes in barometric pressure, the external environment presents additional problems for commercial flights. The concentration of ozone, which is very low at sea level, increases with altitude and peaks in the stratosphere. Ozone, which is important to filter ultraviolet radiation, is toxic to the respiratory system, even at concentrations below 1 part per million (ppm), which can be reached at some common flight altitudes. To manage this problem, planes have catalytic ozone converters installed to reduce the concentration of the gas. The regulations of the Federal Aviation Administration establish a maximum mean concentration of 0.1 ppm and a maximum peak concentration of 0.25 ppm.[1]

The temperature falls by approximately 2ºC for every 300 m increase in altitude, necessitating warming of the air inside the cabin.[27] This air normally has a low humidity (5%), which can cause problems for some individuals. Most commercial aircraft recirculate approximately 50% of the air to improve humidity and energy efficiency. The air must be filtered to retain particles smaller than 0.3 μm in diameter using high-efficiency particulate air (HEPA) filters similar to those used in hospital operating theaters. In addition to particles in suspension, this system is considered effective for the retention of bacteria, fungi, and even viruses released during speech, coughing, or sneezing (Figure 3). The air is renewed 15 to 20 times per hour, although this may vary according to the model and the zone of the plane. The cabin ventilation system generates transverse airflow and is able to renew the air more effectively than in buildings with air conditioning. Complex electronic systems with sensors located throughout the cabin control the temperature and regulate valves in order to maintain a temperature that is as homogeneous as possible. Finally, it is worth mentioning that the carbon dioxide content of this filtered and conditioned air is usually very low (1000 ppm).

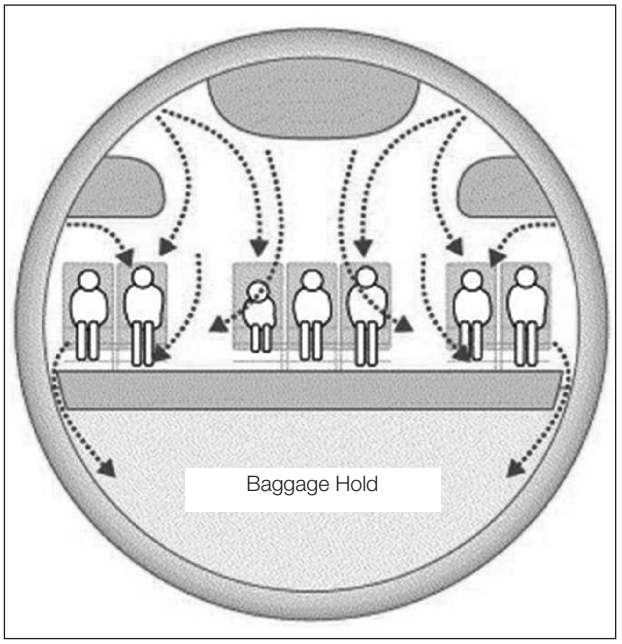

Figure 3. Schematic of the cabin ventilation system in a commercial aircraft.

Physiologic Effects of Commercial Flights

Hypobaric Hypoxia

The partial pressure of inspired oxygen (PiO_2) is a function of the atmospheric pressure and the vapor pressure of water.[37] As the vapor pressure of water at the same body temperature remains stable with altitude, PiO_2 will decrease with altitude (hypobaric hypoxia).[38]

Breathing ambient air at 2438 m (8000 feet) is equivalent to breathing 15.1% oxygen at sea level, meaning PiO_2 falls from 150 mm Hg at sea level to 107 mm Hg at 2438 m.[38,39] In healthy subjects, this can represent a reduction in PaO_2 from 98 to 55 mm Hg,[35,39,40] which is usually well tolerated and does not produce symptoms. However, in patients with chronic respiratory diseases and some degree of baseline hypoxemia, the reduction in PiO_2 during the flight can cause more marked reductions in oxyhemoglobin saturation.[41-43]

Acute exposure to a hypobaric environment triggers hyperventilation, which is essentially induced by stimulation of peripheral chemoreceptors and is usually mediated by an increase in tidal volume.[38] It also generates an increase in cardiac output to compensate for the residual systemic hypoxia. This increase is mainly mediated by tachycardia[31] and is usually proportional to the drop in oxygen saturation.[44] The increased pulmonary perfusion caused by the rise in cardiac output is associated with hypoxic vasoconstriction of the pulmonary artery and increased systolic pulmonary pressure.[45] As a consequence of the increase in pulmonary vascular resistance, there is a redistribution of pulmonary blood flow and an increase in perfusion of certain areas of the lungs compared with the situation at sea level.[45]

Altitude is also associated with limitation of oxygen diffusion from the atmosphere into the pulmonary capillaries as a consequence of the interaction of various factors.[46] Both the reduced PiO_2 and the reduction in affinity of hemoglobin for oxygen in conditions of low PaO_2 lead to a more marked drop in the oxygen content of the pulmonary capillaries than at sea level. Finally, the transit time of blood through the pulmonary capillaries is shortened due to the tachycardia caused by the altitude and this limits the time available to establish an adequate oxygen equilibrium.[47] The net result is an increase in the alveolar–arterial oxygen difference.[42,48,49]

In addition, the oxyhemoglobin saturation is significantly reduced during physical exercise in a hypobaric environment.[50] Exercise at high altitudes also increases the alveolar–arterial oxygen difference in subjects who normally reside at sea level, while it does not affect those native to high altitudes.[51] Studies performed using the multiple inert gas elimination technique have shown that hypobaric hypoxia is associated with a greater heterogeneity in the ventilation–perfusion ratio and a limitation of diffusion that together worsen hypoxemia as exercise intensity increases.[52] Limited diffusion secondary to reduced PiO_2 appears to exert the greatest influence on blood gas alterations during exercise in a hypobaric environment.[51] Additionally, the interstitial edema caused by extravasation of fluids into the extravascular space appears to potentiate the ventilation–perfusion imbalance.

The changes described have few consequences in healthy subjects, who might only note a slight increase in tidal volume and heart rate. However, hypobaric hypoxia represents a risk for some patients with chronic respiratory disease, in whom it can aggravate preexisting hypoxemia and favor the development of cardiovascular complications. In fact, it is recognized that hypoxia reduces the ischemic threshold in men with exercise-induced ischemic heart disease as well as favoring some atrial arrhythmias and being associated with ectopic ventricular beats as a result of increased sympathetic activity.[38]

Expansion of Trapped Gases

With increasing altitude, barometric pressure is reduced and gases expand if they are trapped in the body, unable to escape.[9] This phenomenon is explained by Boyle's law, which establishes that the volume of a gas is inversely proportional to the pressure:

$$P \times V = P' \times V'$$

Although the expansion of the trapped gases is limited, it occurs rapidly, and in healthy subjects can cause discomfort in organs such as the ear, paranasal sinuses, teeth, and gastrointestinal system. In patients with respiratory diseases, and even in young, apparently healthy individuals with small apical bullae, the phenomenon can generate more serious problems.[53-56]

Ears. Air trapping can occur in the ears due to partial or complete obstruction of the Eustachian tube, which normally equalizes air in the middle ear with the outside. This can occur both during ascent and descent and is also one of the main problems associated with underwater diving. It can be the result of a chronic intrinsic or acquired obstruction or an acute process caused by an infection or allergic reaction. With increasing altitude, the air expands and exerts a pressure on the tympanic membrane, which expands outward. When a pressure increase of 12 to 15 mm Hg is reached, a small bubble of air is expelled into the nostrils and is sometimes accompanied by a small noise. Upon descent, the reverse situation occurs. The external pressure increases and the tympanic membrane is pressed inwards. It is much more likely for obstruction to occur in this situation since the Eustachian tube functions less effectively in this direction. This air block can produce sounds, nausea, and pain in the ears that is sometimes very intense, particularly if the finally phase of the descent occurs very rapidly. A useful maneuver to prevent this obstruction involves repeated swallowing of saliva. Consumption of liquids or food can also help. If the condition persists, gentle Valsalva maneuvers are recommended.[38]

Paranasal sinuses. The paranasal sinuses can present similar problems to those experienced in the ear. In this case, the obstruction may be due to chronic lesions such as polyps or to acute problems such as mucus generated in response to infections or allergies. In general, the problem appears during descent and in 70% of cases affects the frontal sinuses. The pain can become very intense.[53-56]

Barodontalgia. Some subjects may experience dental pain, mainly during ascent to between 1500 and 3000 m. It was initially thought that small pockets of air trapped during dental restoration or other manipulations were the cause of the problem. However, it has not been possible to confirm that hypothesis, despite the association of symptoms with different types of dental complaints.

Gastrointestinal tract. The gastrointestinal tract usually contains some quantity of gas, and consequently, gastrointestinal discomfort is common during air travel. Nevertheless, such problems are of minor significance at the cabin pressures reached during commercial air travel.

Lungs. In healthy subjects without structural abnormalities there are usually no problems of this type associated with the lungs since pulmonary gas pressure is rapidly equalized with the ambient pressure. Nevertheless, some young, apparently healthy subjects may have apical bullae, which can burst during ascent and cause a pneumothorax. In some cases this may be a tension pneumothorax and become serious.

Given that the gas in the body cavities is saturated with water vapor, the expansion caused by increased altitude is greater than that calculated according to Boyle's law. Given that body temperature remains constant, in the case of bullae or closed pneumothorax

the increase in volume can be calculated with the following formula:

$$\Delta\text{Volume} = \frac{\text{Pressure of gas at sea level–water vapor pressure}}{\text{Pressure of gas at 2438 m–water vapor pressure}}$$

If it is assumed that the gas pressure is 760 mm Hg at sea level and 365 mm Hg at an altitude of 2438 m, and that water vapor pressure remains constant at 47 mm Hg, it can be estimated that the volume of trapped gas will increase by 37.6% during ascent.

The problem is much more severe in patients with chronic obstructive pulmonary disease (COPD), since those patients usually have regions of emphysema that are poorly connected with the exterior or separated from it and can cause rupture and pneumothorax, in addition to the problems generated by hypoxia.

Airline companies usually recommend that individuals do not fly within 6 weeks of the resolution of a spontaneous pneumothorax, although the scientific evidence supporting this recommendation is very limited.[38] If the pneumothorax has been treated surgically or by pleurodesis with talc it is highly unlikely that there will be a relapse during flight.

Diving and flight. A particular problem may occur following scuba diving activities. Dissolved nitrogen can accumulate in the tissues (residual nitrogen) during scuba diving, particularly when diving is deep and repeated. During ascent, that nitrogen may be released and give rise to symptoms of decompression, which in some cases can be severe. In general, it is recommended that individuals do not fly within 24 hours following scuba diving, and that they abstain longer periods if diving required decompression breaks. Tables and computer programs are available that can help determine the amount of residual nitrogen and the recommended delay before flying.[53-56]

Cabin Humidity and Dehydration

As mentioned, cabin humidity is usually less than 10% to 20%.[12] This can cause skin dryness and discomfort in the eyes, mouth, and nostrils. The dehydration caused by a long flight can also be significant in patients with bronchiectasis. If nasal irritation is particularly acute, use of a hypertonic saline spray is recommended.[1]

Restricted Movement

Prolonged immobility, particularly in a sitting position, contributes to the accumulation of blood in the legs, and this can cause swelling, tightness, and discomfort in the lower limbs. In turn, immobility can favor the development of deep vein thrombosis (DVT).[1]

Psychological Aspects

For some subjects, the aircraft environment and the flight itself can trigger increased anxiety, which can lead to an exaggerated perception of some respiratory symptoms or contribute to the deterioration of an existing respiratory condition.

Assessment of Respiratory Diseases

It is difficult to establish definitive guidelines based on currently available information. In fact, a wide variety of procedures are used for the assessment of patients with respiratory disease. In a review of 109 in-flight requests for oxygen, information on oximetry or spirometry results were only available in 61% of cases.[7] Furthermore, a 1997 survey of specialists in respiratory medicine in England and Wales revealed that they followed highly diverse criteria in prescribing use of oxygen in flight.[57]

In any case, to establish a medical opinion on risk in air travel, the type, reversibility, and degree of functional impairment caused by the disease must be assessed along with the tolerance of the patient for the predicted flight altitude and the length of exposure.

General Clinical Assessment

Although all patients with chronic respiratory disease may benefit from a clinical assessment prior to undertaking air travel, such assessment should be considered obligatory in those situations shown in Table 1. The following procedures should be considered in this preliminary examination:

– Medical history, in which special attention should be paid to recognizing all cardiorespiratory disease, with particular interest in comorbidity that could be worsened with hypoxemia (cerebrovascular disease, ischemic heart disease, heart failure). It is also important to assess dyspnea and other respiratory symptoms and compile previous experiences of the patient on other flights.

– Measurement of oxyhemoglobin saturation by pulse oximetry (SpO_2) or arterial blood gas analysis,[58] following a period of rest sufficient to guarantee stability of the recordings. In the case of clinical suspicion of hypercapnia, blood gas analysis should obviously be performed.

– Forced spirometry[59,60] and single-breath determination of the diffusing capacity of the lung for carbon monoxide (DLCO).[61]

– Walk test. The medical departments of some airlines propose walking for 50 m as a way to assess tolerance of flight conditions. In such a test, the aim is to verify that the patient is capable of walking 50 m without limitation due to dyspnea.[7] Although it is a crude procedure that has not been sufficiently validated, it allows an estimate to be made of the cardiorespiratory reserve by assessing the increase in ventilation and cardiac output in response to exercise.

In principle, there is no reason to use a 50 m walk test in place of the 6 minute walk test, which is commonly used in many patients with respiratory disease and is well standardized.[62] Criteria for concern should be the inability of the patient to continue walking for 6 minutes, a distance covered of less than 150 m, or the development of severe dyspnea (score of more than 5 on the Borg scale).[36]

TABLE 1
Respiratory Indications for Clinical Evaluation Prior to Air Travel

Moderate to severe chronic obstructive pulmonary disease
Persistent severe asthma
Severe restrictive disease (including diseases of the chest wall and respiratory muscles), especially with hypoxemia or hypercapnia
Cystic fibrosis
History of intolerance of air travel due to respiratory symptoms (dyspnea, chest pain, confusion, or syncope)
Comorbid conditions that are worsened by hypoxemia (cerebrovascular disease, ischemic heart disease, heart failure)
Pulmonary tuberculosis
Patients from areas with recent local outbreaks of severe acute respiratory syndrome
Recent pneumothorax
Risk or previous episode of venous thromboembolic disease
Prior use of oxygen therapy or ventilatory support

TABLE 2
Respiratory Contraindications for Air Travel

Absolute
Acute respiratory failure
Sputum-positive tuberculosis
Passengers from areas with recent local outbreaks of severe acute respiratory syndrome (SARS) with respiratory symptoms
Contacts of probable or confirmed cases of SARS who have been exposed in the last 10 days
Undrained pneumothorax
Thoracic surgery within the last 2 weeks
Lung contusion
Subcutaneous or mediastinal emphysema
Relative
Resolution of a spontaneous pneumothorax in the last 6 weeks
Major thoracic surgery within the last 6 weeks
Scuba diving in the last 24 hours

– Incremental cardiorespiratory exercise test. The incremental exercise test is not recommended for the systematic assessment of all patients, although it could be useful if the results of simulated altitude-induced hypoxia were unclear. It has been confirmed that a peak oxygen consumption (VO_2max) greater than 12.1 mL/min/kg in patients with moderate or severe COPD is associated with a PaO_2 of greater than 50 mm Hg during the flight.[63] That relationship between VO_2max and PaO_2 was confirmed in the first and fourth hour of flight in a study involving 18 patients with severe COPD.[36] In fact, in a multivariate analysis, PaO_2 at sea level and VO_2max were selected as independent predictors of PaO_2 during the first hour of flight. However, in the fourth hour the only independent variable associated with VO_2max was PaO_2.[36]

Identification of at-risk patients. The information collected in the aforementioned procedures should allow identification of patients who should not fly (Table 2) along with those in whom the hypoxemia in flight could prove dangerous.

In general, it is accepted that patients with acute respiratory failure should not fly. This should also apply to patients with sputum-positive tuberculosis. In the case of patients who are negative for the human immunodeficiency virus (HIV), it would be necessary to have taken antituberculosis treatment for at least 2 weeks. In HIV-positive patients, 3 negative sputum stains or a negative sputum culture are required during the course of the treatment. Passengers with respiratory symptoms who come from areas of local transmission of SARS should also be prohibited from flying, as should contacts of probable or confirmed cases of SARS who have been exposed within the last 10 days. Patients with undrained pneumothorax, subcutaneous or mediastinal emphysema, or a pulmonary contusion, or who have undergone a major thoracic surgical procedure in the last 2 weeks are also considered to have a respiratory contraindication for air travel.

Most current guidelines only consider the results of pulse oximetry or baseline arterial blood gas analysis in screening for patients at risk of developing severe hypoxemia.[7,9-17] In fact, PaO_2 greater than 70 mm Hg or SpO_2 above 95% are usually considered acceptable for air travel in the majority of cases.[64,65]

However, in recent years it has been shown that screening based on PaO_2 or SpO_2 alone are insufficient. For instance, a study was performed in which in-flight hypoxemia was assessed in a group of patients with COPD who had a resting PaO_2 of more than 70 mm Hg, without hypercapnia, and a forced expiratory volume in 1 second (FEV_1) less than 50% of reference.[63] In 53% of the patients, PaO_2 was less than 55 mm Hg at an altitude of 2438 m and 33% had a PaO_2 of less than 50 mm Hg. What was even more noteworthy in that study was that 86% of the patients had a PaO_2 less than 50 mm Hg when they undertook low-intensity exercise similar to that necessary to walk along the aisle of the cabin or to go to the bathroom.[63] Similar findings have been obtained in patients with interstitial disease.[35]

Figure 4 shows a proposed algorithm for patient assessment. In those patients who receive home oxygen therapy, it is recommended that the oxygen flow be increased during the flight, usually by 1 to 2 L/min. In other patients, in-flight hypoxemia should be estimated if they have a PaO_2 less than 70 mm Hg or an SpO_2 less than 93%, if the forced vital capacity (FVC) or DLCO is less than 50% of reference, or if other risk factors are present (Table 3).

Estimation of the Degree of In-Flight Hypoxemia

Based on the level of hypoxemia during air travel in healthy subjects, a PaO_2 of more than 50 to 55 mm Hg has been arbitrarily considered acceptable.[9-13] Consequently, it is important to estimate the PaO_2 during the flight, since below 50 mm Hg provision of supplementary oxygen during the flight is recommended.[35]

PaO_2 at altitude can be estimated in 2 ways: through the use of prediction equations or with a hypoxia–altitude simulation (hypoxic challenge) test.

Prediction equations. Various equations have been developed to predict in-flight PaO_2 based on measurements obtained at sea level (Table 4).[13,66-72] Some of them allow PaO_2 to be determined for any given altitude based on values obtained at sea level (Figure 5).[67,70]

In most cases, the equations were established for patients with COPD and the measurements of PaO_2 at altitude were performed in hypobaric chambers or following altitude simulation via respiration with a fraction of inspired oxygen (FiO_2) of 15%. The accuracy improves when measurements of FEV_1[28,66] or FEV_1/FVC[69] are included. In addition, greater accuracy is obtained when they are applied to COPD patients with an FEV_1 less than 60% of reference.

Despite the simplicity of equations to estimate in-flight hypoxia and their widespread availability, they also have drawbacks. The most important is the consequence of their very large 90% confidence interval, which is ±7.5 mm Hg, mainly due to the use of very small samples in their calculation. It is notable that in 18 patients with severe COPD differences have been detected between the actual PaO_2 during the flight and that estimated in the equation of Gong et al[67] of –6 ±6 mm Hg (range, –15 to 6 mm Hg).[36]

In almost all cases, patient series used to develop the equations have involved healthy men or men with COPD, meaning that accurate information on women is lacking. Nor have flight duration and cabin conditions been considered. In addition, the equations have not been validated with another hypoxia test repeated after the test used to generate them. It is possible that equations that include FEV_1 underestimate the severity of hypoxemia triggered by altitude in hypercapnic patients,[69] since some authors have demonstrated that PaO_2 at altitude is inversely proportional to $PaCO_2$ at sea level.[63] In the same way, equations that use FEV_1 or FEV_1/FVC in healthy subjects probably overestimate PaO_2 at altitude.[73] It is also likely that the cause of the hypoxemia should be taken into account. For instance, hypoxemia as a result of shunt is affected very little by altitude, while that caused by ventilation–perfusion imbalance is highly dependent upon PiO_2.[74,75]

Recently, a specific prediction equation that includes DLCO was developed for patients with restrictive disease.[71] Another equation relevant to patients with COPD or interstitial disease has also been proposed.[72] In addition, in recent years models have incorporated $PaCO_2$, both for healthy subjects and patients with COPD.[70]

In the light of available data, the equation published by Muhm[70] would be the most recommendable in healthy subjects and patients with COPD, while that of Christensen et al[71] would be advisable for patients with restrictive disease.

Hypoxia–altitude simulation test. Although hypobaric hypoxia is the ideal method to estimate the degree of hypoxemia during a commercial flight, it can not be used in ordinary clinical practice due to the limited availability of hypobaric chambers (Appendix 2). As an alternative, it is recommended to resort to the isobaric hypoxia–altitude simulation (hypoxic challenge) test, initially described by Gong et al.[67] This test assumes that respiration of a hypoxic

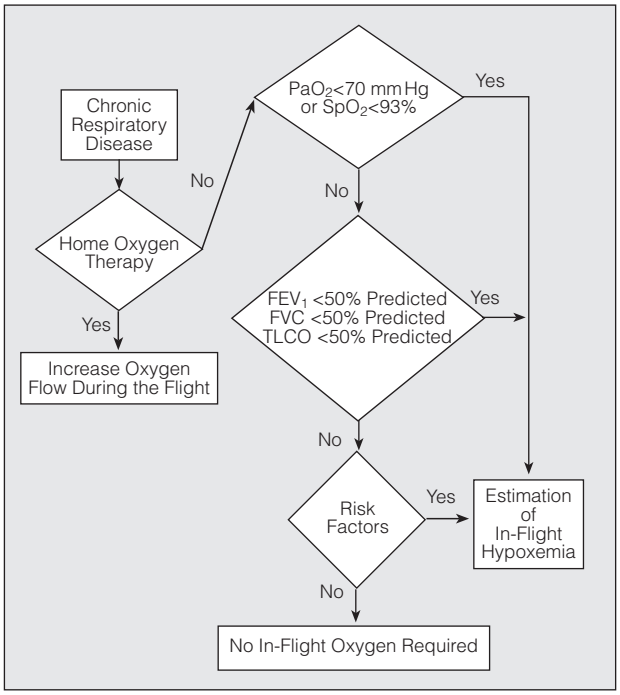

Figure 4. Algorithm proposed to assess the need for supplementary oxygen during the flight in patients with chronic respiratory diseases. SpO_2 indicates oxygen saturation measured by pulse oximetry; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; DLCO, diffusing capacity of lung for carbon monoxide.

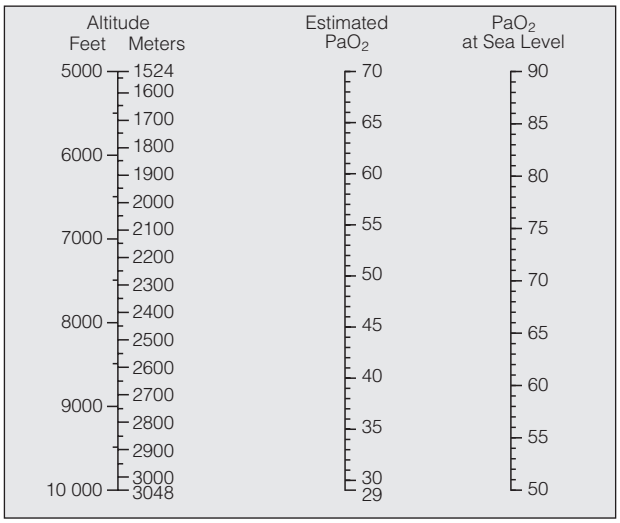

Figure 5. Nomogram for the determination of estimated in-flight PaO_2 from PaO_2 at sea level and at altitude. Taken from Gong et al.[67]

TABLE 3
Additional Risk Factors for the Development of Severe Hypoxia During Air Travel

Hypercapnia
Lung cancer
Restrictive disease
Ventilatory support
Concomitant heart or cerebrovascular disease
Severe anemia
Hospital admission for exacerbation of lung or heart disease within the last 6 weeks

TABLE 4
Equations for the Prediction of In-Flight Hypoxemia*

Equation	Reference
PaO_2 ALT=22.8–(0.00274×Alt)+(0.68×PaO_2 SL)	67
PaO_2 ALT=1.59+(0.98×PaO_2 SL)+(0.0031×Alt)–(0.00006×PaO_2 SL×Alt)–(0.00006×$PaCO_2$ SL×Alt)+(0.000000092×Alt^2)	70
PaO_2 2438 m=0.410×PaO_2 SL+17.652	28
PaO_2 2438 m=(0.417×PaO_2 SL)+17.802	69
PaO_2 2438 m=(0.519×PaO_2 SL)+(11.855×FEV_1 [L])–1760	28
PaO_2 2438 m=(0.453×PaO_2 SL)+(0.386×FEV_1 [% predicted])+2440	28
PaO_2 2438 m=(0.294×PaO_2 SL)+(0.086×FEV_1 [% predicted])+23.211	69
PaO_2 2438 m=(0.245×PaO_2 SL)+(0.171×FEV_1/FVC [% predicted])+21.028	69
PaO_2 2438 m=(0.238×PaO_2 SL)+(20.098×FEV_1/FVC)+22.258	69
PaO_2 2438 m=PaO_2 SL×$e^{-(0.02002-[0.00976\times FEV_1\ [L]])\times(PiO_2G-PiO_2ALT)}$	66
PaO_2 2438 m=PaO_2 SL×$e^{-(0.01731-[0.00019\times FEV_1\ [\%\ predicted]])\times(PiO_2G-PiO_2ALT)}$	66
PaO_2 2438 m=5.55+(0.390×PaO_2 SL)+(0.2475×DLCO [% predicted])	71
PaO_2 2438 m=(0.54×PaO_2 SL)+4700	72

*Alt indicates altitude in feet; PaO_2 ALT, PaO_2 estimated at altitude (mm Hg); PaO_2 2438 m, PaO_2 estimated at 2438 m (8000 feet); PaO_2 SL, PaO_2 at sea level (mm Hg); PiO_2 G, partial pressure of inspired oxygen saturated with water vapor on the ground; PiO_2 ALT, partial pressure of inspired oxygen saturated with water vapor at altitude; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; DLCO, diffusing capacity of the lung for carbon monoxide; $PaCO_2$ SL, partial pressure of carbon dioxide at sea level (mm Hg).

gas mixture at sea level (normobaric hypoxia) simulates the hypobaric hypoxia characteristic of higher altitude.[69] The maximum altitude corresponding to cabin pressure (2438 m) can be simulated by respiration of a mixture of 15% oxygen in nitrogen.

No specific preparation is required for the test. It is recommended that the test be performed without interruption of the patient's usual medication, attempting to avoid changes in the dose or intervals of the medication.[69]

Once patients are seated, they can be made to breathe a hypoxic gas mixture using a Douglas bag, a plethysmography chamber, or a Venturi mask.

The most traditional and simple method is to ask the subject to breathe the gas mixture contained in a 30 to 100 L Douglas bag, which is filled with 15% oxygen and nitrogen as a carrier using pressurized cylinders. In this case, the patients can breath through a mouthpiece with a nose clip, or through a face mask with a valve to prevent rebreathing.[7,14]

The second option involves filling a sealed plethysmography chamber with a gas mixture (15% oxygen in nitrogen) that can be kept constant by introducing oxygen or nitrogen through a port. This procedure has the advantage of not requiring a mask or mouthpiece[76] and also allowing titration of the oxygen flow required to correct the hypoxemia by administration of oxygen through nasal prongs within the hypoxic environment of the chamber. However, while the patient remains in the chamber it is not possible to obtain samples of arterial blood and monitoring is therefore limited to SpO_2.

As a third possibility, a Venturi mask can be used in which oxygen is replaced with nitrogen as the carrier gas. It has been confirmed with various devices that a Venturi system at 35% generates an FiO_2 of 16%, while 40% produces an FiO_2 of 14%, both in healthy subjects and patients with COPD.[73] However, it must be remembered that not all commercial models based on the Venturi principle are able to administer oxygen with an error of less than 1%, as claimed in their specifications. In addition, the FiO_2 can be reduced if the inspiratory flow of the patient exceeds the total flow generated by the apparatus. Although its role is more limited, the dead space inside the mask also affects the concentration of oxygen provided.[72] It is also necessary to consider that nitrogen is 14% less dense than oxygen, meaning that the carryover capacity for air through the Venturi system is lower than that of oxygen, thereby making the FiO_2 achieved less accurate.[77] Thus, it appears reasonable to suggest that if this system is used to administer the hypoxic gas mixture then FiO_2 should be monitored simultaneously.

During the test, the patient will be asked to breathe at tidal volume and the test will be ended after 20 minutes[67,69] or when a stable situation is achieved, defined as the absence of variability in SpO_2 (±2%) or heart rate (±5 beats per minute) for at least 2 minutes.[67]

It is recommended that SpO_2 be monitored continuously and that arterial blood gas analysis be performed at the beginning and end of the test. In terms of pulse oximetry, it should not be forgotten that true oxygenation can be slightly overestimated in smokers, given that the technique does not discriminate between oxyhemoglobin and carboxyhemoglobin.[78] Furthermore, most pulse oximeters display a certain degree of inaccuracy and variability in the saturation range between 88% and 92%.[79] Therefore, SpO_2 should only be used to monitor the test, while interpretation of the test results should be based on PaO_2.

In both healthy subjects and patients with COPD, the hypoxic challenge test provides a measure comparable to that obtained by simulating the same altitude in a hypobaric chamber.[69] The relationship between isobaric hypoxia and hypobaric hypoxia appears not to be affected by the age or the sex of the subjects.[69] In turn, it has also been

demonstrated that there is a good correlation between the PaO_2 obtained during simulation of altitude-induced hypoxia and that determined during flight,[32] although this correlation is weakened when the interval between the 2 measurements is longer than 4 months.[32]

In terms of safety, the tolerance of hypoxic challenge is good and only mild side effects such as tachycardia, dyspnea, vertigo or nausea, headache, and sleepiness have been described.[67]

Hypoxic challenge offers certain advantages over prediction equations. It provides a more accurate assessment of the individual's response to hypoxia. In addition, it allows assessment of the possible effects of hypoxia, such as symptoms or electrocardiographic (ECG) abnormalities. Although initial studies involved continuous ECG monitoring,[67,69] few arrhythmias related to hypoxia were identified and all of them were benign; consequently, systematic ECG monitoring is not recommended.[7] However, it may be considered on an individual basis in patients with cardiovascular comorbidity.

Despite these considerations, hypoxic challenge is a procedure that also presents limitations.[80] It does not reproduce cabin conditions of pressure or air density. However, in order for reduced air density or flow turbulence to generate an increase in FEV_1 or a reduction in work of breathing, altitudes of more than 3000 m are required,[81] suggesting that these factors will have little influence. In addition, the potential beneficial effect of the reduced air density will never be greater than the negative effect caused by the reduction in PiO_2, the increase in lung elasticity and air trapping, and the poor distribution of ventilation.[80,82]

The length of the flight is also not taken into account during hypoxic challenge. However, changes in arterial blood gases during a flight lasting 5 hours have recently been analyzed in patients with COPD.[36] It has been demonstrated that when patients remain seated PaO_2 falls until cruising altitude is reached and then remains stable for the rest of the flight.[36]

There is less consensus regarding the application of these recommendations in children with respiratory diseases. Little information is available on physiologic changes at altitude in children. In addition, the spectrum of disease can be very broad. In premature babies with acute viral respiratory infection there is a greater risk of apnea due to immaturity of the breathing pattern. In that case, environmental hypoxia can increase the risk of apnea and it is therefore recommended that infants do not fly until 6 months after the date for full-term birth. On the other hand, some children with cystic fibrosis are better adapted to a hypoxic environment, probably through changes in the dissociation characteristics of hemoglobin. As a result, the current recommendation considers that children with an FEV_1 less than 50% of reference for cystic fibrosis or other chronic lung disease should undergo a hypoxic challenge test and that if SpO_2 is less than 90% during the test then provision of oxygen during the flight should be prescribed.[7,83] The most recommendable route for administration of the hypoxic gas mixture in children is breathing in a plethysmography chamber.

Prescription of Supplementary Oxygen During the Flight

Supplementary oxygen is recommended during air travel for patients who have an estimated in-flight PaO_2 of less then 50 mm Hg obtained with prediction equations or, preferably, a hypoxic challenge test (Figure 6).[9,76] The criteria on which this cutoff is based are arbitrary.[67] Since healthy individuals can reach a PaO_2 of 55 to 60 mm Hg at cabin altitude,[35] 50 mm Hg was considered to represent the lower limit for a clinically acceptable PaO_2.[67] Therefore, that cutoff is based on expert consensus and does not have scientific support.[35]

Patients with an estimated PaO_2 greater than 55 mm Hg could fly without a requirement for supplementary oxygen. Finally, the group of patients with an estimated PaO_2 between 50 and 55 mm Hg should be assessed on an individual basis. In this case, if there is serious deterioration of resting lung function, marked exercise limitation in either the walk test or the incremental cardiorespiratory exercise test, or comorbidity, provision of oxygen during the flight could also be recommended (Figure 6).

Oxygen is usually provided during the flight through nasal prongs. In patients with severe COPD subjected to conditions of hypobaric hypoxia similar to those in the cabin of a commercial aircraft, it has been shown that provision of oxygen through nasal prongs at a rate of 3 L/min produces a greater increase in PaO_2 than when administered using a Venturi mask at 24% or 28%.[84] In fact, Ventimask systems may favor dilution of ambient air at relatively low flow rates.[85]

An oxygen flow of 2 L/min appears sufficient to correct the hypoxemia in most cases. It has been confirmed that provision of oxygen through nasal prongs at 2 L/min in healthy subjects and patients with obstructive or restrictive disease who breathe an ambient FiO_2 of 15% achieves an SpO_2 similar to that recorded when they breathe at an FiO_2 of 21%.[76] In restrictive diseases, a flow rate of 2 L/min also appears to be sufficient to maintain adequate oxygenation during the flight, although when the patient moves about the aircraft it may be advisable to increase the flow to 4 L/min, so long as an extension is available.[71]

Finally, provision of supplementary oxygen should be considered a safe and effective procedure for the management of many patients with chronic respiratory diseases who undertake a journey by air.[41,65,84] For example, it has recently been described that provision of oxygen during flights of up to 13 000 km allowed a group of patients with severe lung disease to reach their destinations satisfactorily.[86] In that study, only a few episodes of near fainting were observed due to insufficient oxygenation when going to the bathroom without supplementary oxygen.[86]

Specific Recommendation for Some Respiratory Diseases

Chronic Obstructive Pulmonary Disease

COPD and the requirement for its treatment with oxygen during flight is the most common cause of medical

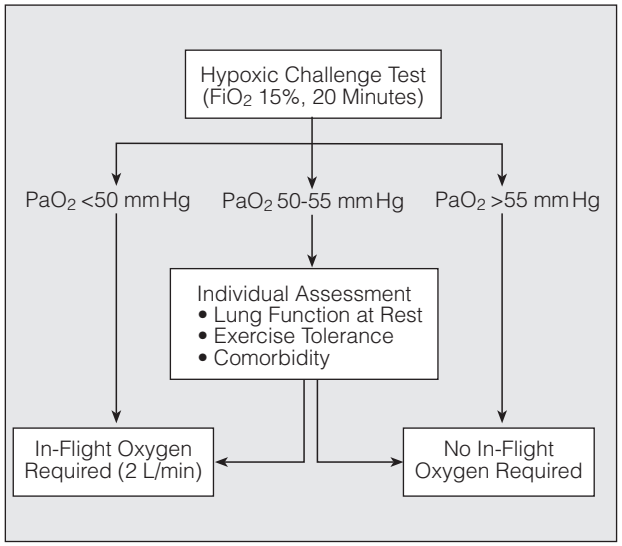

Figure 6. Algorithm for the interpretation of hypoxic challenge. FiO_2 indicates inspired oxygen fraction.

consultation prior to air travel.[87] However, the response of physicians cannot currently be clear and robust, since there is insufficient scientific evidence and many elements remain to be clarified.

In general, the first recommendation for a patient with COPD and hypoxemia would be to avoid air travel and look for other means of transport. This indication might have been valid some years ago but it is currently insufficient for many patients, since it may affect their quality of life and in some cases their work. In fact, a small survey performed in the United States of America on patients with severe COPD showed that each year approximately 1 in 5 traveled by air.[88] However, those results cannot be extrapolated to Spain, where the proportion is likely to be lower.

As for other diseases, it is accepted that patients with COPD should maintain a PaO_2 of more than 50 mm Hg during a flight.[13,35,89] With this threshold, no problems have been observed in studies involving hypoxic challenge and it seems reasonable given the clinical experience accumulated in patients with COPD treated by continuous home oxygen therapy. However, this level is arbitrary and no studies have analyzed its possible consequences in periods of time closer to those of flights, although flight duration appears to have less effect than the altitude reached.[29]

Despite the potential impact of COPD, few studies have addressed the problem of hypoxemia at high altitude during air travel in this setting. Furthermore, the studies performed have involved small samples of patients without severe hypoxemia, the majority eucapnic, and without significant cardiovascular comorbidity.[28,32,65,90,91] The results of those studies indicate that patients can have reductions in PaO_2 of up to 25 mm Hg when they reach an in-flight altitude of 2438 m (8000 feet). This situation is not uncommon in normal flights,[29] and although the incidence of medical problems appears minimal in the general population,[35,92] the same is not true of COPD patients, in whom symptoms and the requirement for in-flight medical assistance are more common.[88] Nevertheless, these events do not normally appear to be particularly serious, and when they are, they are usually cardiovascular in origin.[88,92] Although the interpretation of these data may be erroneous due to the limitations of their collection, it is also possible that the tolerance of hypoxemia in patients with COPD (without other factors that could alter oxygen transport such as heart disease or anemia) is greater than might be expected.

According to current knowledge, it could be recommended that all patients with moderate or severe COPD who wish to travel by air should be clinically assessed, with attention to the following elements: *1)* ruling out the presence of exacerbation or that the patient is in an early phase of recovery from an exacerbation, *2)* identifying the treatment being taken, and *3)* reducing comorbidity. Once clinical stability has been confirmed and treatment optimized, arterial blood gas analysis and spirometry should be performed in the days prior to flying. The values obtained for PaO_2 must be adjusted to sea level; in some regions of Spain that may imply an increase of up to 10 mm Hg.

In order to simplify the assessment, the following algorithm could be recommended in response to the presence of hypoxemia (Figure 7):

1. PaO_2 >70 mm Hg. In general, patients with this PaO_2 will not present severe hypobaric hypoxemia, making systematic estimation of in-flight PaO_2 unnecessary. Nevertheless, the presence of symptoms (dyspnea or chest pain) during previous flights should be assessed, and if they are present, oxygen support at low flow rates (1-2 L/min) should be recommended. It also seems wise to extend that treatment option to those cases and in which the in-flight cabin pressure corresponds to an altitude of greater than 2438 m (8000 feet) and the patient has very severe COPD (FEV_1 ≤30%), where limitations may be present in the mechanisms of compensation for hypoxemia, or diseases that alter oxygen transport.

2. PaO_2 =60-70 mm Hg. An estimate of in-flight PaO_2 should be made using a prediction equation or, preferably, hypoxic challenge. Prescription of oxygen at low flow rates is recommended in the following situations:

– Estimated in-flight PaO_2 less than 50 mm Hg
– Flights in which the cabin pressure corresponds to an altitude greater than 1859 m (6000 feet)
– Presence of cardiovascular comorbidity and/or anemia

3. PaO_2 <60 mm Hg. Patients in this situation usually already receive continuous home oxygen therapy. The goal would be maintenance of the same oxygen levels during the flight, necessitating an increase of 1 to 1.5 L/min over the patient's usual oxygen support. Such treatment should not normally create problems in eucapnic COPD patients, in whom a tendency toward hypocapnia due to hyperventilation has been observed. However, in the presence of hypercapnia, prior assessment of variations in gas exchange following increased oxygen support should be undertaken.

It is important to mention that patients who are not receiving continuous home oxygen therapy have a lower sense of the severity of the disease and a substantial

proportion may not consult their doctor prior to undertaking air travel.[88] Thus, improved treatment education should be developed for this patient population.

Alongside preflight planning based on PaO_2, other general measures to prevent deterioration of hypoxemia include the following:

– Avoid excessive physical effort: do not carry weight and reserve a seat close to the bathroom. However, this should not be a contraindication for the necessary movement of the lower limbs to prevent DVT
– Avoid sleep
– Do not eat large meals

It is advisable for airline companies to have trained staff available who are able to monitor SpO_2 in patients who require oxygen during the flight (SpO_2 between 85% and 93% could be acceptable). In addition, they might be able help to detect abnormalities in heart rhythm, which although rare, show a high between-individual variability.[93] This monitoring is essential if the patient has to travel urgently whilst clinically unstable.

While awaiting new studies that improve upon the substantial limitations in our understanding, the overall message is that all patients with COPD should be assessed by their pneumologist prior to air travel. Supplementary oxygen should be provided for those patients whose estimated in-flight PaO_2 is less than 50 mm Hg, taking particular care with those who have cardiovascular comorbidity.

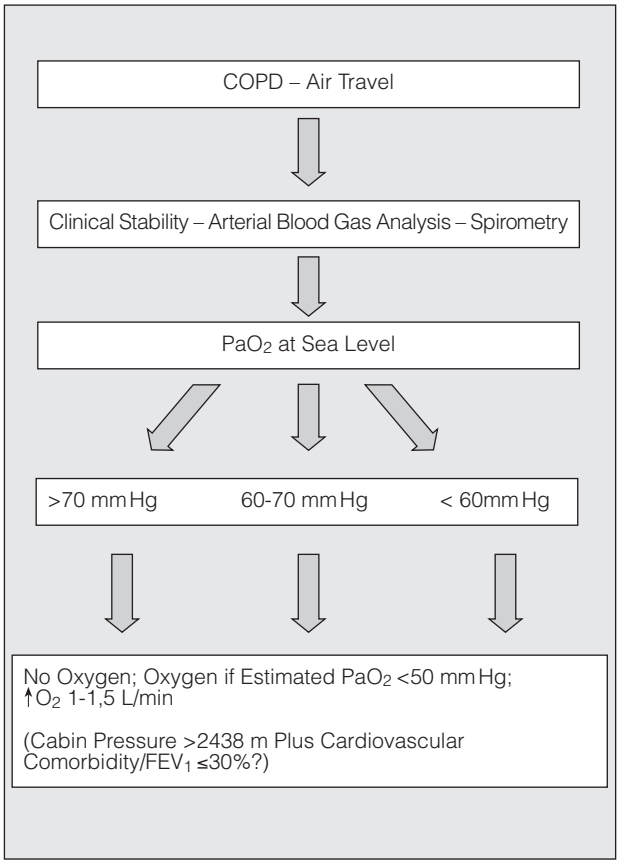

Figure 7. Simplified algorithm for the prescription of in-flight oxygen therapy in patients with chronic obstructive pulmonary disease.
COPD indicates chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second.

Infectious Disease

Commercial flights represent a favorable environment for the spread of pathogens transported by passengers or flight personnel, as was shown during the recent outbreak of SARS. Few studies or data are available on this topic and it is difficult to quantify the global repercussions, which may be underestimated, since almost all of the diseases involved have incubation periods that are shorter than the length of the trip, some of the diseases are treated as trivial processes, and the studies that have been performed have included a significant proportion of passengers who could not be located.[94] The International Health Regulations adopted worldwide in 1969 to limit the spread of disease are in the process of revision.[95,96] Recently, the World Health Organization (WHO) published guidelines on infectious diseases and air travel.[97]

Risk factors. The respiratory infections that have been the object of the greatest interest are pulmonary tuberculosis, SARS, and infections caused by the influenza virus. Since the microorganisms responsible for those infections are mainly transmitted through the air, the risk of transmission during flights is affected by duration, the proximity of the index case, and the cabin ventilation, in addition to the pathogenic characteristics, the epidemiology of the infection in each region, and the immune status of the subject.

The use of appropriate filters and correct recirculation of air in the plane reduces the risk of infection. Although the safety of HEPA filters in protection against viruses has been questioned,[98] a more serious concern is the absence of legislation obliging their use in most countries. HEPA filters were found not to be used on 15% of flights carrying more than 100 passengers in the USA, and that figure is considerably higher in small planes that undertake local flights.[99]

Based on the cases analyzed and studies involving mathematical models, individuals seated in either of the 2 rows of seats closest to the affected passenger are at the highest risk for transmission of *Mycobacterium tuberculosis* and if ventilation is doubled, the risk is reduced by half. The probability of transmission is also reduced to almost zero in passengers seated 15 rows from the zone of infection.[100,101] However, this "safe distance" does not apply in the case of a patient with SARS, who could infect any other healthy passenger seated in the next 7 rows.[102]

Studies performed by the WHO have failed to demonstrate that air recirculation by itself facilitates transmission of infectious disease on board aircraft. However, it should be confirmed that the cabin ventilation system functions correctly and continuously while passengers are on board, independently of whether or not the plane is in flight or held on the runway, as inadequate functioning of the system favors infection.[103]

Calls have recently been made in scientific journals and in the general media for serious consideration to be given to regulations on the use of HEPA filters and for an increase in the number of checks made on aircraft by the authorities.[104,105]

Tuberculosis. A third of the world's population is infected by *M tuberculosis*, and consequently, it is the most extensively studied model of transmission during air travel. Evidence is available that transmission from smear-positive individuals is more common during long flights (longer than 8 hours) and can affect both the passengers and crew members.

Seven episodes of possible tuberculosis transmission during airplane journeys have been studied, 2 of the episodes corresponding to strains resistant to isoniazid and rifampicin. Possible transmission of the infections (Mantoux conversion) to other passengers or crew members could only be established in 2 of the episodes, although it was not possible to demonstrate development of the disease as a result of exposure during a commercial flight in any of the cases.[94,106] In the remainder, the studies found no evidence of transmission,[107] were inconclusive,[108,109] or the likelihood of transmission was considered very low.[110] In all of the cases, the index patient had substantial radiographic involvement and sputum stains revealed acid-fast bacilli with positive sputum cultures.

Despite the fact that acquisition of the disease and possibly transmission of the infection is less likely than in other modes of transport, a great deal of anxiety has been generated among the public, health authorities, and airline companies, and consequently, the WHO has published guidelines with a protocol that ends with a series of recommendations for passengers, physicians, health authorities, and airlines (Appendix 3).[111]

Severe acute respiratory syndrome. The epidemic outbreak of SARS, for which the causative agent is a coronavirus, is the most recent and representative example of a disease transmitted by a very small number of travelers to other countries and continents within a few weeks.[112]

Studies showed that in 5 of the 40 flights investigated for carrying patients infected with the SARS virus transmission of the virus to other passengers was likely to have occurred.[102.113-116] The majority of the patients who were infected had been seated in the 5 rows closest to the index case, although at least in 1 flight lasting 3 hours (Hong Kong–Beijing) an outbreak occurred that affected a high percentage of passengers seated up to 7 rows from the index case and subsequently in more than 300 secondary cases.[102] Possible explanations for that outbreak have been sought, and although no conclusive results have been obtained, it has been suggested to have occurred mainly through aerial transmission from a direct or indirect contact, that some of the passengers were infected prior to the flight, or that it occurred as a result of defective cabin ventilation. The cabin crew may have an increased risk of acquiring the disease due to their movement through the aircraft.[102]

The WHO developed a series of recommendations and guidelines, which included a series of measures that should be followed by all countries (Appendix 4).[114,115] Once those measures were put into practice, no new cases of long-distance propagation of the disease were identified.[101]

Influenza. Epidemic infection with the influenza A virus appears between the months of October and April in the northern hemisphere and between May and September in the southern hemisphere. In a recent study undertaken in Switzerland, almost 13% of passengers who suffered fever during a journey to subtropical or tropical regions had a significant antibody titer against influenza viruses when they returned and in more than 6% it was possible to demonstrate a seroconversion of more than 4 times the initial titer. The most common pathogens in fever episodes outside the periods of local epidemic were influenza viruses.[117] That source may be the cause of some of the limited outbreaks that occur during the nonepidemic period.[118,119] Other viruses such as influenza B and parainfluenza also have demonstrated pathogenic capacity.[120,121] As in conventional epidemic outbreaks, a series of risk factors affect acquisition of infection, such as age over 65 years, presentation of comorbid conditions, and close contact with the index case, meaning that tourism in groups can facilitate infection.[120]

Nevertheless, only 3 studies have reported infection during air travel.[103,118,121] The passengers seated in the rows closest to the index case were the most often affected, although given the high infectiousness of the virus, between 25% and 70% of the passengers was possible in flights lasting longer than 3 hours and up to 20% of secondary familial contacts developed the disease. Suspension or failure of the ventilation system favors disease transmission, as demonstrated in a flight in which an individual with flu infected 72% of the passengers.[103]

Some countries recommend flu vaccination for those passengers undertaking journeys to the southern hemisphere during the summer and who were not vaccinated during the previous year.[122]

Respiratory transmission of other diseases

Some microorganisms that do not produce respiratory symptoms, or at least are not associated with respiratory conditions as the principal symptoms, are nevertheless transmitted through the airways. Among them, meningococcus and measles virus are the most noteworthy as a result of their infectiousness, morbidity and mortality.

Between 1999 and 2001, 21 cases were studied of patients with meningococcal disease who had traveled by plane during the infectious period without evidence of a single secondary case. Nevertheless, given the severity of the disease, it is advised that individuals seated near the index case begin prophylactic treatment in the 24 hours following the case being reported, so long as less than 14 days have elapsed since the contact.[101,123]

The measles virus is highly contagious, with up to 80% of exposed individuals developing the disease, and cases have been described of transmission during air travel.[124-127]

Currently, the vaccination schedule in the different autonomous communities of Spain includes vaccination against meningococcus from the age of 2 years and measles from 15 months, making the risk of transmission of those diseases presumably minimal, although individuals without antibodies or those from other countries who have not been vaccinated could be affected.

No epidemic outbreaks have been reported for the virus that causes the common cold, but this absence is presumably due to the high frequency of the disease and the difficulties associated with investigating it.[101] One study found no evidence that the air recirculation system in the cabin aided appearance of symptoms of infection in the upper airways.[128]

There is currently a great deal of concern regarding spread of the avian flu virus (H5N1). This virus has a shorter incubation period and is more contagious than the SARS virus. The USA has prepared a national plan to prevent the spread of outbreaks through the establishment of a series of specific health measures in airports. In addition to an increase in the number of health care workers, medical consulting rooms have been built that allow the health of passengers to be assessed and isolation rooms created to establish a quarantine area in international airports. Those facilities are in permanent contact with the Centers for Disease Control and Prevention (CDC) and have access to passenger information for all flights in order to identify contacts of a possible index case.[129]

To date, the benefits of such a strategy have not been demonstrated and it is quite unlikely that it would prevent or slow an epidemic caused by introduction of the influenza or SARS virus.[130] Detection of individuals with the disease exclusively in the destination airport would only have consequences for the detection of individuals who developed the clinical features during the flight and of contacts, thereby making the sensitivity low. Most experts are in favor of strategies similar to those followed in the SARS outbreak, including monitoring to detect individuals with symptoms in the departure airport, in an effort to prevent individuals with the disease from boarding the flight.[131-134]

If a case of infection with the avian influenza virus is confirmed, isolation measures similar to those followed for patients and contacts with SARS must be established, treatment with neuraminidase inhibitors should be initiated immediately, and in contacts, prophylactic measures with those drugs should be started during the first 48 hours. If a specific vaccine is available it should be immediately administered to contacts.[135] The WHO has established a global plan in which these elements are considered.[136,137]

Recently, a series of recommendations and considerations were prepared on the management of exposure to an infectious disease during commercial air travel[101]:

– Although passenger transport companies can refuse to transport individuals with a disease, they cannot undertake systematic examination in an effort to identify ill passengers.

– Early diagnosis is necessary to establish measures for the other passengers.

– Governments have the legal authority, in accordance with international law, to establish controls on passengers with transmissible diseases for which declaration is obligatory.

– The authorities may establish measures to quarantine passengers who arrive at their airports.

– Physicians must identify those subjects who are not in a good enough state of health to travel by air and inform them of how a flight might affect their health.

– Prevention is the best course of action and postponement of the journey should be advised.

– Hand washing reduces the risk of transmission of contagious diseases and should be performed as a matter of course during travel and always prior to eating.

– The mouth and nose should be covered in the event of sneezing or coughing and hands should be washed afterwards to protect others.

– In the case of a passenger with suspected SARS during the flight, a US National Institute for Occupational Safety and Health N95 mask should be provided and an isolation zone established in the aircraft.

Cystic Fibrosis

Survival and quality of life have improved in patients with cystic fibrosis, making it not uncommon for them to want to go on holidays and even undertake work that may involve air travel.

Few studies have assessed the effects of commercial flights on patients with cystic fibrosis. There is some disagreement regarding estimation of the level of hypoxemia in those patients. Although in a study performed in a small group of patients aged between 11 and 16 years, hypoxic challenge predicted with a high level of sensitivity and specificity the development of desaturation during the flight, later studies have not confirmed those findings.[138] A study undertaken by the same group that contained a larger number of subjects and involved longer flights (8-13 hours) contradicted the earlier findings and showed that an FEV_1 less than 50% of reference better identified patients who desaturated than did the results of hypoxic challenge.[83]

Only a small percentage of the patients who displayed reductions in SpO_2 to below 90% presented symptoms and required oxygen supplementation.[83] However, it should be noted that the patients included in those studies were stable, had disease that was not very advanced, and were younger than other groups of patients with cardiac or respiratory diseases for whom reduction of PaO_2 to below 50 mm Hg necessitates the implementation of oxygen therapy during the flight. This would explain the greater tolerance of hypoxia seen in patients with cystic fibrosis, confirmed both in acute exposure in hypobaric chambers[139] and during time at altitude.[140] In addition, in patients with cystic fibrosis, the results of hypoxic challenge are particularly variable over time and can change within a few weeks.[141,142]

Consequently, the decision to have a cystic fibrosis patient use oxygen therapy during a flight should not be based exclusively on hypoxic challenge tests but also on clinical parameters and the degree of bronchial

TABLE 5
Specific Recommendations for Patients With Cystic Fibrosis Who Intend to Undertake a Journey by Air

Drink lots of liquids to avoid noxious effects of the dry cabin air on the secretions and mucosa of the airway
If the patient uses a nebulizer, some airlines allow the patient's own nebulizer to be used or provide one for long-haul journeys
If possible, physiotherapy exercises should be performed during stopovers on long journeys

obstruction.[140] Other recommendations to consider in patients with cystic fibrosis who intend to travel by air are summarized in Table 5.

Some authors have described an increase in exacerbations following a holiday,[141,142] related to poorer management of the disease. Correct compliance with treatment and, in particular, physiotherapy improves the conditions in which the return flight is undertaken and reduces the likelihood of complications.[143]

Venous Thromboembolic Disease

The estimated incidence of venous thromboembolic disease (VTD) in the general population is 1 per 1000 person-years.[144] The pathogenesis of DVT was first described by Virchow in 1856, and the description remains valid today. It is based on a triad formed by stasis of venous blood flow, damage to the vascular endothelium, and hypercoagulability. These circumstances coincide in acquired—transient or persistent—or congenital conditions defined as risk factors, present in approximately 75% of patients with VTD.[145]

Extended journeys have been associated with an increased incidence of VTD[146] and have been included in the list of risk factors.[147,148] In 1977, the term "economy class syndrome" was coined following the description of 8 cases of VTD after flights in economy class.[149] The aim was to highlight that the limited space within which to stretch the legs during an extended period of time reduces venous return and favors stasis of venous blood flow.[150] This situation is not exclusive to air travel in economy class. It has also been described in business class[151] and in other forms of travel, such as cars and buses,[152] involving long periods of time with the lower limbs flexed and at rest.

Apart from venous stasis, there is a lack of agreement regarding other factors associated with air travel that could contribute to DVT such as dehydration, favored by the low humidity of the cabin and in some cases increased by the diuretic effect of coffee or alcoholic drinks, and the hypobaric hypoxia associated with pressurized cabins. Dehydration could predispose to DVT as a result of hemoconcentration and blood hyperviscosity, although this hypothesis has not been confirmed. It has been observed in experimental studies that hypobaric hypoxia favors activation of clotting[153,154] and reduces physiologic fibrinolytic activity of endothelial cells[154]; however, those results have not been reproduced in subsequent studies.[155]

Incidence and risk of VTD. Studies addressing the incidence and risk of thrombosis associated with long-distance flights have employed a variety of different methods and yielded disparate results. For passengers with a high risk of thrombosis due to the presence of additional risk factors the incidence of VTD appears to be high, from 3% to 5%.[156,157] In patients at low or moderate risk the incidence drops to between 0% and 1%.[157,158]

Most of the VTD events that were identified were asymptomatic DVT that exclusively affected the venous territory of the calf, although the screening method used in almost all of the studies involved venous compression ultrasound with or without Doppler, raising questions over the results due to the limited sensitivity of the technique for distal clots. The influence of other individual risk factors appears to be decisive in generating DVT.[159]

The incidence of pulmonary embolism has been assessed in cohort studies.[160-162] According to data collected in Paris airports between 1984 and 1998, the incidence of this entity has increased.[160] Significant differences have been described in incidence rates according to distance traveled, ranging from 0.01 per 106 passengers for distances of less than 5000 km to 4.8 cases per 106 passengers in flights of more than 10 000 km.[161] Differences were also seen according to distance traveled in a study performed at Madrid Barajas Airport.[162] In flights lasting more than 8 hours the incidence of pulmonary embolism was 1.65 per 106 passengers and in flights lasting 6 to 8 hours it was 0.65 per 106 passengers, while no cases were observed in flights lasting less than 6 hours. Consequently, 6 hours has been considered the cutoff for recommending general measures for the periodic movement of the limbs.[163]

The relative risk of VTD is difficult to establish due to the heterogeneity of the studies.[152,157,164] Considering only air travel, the risk is not clear (odds ratio, 1.3),[164] and consequently, it could not be considered as an independent risk factor. However, in passengers with additional risk factors for thrombosis, the odds ratio increased in all studies to represent a 3-fold to 4-fold higher risk of VTD. Recently, it has been demonstrated that the immobility during a flight lasting more than 8 hours increases the levels of certain markers of clotting in subjects without risk factors for thrombosis, but it remains to be established whether this represents an increased risk of VTD.[165]

Prophylactic measures. Patients must be assessed individually and the presence of other risk factors for venous thrombosis identified (Table 6) in order to adopt prophylactic interventions. Classification of the risk as moderate or high in these circumstances is not well established. It seems reasonable to extrapolate the impact of each of these factors on VTD.

GENERAL MEASURES. Adequate hydration, regular movement of the lower limbs, and avoiding keeping the legs bent for long periods of time are the measures recommended by most experts. These measure are recommended for general application in flights lasting more than 6 hours.[163]

TABLE 6
Risk Factors for the Development of Venous Thromboembolic Disease That Should be Assessed for Long-Haul Flights

Recent major surgery
Recent fractures or immobilization of the lower limbs with a plaster cast
Recent immobilization as a result of illness
Congenital thrombophilia: antithrombin, protein C, or protein S deficiency, homozygous or heterozygous factor V Leiden mutation, combined deficiencies, heterozygous factor II G20210A mutation, hyperhomocysteinemia, increased plasma concentration of factor VIII, others*
Previous venous thromboembolic disease, especially idiopathic disease
Cancer, especially with metastasis
Antiphospholipid syndrome
Advanced age
Pregnancy, puerperium
Obesity
Superficial venous thrombosis, varicose veins
Oral contraceptives, hormone replacement therapy, tamoxifen
Miscellaneous factors: polycythemia vera, thrombocytosis, paroxysmal nocturnal hemoglobinuria, nephrotic syndrome, inflammatory bowel disease, Behçet syndrome, lupus erythematosus, antipsychotic medication

*Other thrombophilias: increased plasma concentration of factor IX, factor XI, and thrombin-activatable fibrinolysis inhibitor, and dysfibrinogenemias.

COMPRESSION STOCKINGS. In passengers at high risk of thrombosis, compression stockings, generally knee length and with a pressure of 15 to 30 mm Hg have proven to be effective in reducing the incidence of VTD;[166-168]; no adverse effects are associated with their use and they are well tolerated.

PROPHYLACTIC DRUG TREATMENT. The use of acetylsalicylic acid and low molecular weight heparins has been tested in passengers at high risk of thrombosis. A dose of 400 mg acetylsalicylic acid for 3 days proved to be ineffective and caused gastrointestinal discomfort in 13% of subjects.[169] In contrast, a single dose of enoxaparin, both at a therapeutic weight-adjusted dose and as a high-risk prophylactic dose, administered 2 to 4 hours prior to the flight reduced the incidence of DVT without side effects.[169]

The general conclusions on VTD and air travel are summarized in Table 7.

Chronic Respiratory Failure

Few studies have addressed the effects of air travel on patients with respiratory diseases who present respiratory failure or severe abnormalities in control of ventilation. Issues that must be taken into account in relation to air travel in such patients, in addition to the characteristics and length of the flight, are the following: *1)* the total length of the journey (flight time plus predicted waiting time and risk of unexpected delays), *2)* travel from the airport to the final destination, *3)* logistic aspects such as provision of oxygen or the feasibility of charging the batteries of the apparatus or a wheelchair during the flight and at the destination, and *4)* the altitude of the destination point and the length of time the individual will remain there. Most patients can travel despite limitations, so long as the journey is sufficiently prepared and no elements are left to chance.[170]

In general, an increase in oxygen flow of 1 to 2 L is recommended in patients who receive home oxygen therapy.[171] It is also essential to know the conditions of each airline company prior to embarking upon a journey, both in terms of the transport and provision of oxygen and in relation to the accessories required by the patient (wheelchair, ventilator) and the requirement to travel with an escort. Some companies allow the passenger to carry small oxygen bottles (a maximum of 2 bottles less than 0.5 m long and 250 mm in diameter),[172] but other companies do not accept transport of oxygen, although they allow the use of some oxygen concentrators, according to very strict regulations, so long as the user has sufficient batteries available to last the entire duration of the flight.[173]

Restrictive Diseases

Cases have been described of patients with kyphoscoliosis or neuromuscular diseases in whom long air journeys generated right heart failure,[174] presumably linked to the hypoxia maintained during the flight.

From a theoretical point of view, in patients with nonhypercapnic restrictive disease (caused by involvement of the parenchyma), who present a risk of hypoxia during the flight, oxygen would be indicated to reduce the impact of hypoxemia on pulmonary hypertension.

In patients with restrictive diseases who use mechanical ventilation (for extrapulmonary involvement), it is recommendable that they carry the apparatus with them during the flight, even if they only use it at night. Clearly, patients with continuous ventilation should carefully assess the journey since they will need to use the ventilator throughout the travel period, including during airport transfers.

From a logistic perspective, it is very important to confirm the hand luggage that the patient can carry, especially in relation to wheelchairs, the ventilator, and the spare battery. In the case of patients with severe disability, most airlines require the presence of an escort and consider that 1 person can take responsibility for

2 passengers with disability. The patient should also consider the physical space that he or she may require. It is usually recommendable to make direct contact with the airline company to assess all the patient's requirements.[175]

Sleep Apnea-Hypopnea Syndrome

There are few reports in the literature on the impact of air travel in patients with sleep apnea–hypopnea syndrome (SAHS). Some complications have been associated with long journeys followed by a period at altitude. All patients with SAHS should avoid consumption of alcohol immediately before and during the flight. Patients in a severe condition should employ continuous positive airway pressure (CPAP) during long flights. To this end, they should have a dry cell battery available for use as an energy source for the equipment.

Asthma

Although the low humidity of the air in aircraft cabins may favor the development of bronchospasm due to loss of water from the bronchial mucosa, asthma attacks during air travel are thought to be rare.[7] In addition, it is sometimes difficult to differentiate them from dyspnea due to hyperventilation or panic.[7] More recently, a higher incidence of episodes of bronchospasm requiring treatment during flight has been described.[176]

Patients with controlled asthma and no respiratory failure do not present problems for air travel, although they should ensure that they have their medication to hand. Patients with severe asthma with frequent exacerbations and serious attacks should ensure that the disease is well controlled prior to the day of the flight.

Since 2004, the emergency medication in most aircraft includes bronchodilators, both in pressurized cartridges and for injection. However, in case of an attack, patients are recommended to take their normal rescue medication.[177]

Lung Cancer

Patients with primary tumors or metastases can generally fly safely. Nevertheless, it may be necessary to consider measures to alleviate hypoxemia or pain.

Pneumothorax

Pneumothorax is a contraindication for air travel. A patient will only be allowed to fly when the lung has been completely reinflated. The patient should not be allowed to fly until 72 hours after pleural drainage has been withdrawn and with a radiograph performed 48 hours after completion of drainage to confirm resolution of the pneumothorax.[7]

Optionally, some airline companies may accept transport of a passenger with a pleural drain. In that case, since it is difficult to guarantee continuous aspiration during the flight, it is recommended that a Heimlich valve be used.[12] In exceptional cases it may be necessary to evacuate a pneumothorax during the flight. This should only be done by trained staff and when the cabin pressure corresponds to sea level.[12]

Chest Injury

Simple rib fractures do not usually present problems during the flight, particularly when there is no lung damage or prior pulmonary disease.[12] The main problem associated with such fractures is pain, which can reduce ventilation. Therefore, it is important that adequate analgesia is guaranteed during the flight. Multiple fractures may cause thoracic instability and, in that case, the requirement for specialized transport should be considered.

Flights should be postponed in all patients with acute respiratory failure due to lung contusion until lung function returns to normal.[7,12] Likewise, mediastinal or subcutaneous emphysema constitutes a contraindication for travel on commercial flights.[12] In any of those situations, if air travel is essential an air ambulance is required.

Thoracic Surgery

Although individual assessment is necessary, as a general rule patients are advised not to fly until at least 2 weeks after the operation.[7]

Organization and Logistics

Patients with respiratory diseases who require oxygen on board or some form of health care during the flight are

TABLE 7
General Considerations Regarding Venous Thromboembolic Disease and Air Travel

The association between venous thromboembolic disease (VTD) and air travel is weak.
The clearest risk is for presentation of asymptomatic deep vein thrombosis (DVT) restricted to the calf area.
Symptomatic episodes of VTD, including fatal pulmonary thromboembolism, are rare.
The risk is increased in journeys lasting more than 6 hours in patients with additional risk factors. Regular movement of the legs and hydration should be a general recommendation.
In passengers with other risk factors for venous thromboembolism, the decision to implement other prophylactic measures should be made on an individual basis. Knee-length compression stockings are effective and reduce the incidence of DVT.
Low molecular weight heparins are effective in patients at high risk of thrombosis.
In general, a single high-risk prophylactic dose of low molecular weight heparin appears to be sufficient but should be assessed on an individual basis.
Aspirin is ineffective and should not be recommended.

TABLE 8
General Recommendations for Patients With Respiratory Diseases During Air Travel

Obtain a report of the clinical condition of the patient that includes the most recent functional assessment and treatment. This is essential if the stay is for a number of weeks and the destination does not have the usual health care resources.
In countries in which smoking is still allowed inside the aircraft, the patient must be seated in a nonsmoking area.
Avoid excessive alcohol consumption prior to and during the flight, especially in cases of apnea–hypopnea syndrome and risk of venous thromboembolic disease.
Move around during long flights, unless oxygen is required.
If oxygen is required, it should be used if possible while moving inside the plane (with an extension to allow movement).
Prophylactic measures should be taken to reduce the risk of thromboembolism.
Carry required medication, especially rescue inhalers, in hand luggage.
If medication is checked with baggage, ensure that it is not affected by the extreme conditions in the hold.
Use spacer chambers rather than nebulizers.
If continuous positive airway pressure is required on a long-haul flight, carry a dry cell battery, which must be switched off prior to landing.
Patients who require a ventilator must be able to tolerate temporary disconnection of the apparatus during takeoff and landing.
The requirement for oxygen or any other form of medical assistance must be indicated when the reservation is made, at least 48 hours. prior to departure.
If necessary, assistance must be organized with the medical department of the company to transfer the patient within the airport.

considered as ill patients who require medical authorization (medical fitness for air travel [MEDA] case). All patients who report such a condition must be informed when making the reservation of the process that needs to be followed in order to obtain medical authorization, of the limitation and requirements that exist, of the number of escorts required, and of the cost of the service requested. In turn, they must complete the INCAD/MEDIF form provided by the company (Appendix 5), based on IATA recommendations, and send it by fax to the medical department of the airline company to receive authorization and initiate the corresponding procedures.

Oxygen is normally supplied through a mask, although patients may use their own nasal prongs. Three sources of oxygen can be used in aircraft. If cabin pressure is lost, passengers may receive oxygen through masks located above their seats. However, this oxygen source, which has a limited duration, cannot be used for provision of supplementary oxygen to sick patients during the flight. The most common practice is to use cylinders with a capacity of 22 cubic feet. At a flow rate of 4 L/min, those cylinders can provide oxygen for 4 hours,[80,178] making it important to estimate the number of cylinders that the patient will need based on the flow prescribed and the length of the journey. Recently, the American Department of Transportation approved the use of portable oxygen concentrators, which can be used during takeoff and landing and while moving inside the cabin. This equipment can also help the patient while moving inside the plane and in the terminal. To date, the only approved models are manufactured by Inogen (www.inogen.net) and Airsep (www.airsep.com).[33] It should be noted that most companies do not allow the use of liquid oxygen on board. If the patient wishes to transport a portable liquid oxygen system it must be checked in empty and filled on arrival at the destination.

In general, in-flight oxygen is administered at flow rates of 2 or 4 L/min, and exceptionally, at 8 L/min. The medical department of the airline company may require that the patient be accompanied by an escort trained in the used of the oxygen therapy system. In most cases, provision of oxygen during the flight is a service paid for by the passenger. As a guide, from January 2006 the Spanish airline Iberia charges €165 per flight and requires at least 48 hours notice prior to departure of the flight or 24 hours in the case of emergencies. In more exceptional cases, some companies may insist that a second seat is purchased for the oxygen source.

Previous experiences of travel with patients requiring oxygen therapy or mechanical ventilation show that the main problems arise during transfer of the patients.[80] In general, most companies only provide oxygen during the period of time inside the plane or during transfer between planes of the same company. If oxygen is required during boarding or while waiting in the airport, the passenger should inform the medical services of the company to organize specialized transport, such as ambulance transfer to the plane. Transport with oxygen during the flight does not represent an exceptional situation. Data from the airline Iberia indicate that 2000 persons require supplementary oxygen in flight each year.

It is also possible to use CPAP equipment or ventilators during flights. In that case, patients should carry their own equipment, since it is not provided by airlines. It is important to mention that, since the great majority of commercial aircraft do not have plug sockets in the cabin, the patient should carry a dry cell battery to independently power the equipment.

Permission to use CPAP or a ventilator on board must also be requested when making the reservation and requires authorization by the medical department of the company. In general, an escort is not required for the use of CPAP,

whereas mechanical ventilation usually demands the presence of an assistant trained in its use. Patients who are completely dependent on a ventilator and cannot tolerate temporary disconnection of the equipment during takeoff and landing, or in the event of other occurrences, cannot fly in commercial aircraft. In such cases, the use of air ambulances is necessary.

Nevertheless, there is a marked diversity in the regulations, availability, cost, and ease of oxygen provision during air travel,[179] making it advisable for patients or their representatives to determine the criteria established by the company with which they intend to fly. This information can be obtained directly from travel agencies, when making a reservation, or via the webpage of the British Lung Foundation.[180]

Finally, all patients with respiratory diseases who intend to fly are advised to consider certain general recommendations (Table 8) and even to access specific information sources for patients.[180-182]

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APPENDIX 1

Conversion of Altitude Expressed in Feet to Meters

Feet	Meters	Feet	Meters
1000	305	26 000	7925
2000	610	27 000	8230
3000	914	28 000	8534
4000	1219	29 000	8839
5000	1525	30 000	9144
6000	1829	31 000	9449
7000	2134	32 000	9754
8000	2438	33 000	10 058
9000	2743	34 000	10 363
10 000	3048	35 000	10 668
11 000	3353	36 000	10 973
12 000	3658	37 000	11 278
13 000	3962	38 000	11 582
14 000	4267	39 000	11 887
15 000	4572	40 000	12 192
16 000	4879	41 000	12 497
17 000	5182	42 000	12 802
18 000	5486	43 000	13 107
19 000	5791	44 000	13 411
20 000	6096	45 000	13 716
21 000	6401	46 000	14 021
22 000	6706	47 000	14 326
23 000	7010	48 000	14 630
24 000	7315	49 000	14 935
25 000	7620	50 000	15 240

APPENDIX 2
Centers With Hypobaric Chambers in Spain

Centro de Instrucción en Medicina Aeroespacial (CIMA)
Arturo Soria 82, 28027 Madrid, Spain, Dr Francisco Ríos Tejada, Tel: +34 914 101 300, Fax: +34 914 081 312, E-mail: friotej@oc.mde.es
Institut Nacional d'Educació Física de Catalunya (INEFC)
Avda. de l'Estadi, s/n, 08038 Barcelona, Spain, Dr Felip Santamaría, Tel: +34 934 255 445,

APPENDIX 3
Ten Recommendations of the World Health Organization to Prevent Transmission of Tuberculosis During Air Travel[111]

For Passengers

1. Individuals with tuberculosis (TB) with the possibility of between-individual transfer, such as sputum-positive patients, must postpone their journey until they are no longer a potential source of transmission.

For Physicians and Health Authorities

2. If the history of a patient with TB who could transmit the disease shows that he or she has recently undertaken a journey by air (eg, within the last 3 months), the physician should immediately inform the health authorities in the declaration of the TB case.

3. The health authorities should immediately contact the airline company if the person has undertaken a journey lasting at least 8 hours in a commercial aircraft during the last 3 months.

For the Airline Companies

4. Airline companies should work closely with health authorities in the provision of information to passengers and flight crew who may have been exposed to *Mycobacterium tuberculosis* as well as in the identification of those passengers who should be informed.

5. Airline companies should cooperate closely with health authorities in the provision of information to passengers and flight crew who may have been exposed to *M tuberculosis* as well as in the identification of those passengers who should be informed.

6. Airline companies should require the home and work addresses and telephone numbers of passengers so that they can be informed in the event of potential health risks (exposure to *M tuberculosis* or other infectious diseases, exposure to toxins, etc).

7. Airline companies should ensure that all crew receive appropriate training in first aid and the use of universal precautions regarding exposure to biologic fluids. All aircraft must be equipped with emergency medical supplies (including gloves, masks containing high efficiency particulate air [HEPA] filters, and biohazard bags).

8. Airline companies must have prearranged access to physicians with experience in transmissible disease who are available for subsequent consultation by health authorities.

9. Records of all diseases and medical emergencies must be kept for at least 3 years.

10. Long delays should be reduced to a minimum and HEPA filters should be installed and maintained at maximum efficiency (99.97% at 0.3 μm).

APPENDIX 4

Recommendations of the World Health Organization to Prevent Transmission of the Virus That Causes Severe Acute Respiratory Syndrome During Air Travel[115]

1. Establish a screening system organized by the authorities in the affected regions in which all passengers are assessed by health workers at the point of departure.

2. In case of suspicion during the flight, isolation measures should be taken for subjects who are suspected to carry the disease (provision of an exclusive bathroom, covering the mouth and nostrils of the patient with an appropriately protective mask) and the health authorities at the destination point should be informed about the suspicion.

3. Management of contacts. Contacts are considered as all individuals seated in the 2 rows closest to the index case and all those who have had close contact with the index case prior to or during the journey. If the affected individual is a member of the cabin crew, all passengers are considered contacts. It is obligatory for the health authorities to identify and locate the whereabouts of those individuals for the following 14 days and to contact the health authorities immediately if they develop any symptoms.

4. The aircraft should be disinfected according to World Health Organization guidelines.[30]

APPENDIX 5
INCAD/MEDIF Form

To be completed by SALES OFFICE/AGENT	**INFORMATION SHEET FOR PASSENGERS REQUIRING SPECIAL ASSISTANCE** Answer ALL questions — put a cross (×) in "YES" or "NO" boxes. Use BLOCK LETTERS or TYPEWRITER when completing this form.

A NAME/INITIALS/TITLE:

B PROPOSED ITINERARY (airline(s), flight number(s), class(es), date(s), segments(s), reservation status of continuous air journey).

Transfer from one flight to another often requires LONGER connecting time.

C NATURE OF INCAPACITATION:

D IS STRETCHER NEEDED ON BOARD? (all stretcher cases MUST be escorted). No ☐ Yes ☐

Request rate if unknown.

E INTENDED ESCORT (name, sex, age, professional qualification, segments if different from passenger). If untrained, state "TRAVEL COMPANION".

For blind and/or deaf, state if escorted by trained dog.

F WHEELCHAIR NEEDED? No ☐ Yes ☐

Categories are: WCHR WCHS WCHC

Wheelchair category:

OWN wheelchair	Collapsible	Power driven?	Battery type (spillable?)
No ☐ Yes ☐	No ☐ Yes ☐	No ☐ Yes ☐	No ☐ Yes ☐

Wheelchairs with spillable batteries are "dangerous goods" and are permitted on passenger aircraft only under certain conditions, which can be obtained from the airline(s). In addition, certain countries may impose specific restrictions.

G AMBULANCE NEEDED? No ☐ Yes ☐

To be arranged by AIRLINE: No ☐ Yes ☐

Specify ambulance company contact:

Specify destination address:

Request rate(s) if unknown.

H OTHER GROUND ARRANGEMENTS NEEDED No ☐ Yes ☐

If yes, SPECIFY below and indicate for each item: (a) the ARRANGING airline or other organisation, (b) at whose EXPENSE, and (c) CONTACT addresses/telephone numbers where appropriate, or whenever specific persons are designated to meet/assist the passenger.

1	Arrangements for delivery at airport of DEPARTURE	No ☐	Yes ☐	Specify
2	Arrangements for assistance at CONNECTING POINTS	No ☐	Yes ☐	Specify
3	Arrangements for meeting at airport of ARRIVAL	No ☐	Yes ☐	Specify
4	Other requirements or relevant information	No ☐	Yes ☐	Specify

K SPECIAL IN-FLIGHT ARRANGEMENTS NEEDED, such as: special meals, special seating, leg-rest, extra seat(s), special equipment, etc. No ☐ Yes ☐

If yes, DESCRIBE and indicate for each item: (a) SEGMENT(s) on which required, (b) airline-ARRANGED or arranging third party, and (c) at whose expense. Provision of SPECIAL EQUIPMENT, such as oxygen, etc. always requires completion of the MEDIF.

L DOES PASSENGER HOLD A "FREQUENT TRAVELLER'S MEDICAL CARD (FREMEC)" VALID FOR THIS TRIP? No ☐ Yes ☐

If yes, add below FREMEC data to your reservation requests. If no (or if additional data needed by carrying airline(s)), have physician in attendance complete the MEDIF.

FREMEC / (FREMEC number) | (Issued by) | (Valid until) | (Sex) | (Age) | (Incapacitation)

(Incapacitation *continued*) | (Limitations)

APPENDIX 5
INCAD/MEDIF Form *(continued from page 124)*

MEDICAL INFORMATION SHEET — (MEDIF)

(for official use only)

To be completed by ATTENDING PHYSICIAN

This form is intended to provide CONFIDENTIAL information to enable the airlines' MEDICAL Departments to assess the fitness of the passenger to travel. If the passenger is acceptable, this information will permit the issuance of the necessary directives designed to provide for the passenger's welfare and comfort.

The PHYSICIAN ATTENDING the incapacitated passenger is requested to ANSWER ALL QUESTIONS. Enter a cross "x" in the appropriate "yes" or "no" boxes, and/or give precise concise answers).

COMPLETING OF THE FORM IN BLOCK LETTERS OR BY TYPEWRITER WILL BE APPRECIATED.

- The form must be returned to:

(Carrier's Designated Office)

Airlines' Ref. Code MEDA01	PATIENT'S NAME, INITIAL(S), SEX, AGE:	
MEDA02	ATTENDING PHYSICIAN - Name & Address	
	- Telephone Contact	Business: / Home:
MEDA03	MEDICAL DATA: - DIAGNOSIS in details (including vital signs)	
	- Day/month/year of first symptoms:	Date of operation / Date of diagnosis
MEDA04	- PROGNOSIS for the flight(s):	
MEDA05	- Contagious AND communicable disease?	No ☐ Yes ☐ Specify:
MEDA06	- Would the physical and/or mental condition of the patient be likely to cause distress or discomfort to other passengers?	No ☐ Yes ☐ Specify:
MEDA07	- Can patient use normal aircraft seat with seatback placed in the UPRIGHT position when so required?	Yes ☐ No ☐
MEDA08	- Can patient take care of his own needs on board UNASSISTED* (including meals, visit to toilet, etc.)?	Yes ☐ No ☐ If not, type of help needed:
MEDA09	- If to be ESCORTED, is the arrangement satisfactory to you?	Yes ☐ No ☐ If not, type of escort proposed by YOU:
MEDA010	- Does patient need OXYGEN** equipment in flight? (If yes, state rate of flow)	No ☐ Yes ☐ ☐ Litres per Minute No ☐ Yes ☐ Continuous?
MEDA011	- Does patient need any MEDICATION*, other than self-administered, and/or the use of special apparatus such as respirator, incubator, etc.**?	(a) on the GROUND while at the airport(s): No ☐ Yes ☐ Specify:
MEDA012		(b) on board of the AIRCRAFT: No ☐ Yes ☐ Specify:
MEDA013	- Does patient need HOSPITALISATION? (If yes, indicate arrangements made or, if none were made, indicate "NO ACTION TAKEN")	(a) during long layover or nightstop at CONNECTING POINTS en route: No ☐ Yes ☐ Action:
MEDA014		(b) upon arrival at DESTINATION: No ☐ Yes ☐ Action:
MEDA015	- Other remarks or information in the interest of your patient's smooth and comfortable transportation:	None ☐ Specify if any**:
MEDA016	- Other arrangements made by the attending physician:	

NOTE(*): Cabin attendants are NOT authorized to give special assistance (e.g. lifting) to particular passengers, to the detriment of their service to other passengers. Additionally, they are trained only in FIRST AID and are NOT PERMITTED to administer any injection, or to give medication.

IMPORTANT: FEES, IF ANY, RELEVANT TO THE PROVISION OF THE ABOVE INFORMATION AND FOR CARRIER-PROVIDED SPECIAL EQUIPMENT(**) ARE TO BE PAID BY THE PASSENGER CONCERNED.

Date:	Place:	Attending Physician's Signature:

PASSENGER'S DECLARATION

"I HEREBY AUTHORIZE .....
(Name of nominated physician)

to provide the airlines with the information required by those airlines' medical departments for the purpose of determining my fitness for carriage by air and in consideration thereof I hereby relieve that physician of his/her professional duty of confidentiality in respect of such information, and agree to meet such physician's fees in connection therewith.

I take note that, if accepted for carriage, my journey will be subject to the general conditions of carriage/tariffs of the carrier concerned and that the carrier does not assume any special liability exceeding those conditions/tariffs.

I agree to reimburse the carrier upon demand for any special expenditures or costs in connection with my carriage."

(Where needed, to be read by/to the passenger, dated and signed by him/her or on his/her behalf.)

Place:	Date:	Passenger's Signature: