

BTS STATEMENT

Managing passengers with respiratory disease planning air travel: British Thoracic Society recommendations

British Thoracic Society Standards of Care Committee

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Air Travel Working Party

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Contents

Introduction

Need for recommendations for managing passengers with respiratory disease planning air travel

Purpose of recommendations

Methods of production

Summary of key points and recommendations

The flight environment and effects of altitude

Pre-flight assessment for adults

Hypoxic challenge testing

Pre-flight assessment for infants and children

Logistics of travel with oxygen

Logistics of travel with ventilator support

Disease-specific recommendations

Background literature review

The flight environment

Clinical pre-flight assessment in adults

Clinical pre-flight assessment in infants and children

Research questions

Appendices (A 1-7)

- Appendix 1 Reviewers
- Appendix 2 AHCPR grading scheme for recommendations
- Appendix 3 Referral centres with decompression chambers
- Appendix 4 Major destinations exceeding 8000 ft (2438 m)
- Appendix 5 Sample MEDIF form
- Appendix 6 Figures 1-4
- Appendix 7 Examples of equations for predicting hypoxaemia

References

INTRODUCTION

Need for new recommendations in 2010 for passengers with respiratory disease planning air travel

Since the first British Thoracic Society (BTS) recommendations published in 2002[1] and web update in 2004,[2] data from several studies have confirmed previous findings suggesting that neither resting sea level oxygen saturations nor FEV₁ reliably predict hypoxaemia, or complications during or after air travel in passengers with pulmonary disease.[3-7] It has therefore become clear that there is thus no reliable threshold for these variables which will enable clinicians to determine accurately the safety of air travel or the need for in-flight oxygen in an individual patient. Nevertheless, the need for practical recommendations remains, and there is thus an urgent requirement for new advice to guide physicians in this area. The 2010 guidance has been thoroughly revised, with completely new sections on bronchiectasis, cancer, co-morbidity with cardiac disease, hyperventilation and dysfunctional breathing, obesity, pulmonary arteriovenous malformations and sinus and middle ear disease, in addition to a considerably expanded section on infection.

Air travel remains popular. Although slightly down on the previous year, UK airports handled over 235 million passengers in 2008.[8] It is estimated that worldwide, around 2 billion passengers flew in 2006, 760 million of them internationally.[9] Despite ongoing security, economic and environmental concerns, air travel is likely to

remain convenient for many, and in the longer term passenger numbers are likely to increase further. Given the rising age of Western populations, the age of air travellers is also likely to increase, with greater propensity for medical impairment. Over 30 years ago it was already estimated that around 5% of commercial airline passengers had a pre-existing medical condition.[10]

With the introduction of ultra long haul flights, passengers will be exposed to a cabin altitude of up to 8000 ft for up to and in some cases exceeding 20 hours. As well as escalating the potential for inter-current medical incidents, since longer flights increase the odds of such an event, the associated physiological disturbances associated with moderate but prolonged hypoxia, prolonged immobility and protracted exposure to reduced barometric pressure remain unknown. One study in children has suggested that longer flights may be associated with an increased risk of oxygen desaturation, perhaps partly reflecting a progressive fall in cabin PO₂. [11]

There are still no established methods for quantifying in-flight medical emergencies.[12] However, a North American service offering expert assistance by radio link for in-flight medical emergencies which logs over 17,000 calls annually, calculates that respiratory events were responsible for 10-12% of calls annually in the period between 2004 and 2008, the third most frequently recorded diagnostic category (personal communication Dr Paulo Alves, MedAire Inc, 2009). Respiratory symptoms were also the third most frequent cause of medical diversion after cardiac and neurological events. Physicians should therefore be aware of the potential effects of the flight environment in passengers with lung disease. Since tourist coaches crossing high Alpine passes reach 10,000 ft (3048 m), moderate short-lived hypoxaemia is apparently usually well tolerated by individuals acclimatised at or near sea level. We nevertheless consider that greater awareness of the challenges presented by air travel enables physicians to encourage patients to fly safely wherever possible, thereby also increasing comfort and safety for fellow air passengers.

While pilots are subject to regular medical examination, passengers are not. For potential passengers with lung disease it is valuable for their physician to have recommendations for assessing their patients' fitness for air travel. Over ten years ago a UK-wide survey of respiratory physicians indicated many would welcome advice.[13] Other information sources include British and European,[14-16] North American and Canadian[17-18] COPD guidelines, a British aviation medicine

textbook,[19] supplements to the Aviation, Space & Environmental Medicine Journal[20-22] and air travel publications[23] However, these documents are not always readily accessible to physicians and not all provide consistent, practical or comprehensive coverage.

To meet the need for consistent, practical and comprehensive advice, the British Thoracic Society (BTS) Standards of Care Committee established an Air Travel Working Party and published the first national recommendations for managing patients with lung disease planning air travel in 2002. There was insufficient evidence to produce formal guidelines. The 2002 recommendations were updated (web-only) in 2004, but research published since then, as outlined above, led us to conclude that there is now a need to review existing advice, as well as expand it to include a broader range of pulmonary conditions.

As before, the following recommendations are an expert consensus view based on literature reviews and aim to provide practical advice for respiratory specialists in secondary care. Information for general practitioners and patients is available from the BTS website (www.brit-thoracic.org.uk). They apply to commercial flights only (including scheduled repatriation with a medical or nurse escort), and exclude emergency aeromedical evacuation situations. Medical practitioners should however be aware that, should they assist at an in-flight medical emergency, most airlines will indemnify them, the aircraft will have medical equipment, and in many cases they can access specialist advice such as MedAire's MedLink service.

Purpose of recommendations

These reflect the original aims set out in the 2002 and 2004 documents. In essence we aim to:

1. Enhance safety for passengers with lung disease travelling on commercial flights and reduce respiratory complications, whether they manifest as in-flight medical incidents or unscheduled use of healthcare resources while away or after returning
2. Promote further understanding among healthcare professionals that patients with respiratory disease may require clinical assessment and advice before air travel
3. Provide an authoritative up-to-date literature review of the latest available evidence
4. Provide consistent, practical and comprehensive advice for healthcare professionals managing these patients

5. Formulate key research questions to provoke further investigation. This in turn will help generate a strengthened, high quality evidence base from which clearer evidence-based guidelines can be proposed
6. Promote the development of methods for monitoring the size of the problem

Methods of production (including search terms)

As in 2002 and 2004, the Working Party defined the remit of the recommendations. Independent literature searches were performed by Working Party members and individual draft sections prepared, using where relevant the 2002 and 2004 documents as a starting point. From these draft sections a draft document was generated summarising the current evidence and containing recommendations regarding (1) the flight environment, (2) physiological effects of exposure to altitude, (3) clinical assessment, (4) respiratory disorders presenting a possible risk for potential air travellers, (5) oxygen supplementation. The document was reviewed by the Working Party and re-drafted before presentation at an Open Meeting at the 2009 BTS Winter Meeting. It was circulated to the BTS Standards of Care Committee (SOCC) and reviewers listed in Appendix 1. A final draft was then produced incorporating feedback after discussion and further review by the BTS SOCC.

The search engines used were Medline (English language) 1966-2009 and the Cochrane Library Database. The word titles were:

accidents, altitude, anoxia, aeroplane, aerospace medicine, AIDS, airplane, angina, anxiety, anxiety disorders, arrhythmia, aspirin, asthma, aircraft, aircraft emergencies, air travel, aviation, bronchiectasis, bronchitis, cabin pressure, cancer, cardiac failure, cardiac surgery, child, children, chronic bronchitis, chronic lung disease, COPD, coronary artery disease, cross infection, cystic fibrosis, decompression chamber, desaturation, diffuse parenchymal lung disease, dysrrhythmia, emergency/ies, emphysema, exercise testing, fibrosing alveolitis, fitness for air travel, fitness to fly, flight, heart failure, heparin, hereditary haemorrhagic telangiectasia, HIV, hyperventilation, hypoxia, hypoxic challenge, hypoxia inhalation simulation test/ing, hypoxia/c inhalation test, infection, infectivity, in-flight emergencies, influenza, inhalers, interstitial lung disease, ischaemic heart disease, kyphoscoliosis, lung diseases (restrictive), lung diseases (interstitial), malignancy, mycobacterium tuberculosis, myocardial infarction, nebulisers, neonate, newborn, neuromuscular disease, obstructive lung disease, obstructive sleep apnoea syndrome, opportunistic infections, oxygen, passenger, paediatric, panic, panic disorder, PAVMs, PCP

transmission, pediatric, peripheral oxygen delivery, pleural effusion, pneumothorax, pulmonary arteriovenous malformations, pulmonary metastasis, pre-flight test, pre-flight assessment, pulmonary fibrosis, pulmonary hypertension, pulse oximetric saturation, rehabilitation, respiratory failure, respiratory physiology, respiratory tract disease, respiratory tract infections, SARS, saturation, thoracic surgery, tissue oxygen delivery, travel, traveller, valvular disease, venous thromboembolism, walking test, warfarin

Conflicts of interest

All members of the Air Travel Working Party have submitted a written record of possible conflicts of interest to the British Thoracic Society Standards of Care Committee. These are available for inspection on request from the Chairman of this Committee. Preparation and publication of the document were paid for entirely by the British Thoracic Society and no external funding was received.

SUMMARY OF KEY POINTS WITH AHCPR GRADING

The flight environment and effects of altitude

Commercial aircraft are pressurised to cabin altitudes of up to 8000 ft (2438 m) although this ceiling may be exceeded in emergencies. Cabin altitudes in the Boeing 787 Dreamliner are anticipated to remain below 6000 ft (1829 m). At 8000 ft (2438 m) the partial pressure of oxygen falls to the equivalent of breathing 15.1% oxygen at sea level. In a healthy passenger the arterial oxygen tension (PaO_2) at 8000 ft (2438 m) is influenced by age and minute ventilation, but will fall to between 7.0 and 8.5 kPa (53-64mmHg, SpO_2 85-91%). Values when exercising or sleeping may be lower than this. Altitude exposure may thus exacerbate hypoxaemia in patients with pulmonary disease, and particular caution seems justified in those who are hypoxaemic at sea level. The physiological compensation for acute hypoxaemia consists of mild to moderate hyperventilation, limited by the fall in arterial carbon dioxide tension (PaCO_2), and a moderate tachycardia.

FEV_1 and SpO_2 provide useful information about the severity of the patient's condition. However, as noted previously, there is now considerable evidence suggesting that neither resting sea level oxygen saturations nor FEV_1 accurately predict hypoxaemia or complications during or after air travel in patients with pulmonary disease.[3-7] Whereas in 2002 and 2004 we made firm recommendations, employing SpO_2 and to a lesser extent FEV_1 , in decisions about whether a patient

required hypoxic challenge testing (HCT), it is now clear that there is no reliable threshold in these variables which enables clinicians to determine with accuracy the safety of air travel or the need for in-flight oxygen. Further research is required to determine whether a symptom-based approach, for example using the MRC dyspnoea scale[24], or exercise testing, might prove a more valuable tool.

Meanwhile healthcare professionals are frequently asked for advice, and recommendations are still required. We therefore suggest a practical approach to individuals who may be at increased risk of hypoxaemia or other complications of air travel. Physicians should take into consideration the patient's previous flight experience, the flight duration and destination and, if relevant, the time since the last exacerbation of their chronic condition. Generic advice should be given to all patients as detailed below (a patient information leaflet is available at www.brit-thoracic.org), and further evaluation carried out in those likely to be at greatest risk (see categories below) or about whom the physician is particularly concerned. In all cases the patient's usual care, such as bronchodilator therapy, should be optimised before air travel.

Complex patients can be referred for testing in a hypobaric chamber (see Appendix 3). Patients should be aware that even with in-flight oxygen and/or ventilator support, safety cannot be guaranteed. Air travel is almost always possible with appropriate medical support, but the logistics and economic costs may outweigh the benefits in individual cases. Ultimately it should be made clear that it is the patient's choice if they decide to fly. Patients should also be aware that the airline has the right to refuse carriage if the safety of the passenger is in doubt.

Pre-flight assessment for adults

If there is doubt about the fitness of the patient to fly, and especially if there are co-morbidities affecting fitness (such as cardiovascular disease or immunosuppressant therapy), assessment is recommended. In general the patient should be stable and have recovered from any recent exacerbation before travel. The following should be assessed with history and examination as a minimum:

- history of air travel intolerance with significant respiratory symptoms (dyspnoea, chest pain, confusion or syncope) (C)
- severe COPD or asthma (B)

- bullous lung disease (B)
- severe restrictive disease (including chest wall and respiratory muscle disease), especially with hypoxaemia and/or hypercapnia (C)
- patients with cystic fibrosis (C)
- co-morbidity with other conditions worsened by hypoxaemia (cerebrovascular disease, cardiac disease or pulmonary hypertension) (C)
- pulmonary tuberculosis (C)
- within six weeks of hospital discharge for acute respiratory illness (C)
- recent pneumothorax (B)
- risk of or previous venous thromboembolism (B)
- pre-existing requirement for oxygen, CPAP or ventilator support (C)

Advance planning is essential. Patients and/or their carer(s) must:

- Book any extra services required with the airline in advance including in-flight oxygen, wheelchairs, and formalise any agreement to take on board nebulisers or ventilators including CPAP machines. (C) Airlines may charge varying fees for such services; information is available from the Grown Up Congenital Heart Patients Association (www.guch.org.uk), the Pulmonary Hypertension Association (www.phassociation.org) and the US National Home Oxygen Patients Association (www.homeoxygen.org)
- Arrange medical insurance where possible. If medical insurance is declined and/or patients travel without it, they must be aware of the costs of emergency treatment and repatriation (C)
- Ensure an adequate supply of prescription medicines in carry-on and checked baggage. (C) At the time of writing a doctor's letter is required for paediatric liquid medicines in excess of 100ml taken into the aircraft cabin
- Obtain a doctor's letter if taking unusual, numerous, trial or controlled medication, syringes and/or needles, or if patients have metallic implants (such as coils inserted during bronchial or pulmonary artery embolisation) (C)
- Arrange vaccinations if required (advice for healthcare professionals is available at www.travax.scot.nhs.uk with consistent patient advice at www.fitfortravel.nhs.uk) (B)
- Ask their physician whether an emergency supply of antibiotics, with or without prednisolone, are required (C)
- Use flight hosiery with or without anticoagulation as outlined below if at increased risk of venous thromboembolism (VTE) (C)

- Consider reserving an aisle seat near the restrooms (C)
- Keep mobile, using exercises if not occupying an aisle seat, and well hydrated (C)
- Avoid or minimise alcohol use and sedatives (C)

Frequent Traveller's Medical Card (FREMEC)

Patients with medical needs who fly frequently can obtain a FREMEC which contains important medical information. This card replaces forms otherwise necessary for every flight. Once registered, the reservations office keeps requirements on record so that special assistance can be arranged whenever the patient flies. FREMEC is issued by many airlines and the period of validity is dependent on the nature of the condition. If a patient chooses to fly with an airline other than that which issued the FREMEC card they should confirm its validity with the new airline.

Contraindications to commercial air travel

- infectious tuberculosis (B)
- an untreated pneumothorax (C)
- major haemoptysis (C)
- usual oxygen requirement at sea level at a flow rate exceeding 4L/min (C)

Hypoxic challenge testing (HCT)

The role of HCT may have been overstated in the past, and further research is required to determine its place in assessing respiratory patients planning air travel. In the meantime, there is no evidence to justify amending previous recommendations for patients in whom the physician considers a hypoxic challenge test is required. The UK Flight Outcomes Study showed that, even in centres with an interest in this area, only 10% of British patients undergo a walk test as part of their fitness to fly assessment.[6] We have therefore removed the reference to walk testing. The recommended course of action, depending on the outcome of HCT, is shown in table 1, with SpO₂ thresholds included for units who prefer to use saturations rather than arterial blood gas estimations. Normal temperature and PaCO₂ are assumed; in cases of hyperventilation caution is needed in interpreting the results. Where there is doubt, it seems sensible to err on the side of recommending oxygen.

Table 1 Results of hypoxic challenge test (15% FiO₂ for 15 minutes) with AH CPR grading (Appendix 2)

Hypoxic challenge test result	Recommendation
<ul style="list-style-type: none"> • PaO₂ ≥ 6.6 kPa (> 50 mmHg) or SpO₂ ≥ 85% 	In-flight oxygen not required (B)
<ul style="list-style-type: none"> • PaO₂ < 6.6 kPa (< 50 mmHg) or SpO₂ < 85% 	In-flight oxygen required at 2L/min via nasal cannulae (B)

Pre-flight assessment for infants and children

- For infants born at term (>37 weeks) it is prudent to wait for one week after birth term (corrected gestational age 40 weeks) before flying to ensure they are healthy (C)
- Infants born prematurely (<37 weeks) with or without a history of respiratory disease who have not yet reached their expected date of delivery do not require HCT, which is unreliable in this group,[25] but should have oxygen available during the flight and delivered between 1 and 2 L per minute in the event of becoming symptomatic or the SpO₂ falling <85% as measured by in-flight pulse oximetry (B)
- Infants with a history of neonatal chronic respiratory problems should be discussed with a specialist respiratory paediatrician and HCT performed. In the light of recent evidence it is advised that infants with SpO₂ <85% on testing should have supplementary in-flight oxygen available (C)
- In children with cystic fibrosis (CF) or other chronic lung disease who are old enough to do spirometry and who have FEV₁<50% predicted, hypoxic challenge testing is recommended as described in Box A (B)
- Infants and children who are oxygen dependent at sea level will need their oxygen flow rate doubled at cruising altitude and should not need HCT (B)
- Infants and children who have had oxygen stopped in the last six months should have HCT (C)

Box A Hypoxic challenge testing in infants or young children

The infant or young child, receiving oxygen via nasal cannulae, is placed in a whole body box with a parent or carer, and SpO₂ monitored for 15 to 20 minutes. The air in the body-box is then diluted to 15% oxygen with nitrogen. If SpO₂ falls below 85%, supplementary in-flight oxygen is recommended. The flow required is determined by the oxygen flow, which restores SpO₂ to the original value. This will usually be between 1 and 2 litres per minute. Where whole body box facilities are not available, a tight-fitting non-rebreathing facemask may be used through which high flow 14% oxygen is administered, although this may not be as reliable as the body box technique. In older children, hypoxic challenge testing may be performed using a mouthpiece rather than in the body box. Provision of in-flight oxygen must then be discussed with the airline.

Logistics of travel with oxygen

- Oxygen-dependent patients can fly
- Patients can take their own small, full cylinders on board, but this must be agreed with the airline in advance and patients should know whether their equipment is insured against loss and/or damage
- If additional oxygen is required, it is usually supplied by the airline and must be booked in advance. The airline medical department will issue a MEDIF form (see www.iata.org or Appendix 5) or their own medical form. This requires completion by the patient and GP or hospital specialist, with information about the patient's condition and oxygen requirements. The airline's Medical Officer or External Advisors will then evaluate the patient's needs
- The airline must be consulted in advance if humidification equipment is required
- Airlines will only provide supplementary oxygen on board the aircraft
- In-flight oxygen is usually prescribed at a rate of 2L or 4L/min and should be given by nasal cannulae. For patients requiring oxygen only at altitude, it need not be switched on until the plane is at cruising altitude (when the seatbelt signs are switched off), and can be switched off at the start of descent (when the seatbelt signs are switched on). For patients on oxygen at sea level, the rate should only be increased while at cruising altitude

- Some airlines do not permit use of supplemental oxygen during take-off or landing; patients requiring oxygen at sea level should therefore be discussed first with the airline
- Many airlines now use pulsed dose (breath-activated) systems. Some devices may pose problems for frail, very young (less than 6 years) or very small (\leq approximately 13kg) passengers who often have irregular or shallow breathing patterns. It would be prudent either to ensure such patients can activate the system before travelling, or agree an alternative with the airline
- Lightweight battery operated portable oxygen concentrators (POCs) are now used by many patients, and many airlines allow their use on board. In the United States there is legislation specifically allowing certain types for use in all phases of flight (summary available at <http://rgl.faa.gov>). Currently only the AirSep LifeStyle POC and Inogen One POC units are permitted. Enough batteries for the flight and possible delays must be taken, and the airline must be informed in advance of travel
- The need for oxygen on the ground and while changing flights must be considered, as airlines do not provide oxygen for use at airports. A direct flight is thus preferable. If connecting flights are unavoidable, separate arrangements must be made for oxygen whilst on the ground during stopovers. The main oxygen distributors have their own international distribution network and can supply oxygen at intended destinations if active in those areas. A charge is likely to be made for this service

Logistics of travel with ventilator support

- Ventilator-dependent patients should inform the airline of their requirements at the time of reservation, and a doctor's letter is required outlining the diagnosis, necessary equipment, recent blood gas results and ventilator settings. A medical escort is required for fully dependent (intubated) patients as the ventilator may have to be switched off for take-off and landing and the patient ventilated manually. Arrangements must be made for proceeding through air terminals before and after the flight

Disease-specific recommendations

Asthma and COPD

- FAA and European regulations mandate inclusion of a bronchodilator inhaler in the aircraft emergency kit[26] on aircraft registered in Europe or the USt. For an acute exacerbation on board the patient's own bronchodilator inhaler (or airline emergency kit inhaler if available) should be administered and the dose repeated until symptomatic relief is obtained. A bronchodilator administered via a spacer is as effective as a nebuliser.[27] While many airlines permit use of dry cell battery operated nebulisers (except during take-off and landing) passengers must check in advance.[28] Nebulisers are not included in the airline medical kit because the aircraft oxygen system cannot provide the high flow rates needed to ensure correct dose delivery, and compressor devices are heavy and bulky[29]
- Patients with severe or brittle asthma, or severe COPD, should consult their respiratory specialist beforehand and consider taking an emergency supply of prednisolone in their hand luggage in addition to supplies of their usual medications

Bronchiectasis

- Neither nebulised antibiotics nor nebulised bronchodilators should be required on board

Cancer

- Anaemia should be corrected (to Hb \geq 8.5 g/dl) before air travel; hyponatremia, hypokalaemia and hypercalcaemia should also be corrected
- Patients with major airway obstruction, including upper airways stridor, should have completed treatment (radiotherapy, chemotherapy and/or stenting) before travel. Sufficient time should have elapsed to enable the physician to confirm stability
- Patients with lymphangitis carcinomatosa or superior vena caval obstruction (SVCO) are likely to be very dyspnoeic, and those with SVCO may be in poor physical condition. Air travel should be undertaken only if essential and in-flight oxygen should be available
- Where possible large pleural effusions should be well drained before travel
- Patients with major haemoptysis should not fly
- A doctor's letter is required for patients taking controlled drugs, with details of the patient's name, address, date of birth, outward and return dates of travel, the country being visited and the drugs being carried, including doses and

total amounts. The patient, carer or physician should also consult the Home Office website to determine local controlled drug importation rules (www.homeoffice.gov.uk)

- Neutropenic patients should be made aware of the risk of infection (and its peak timing after chemotherapy) arising from close proximity to other passengers, whether on the ground or in the air
- Patients should not fly within 24 hours of a seizure. The patient and carer(s) should be aware that medical insurance is likely to be refused if the patient has cerebral metastases, and that the cost of repatriation would be significant

Cardiac disease

It is anticipated that the British Cardiovascular Society will shortly publish detailed guidance on the safety of air travel with cardiac disease. Meanwhile physicians should use their discretion to undertake HCT or recommend in-flight oxygen for patients with co-existent cardiac and pulmonary disease. Where measured haemodynamics or correlates of ventricular function are more severe than symptoms would suggest, physician discretion should determine the use of in-flight oxygen. We have made the following specific recommendations.

Coronary artery disease

At 8000 ft (2438 m) there is a 5% fall in ischaemic threshold (measured as the product of heart rate and systolic blood pressure at the electrocardiographic threshold for ischaemia).[30]

- Patients who have undergone elective percutaneous coronary intervention can fly after two days
- Patients at low risk after ST-elevation myocardial infarction (STEMI), namely restoration of TIMI grade 3 flow on angiography, age < 60, no signs of heart failure, normal ejection fraction and no arrhythmias, can fly within three days
- The remainder of patients with STEMI may travel after ten days unless awaiting further investigation or treatment, such as revascularisation or device implantation. For patients with complications, such as arrhythmias or heart failure, advice in the relevant section below should be followed
- Patients with non ST-elevation myocardial infarction (NSTEMI) should undergo angiography and revascularisation before considering air travel

- Patients who have undergone uncomplicated coronary artery bypass grafting should be able to fly within 14 days but must first have a CXR excluding pneumothorax
- Patients with stable angina up to Canadian Cardiovascular Society (CCS) functional class III are not expected to develop symptoms during commercial air travel
- Patients with CCS functional class IV symptoms (defined as the inability to carry on any activity without discomfort), who may also get stable angina at rest, should be discouraged from flying. If air travel is essential they should receive in-flight oxygen at 2 l/min and a wheelchair is advisable
- Patients with unstable symptoms of ischaemic heart disease should not fly

Cyanotic congenital heart disease

- Physicians should use their discretion in deciding whether to perform HCT and/or advise in-flight oxygen
- Those in NYHA functional class IV should avoid air travel unless essential. If flying cannot be avoided they should receive in-flight oxygen at 2L/min

Heart failure

- Patients who are hypoxaemic at sea level, with co-existent lung and/or pulmonary vascular disease, should be considered for assessment with HCT
- Patients in New York Heart Association (NYHA) functional class I-III (without significant pulmonary hypertension) can fly without oxygen
- Patients with severe disease in New York Heart Association (NYHA) functional class IV should not fly unless absolutely essential. If air travel cannot be avoided they should have in-flight oxygen at 2L/min

Hypertension

- Patients with severe, uncontrolled hypertension should have it controlled before embarking on commercial air travel

Pulmonary hypertension

- Those in NYHA functional class I-II can fly without oxygen
- Those in NYHA functional class III-IV should receive in-flight oxygen

Rhythm disturbance, pacemakers and defibrillators

- Patients with unstable arrhythmias should not fly
- Modern pacemakers and defibrillators are compatible with aircraft systems
- Patients with high-grade premature ventricular contractions (\geq Low Grade 4b) should be discouraged from flying, but at the physician's discretion, may fly with continuous oxygen at 2 l/min

Valvular disease

- Patients with valvular disease causing functional class IV symptoms, angina or syncope, should use in-flight oxygen at 2 L/min if air travel is essential

Hyperventilation and dysfunctional breathing

- Patients with a diagnosis of hyperventilation, dysfunctional breathing and/or panic disorders should have full assessment before travel by a clinician skilled in managing these disorders, and appropriate breathing modification exercises and/or pharmacotherapy should be instituted to control the condition before air travel is attempted
- Where there is any doubt as to the cause of breathlessness during a flight, oxygen should be given and skilled medical assistance arranged as soon as possible
- Re-breathing techniques may be used on-board for acute hyperventilation
- Pre-flight evaluation of the patient's response to rapidly acting anxiolytics is advised before air travel

Airborne infections

- For patients with acute and chronic respiratory infections, pre-flight assessment is advised
- Patients with infectious TB must not travel by public air transportation until rendered non-infectious. World Health Organisation (WHO) guidelines state that three smear negative sputum examinations on separate days in a person on effective anti-tuberculous treatment indicate an extremely low potential for transmission, and a negative sputum culture result virtually precludes potential for transmission.[31] This may be over-cautious. While this remains the policy for HIV positive patients, HIV negative patients in whom drug resistant TB is not suspected and who have completed two weeks of effective anti-tuberculous treatment are in practice generally considered non-infectious

- The latest web-based guidelines (national and/or international) should be consulted with regard to travel restrictions related to cases or contacts of patients with respiratory viral infections of high mortality, such as SARS. This is especially important for any outbreak of an emerging respiratory infection. Regular updates are available on the WHO site (www.who.int)

Human immunodeficiency virus (HIV) infection

- HIV positive passengers should check with the Embassy of the country they are visiting for any visa requirements or travel restrictions before they fly
- General measures will help minimise the risk of exposure to blood-borne viruses and are appropriate for all settings where passengers are bleeding, whether or not they are HIV positive. Extensive guidance on such measures is available from the UK Department of Health (www.dh.gov.uk)
- Some HIV positive passengers are at risk of developing opportunistic infection (OI). Patients are usually not deemed fit to travel during the acute phase of an opportunistic infection
- The physician caring for the patient should advise whether a patient who has been treated for a specific OI is fit to travel based on their clinical condition and patient needs. Airline guidance should also be sought
- For advice on pre flight vaccination physicians should consult current British HIV Association guidelines[32] (available at www.bhiva.org)
- Patients should carry a supply of antivirals and other medication in their carry on luggage. If they forget to take their antiviral dose they should take their next dose as soon as practicable and then revert to their normal schedule

Interstitial lung disease

- Patients should be carefully assessed before travel as previously described
- Oxygen should be considered for those staying at high altitude destinations
- An emergency supply of antibiotics with or without prednisolone would appear prudent, together with medical advice on managing steroid dose during intercurrent illness if the patient is already taking oral corticosteroids

Neuromuscular disease and kyphoscoliosis

- All patients with severe extra-pulmonary restriction should undergo HCT before travel

- The decision to recommend in-flight oxygen and/or NIV for these patients must be made on an individual clinical basis

Obstructive sleep apnoea syndrome

- A doctor's letter is required outlining the diagnosis and necessary equipment. It should state that the CPAP machine should travel in the cabin as extra hand luggage (some airlines treat this as excess luggage). A fact sheet for passengers to show airport security personnel is available from the American Sleep Apnea Association (www.sleepapnea.org)
- Alcohol should be avoided before and during the flight
- Dry cell battery-powered CPAP can be used during the flight except during take-off and landing
- On some flights it may be possible to power CPAP using an aircraft power outlet via an appropriate adaptor, but the passenger must check with the airline in advance
- CPAP machines used in-flight should be capable of performing adequately in the low pressure cabin environment
- Patients should ensure that their CPAP machine is compatible with the altitude and power supply at their destination, and that the power supply is within reach of the bed

Obesity

- Obese passengers may have difficulty fitting into standard airline seats and should check in advance with the airline that one seat is sufficient. Those with a BMI > 30 kg/m² should be considered as at moderately increased risk of VTE and follow the advice given for those travelling for more than 4 hours

Pneumothorax

- Patients with a closed pneumothorax should not travel on commercial flights (with the exception of the very rare case of a loculated or chronic localised air collection which has been very carefully evaluated)
- Patients who have had a pneumothorax must have had a CXR confirming resolution before flight. Many would regard it as prudent for a further seven days to elapse before embarking upon flight. In the case of a traumatic pneumothorax the time period following full radiographic resolution should preferably be two weeks

- A definitive surgical intervention undertaken via thoracotomy is likely to be entirely successful and patients should be allowed to fly once they have recovered from the effects of their surgery. A similar intervention undertaken by via video-assisted thoracoscopic surgery will similarly be expected to have a high success rate but cannot be regarded as definitive, and these patients should be aware of a slight risk of recurrence
- Patients having other forms of attempted pleurodesis and those not undergoing attempted pleurodesis after a previous pneumothorax are unlikely to have further episodes precipitated by flight; however spontaneous recurrence could have significant consequences given the absence of prompt medical care. This risk of recurrence is higher in those with coexisting lung disease and does not decline significantly for at least one year. Those not undergoing a definitive surgical procedure may therefore wish to consider alternative forms of transport
- Patients with lymphangioleiomyomatosis (LAM) should be advised that they are at increased risk of pneumothorax and that any unusual clinical symptoms such as chest pain or breathlessness before flight should preclude air travel

Pulmonary arteriovenous malformations (PAVMs)

- For PAVM patients in whom embolisation treatment is planned, delay to non-medical flights is advised until embolisation is completed
- PAVM patients without significant hypoxaemia should be considered as at moderately increased risk of VTE and follow the advice below
- PAVM patients with severe hypoxaemia and no previous events should receive in-flight oxygen and a single pre-flight dose of low molecular weight heparin on outward and return journeys
- PAVM patients with a previous VTE or embolic stroke should receive a single dose of low molecular weight heparin before outward and return journeys
- PAVM patients with severe hypoxaemia and previous embolic strokes should be informed of the increased risk of VTE on flights exceeding 8 hours

Sinus and middle ear disease

- Adults with risk factors for sinus or middle ear barotrauma (mucosal oedema, bacterial infection, thick mucin, intra-and extra-sinus pathology and tumours) should receive an oral decongestant before the flight, and a nasal decongestant spray during the flight just before descent. Women in the first

trimester of pregnancy may wish to avoid topical decongestants and take intranasal steroids instead

- Passengers who develop sinus barotrauma after air travel should receive topical and oral decongestants, analgesics and oral steroids. Antibiotics are advised if a bacterial sinusitis is thought to be the trigger and antihistamines if allergic rhinitis is suspected
- All symptoms and signs of barotrauma should have resolved before flying again; some recommend plain radiography to ensure that mucosal swelling has settled. This usually takes at least a week and may take up to 6 weeks
- Recurrent sinus barotrauma is usually only seen in military aircrew and has been shown to respond to functional endoscopic sinus surgery

Thoracic surgery

- In patients who have undergone thoracic surgery requiring drain insertion, CXR should be performed after drain removal to ensure full expansion of the lung
- Patients who have a pneumothorax after drain removal should not travel on commercial flights until full re-expansion has been confirmed on a chest film
- If the post drain removal CXR confirms full re-expansion, it would be prudent to wait for seven days before embarking upon air travel
- Any symptoms or signs suggesting the possibility of a pneumothorax post drain removal should prompt a further CXR before air travel

Venous thromboembolism

The evidence in this area is unclear, current guidelines conflicting and recommendations controversial. Patients are typically stratified into three groups, but physicians may wish to make decisions on an individual case by case basis, as the evidence for any particular recommendation is limited and firm guidelines cannot be formulated. The risk of VTE is greatest on flights lasting over four hours, and is reduced if passengers occupy an aisle seat.

Low risk for VTE: all passengers not in the categories list below

- Passengers should avoid excess alcohol and caffeine-containing drinks, and preferably remain mobile and/or exercise their legs during the flight

Moderately increased risk of VTE: family history of VTE, thrombophilia, obesity (BMI > 30 kg/m²), height > 1.90 m or < 1.60 m, significant medical illness within previous six weeks, cardiac disease, immobility, pregnancy or oestrogen therapy (including hormone replacement therapy and some types of oral contraception) and post-natal patients within two weeks of delivery

- These patients should be advised to wear below knee elastic compression stockings in addition to recommendations for low- risk passengers. In addition, they should be advised against the use of sedatives or sleeping for prolonged periods in abnormal positions. Passengers with varicose veins may be at risk of superficial thrombo-phlebitis with use of stockings, and the risk/benefit ratio here is unclear

Greatest increased risk of VTE: past history of idiopathic VTE, those within six weeks of major surgery or trauma, and malignancy.

- Pre-flight prophylactic dose low molecular heparin is advised, or formal anticoagulation to achieve a stable INR between 2 and 3, for both outward and return journeys. The recommendations are in addition to the general advice for those at low to moderate risk
- There is no evidence to support the use of low or high-dose aspirin
- Patients who have suffered a VTE should ideally not travel for four weeks or until proximal (above-knee) deep vein thrombosis has been treated and symptoms resolved, with no evidence of pre- or post-exercise desaturation

BACKGROUND LITERATURE REVIEW

The flight environment

To understand fully the implications of air travel on clinical patho-physiology it is necessary to have some familiarity with the physical environment in which they will travel. Thus an appreciation of the nature of the atmosphere and the physical consequences of ascent to altitude are essential.

The atmosphere can be considered as a series of concentric “shells” around the Earth. These are not of equal or constant depth but since most flight occurs within the innermost shell, the troposphere, the model will suffice for our purposes. The troposphere extends from sea-level to an altitude of 36,069 ft (10,980 m) at temperate latitudes, 26,000 ft (7925 m) at the poles and up to 60,000 ft (18,288 m) at the equator.

The troposphere is characterized by a relatively constant decline in temperature on ascent, at a rate of 1.98 °C/1000 ft. until the edge of the troposphere, the tropopause, is reached. Above that altitude the temperature remains constant at -56 °C. Although the decline in temperature is at a constant rate the reduction in atmospheric pressure is more complex, declining in an exponential manner. Sea-level pressure is defined for the purpose of standardisation as 760 mmHg, and the essentially exponential reduction in ambient pressure on ascent means that atmospheric pressure has halved at 18,000 ft and approximately halves again every further 18,000 ft of ascent (see Fig 1). One of the effects of this manner of change in barometric pressure is that even a relative modest ascent will result in a more pronounced reduction in ambient, atmospheric pressure than might be anticipated.

The chemical composition of the atmosphere in the troposphere is quite constant; oxygen 21%, nitrogen 78% and 1% other gases (including argon and carbon dioxide, the latter present at a concentration of just 0.03%). Thus, it is the fall in the partial pressure of oxygen as total ambient pressure falls on ascent that gives rise to hypobaric hypoxia, not a fall in the percentage of oxygen within atmospheric air.

The changes in pressure and temperature have other physical effects, as suggested by the gas laws. Since body temperature remains essentially constant the consequences of a fall in ambient temperature induce fewer adverse consequences for most occupants of aircraft than the change in ambient pressure. Boyle's law

predicts that as pressure falls the volume of a gas will increase proportionately (at a constant temperature). This inverse relationship is of great significance for all who fly; indeed the effects of the pressure reduction on gas volumes is slightly more marked than that predicted by Boyle's law for body cavities containing gas saturated with water vapour. Relative expansion of humidified gas is expressed as follows:

$$\frac{[\text{Initial pressure of the gas in the cavity at sea-level (mmHg)} - 47 \text{ mmHg}]}{[\text{final pressure of gas in the cavity (mmHg)} - 47 \text{ mmHg}]}$$

where 47 mmHg is water vapour pressure at 37°C. Assuming sea level atmospheric pressure of 760 mmHg and atmospheric pressure of 565 mm Hg at 8000 ft, this equation becomes:

$$(760-47) / (565-47) = 713/518 = 1.38$$

This means a 38% expansion for a humidified gas, compared with 34% for a dry gas. This effect arises in all gas filled cavities of the body, but in the lungs there is relatively free communication with cabin air so that gas trapping is rarely of serious concern. However, in cavities in which gas communication is more limited, for instance the middle ear and sinuses, problems can occur on both ascent and descent. Gas expansion can also cause mild intestinal discomfort, with expansion of gastric and colonic gas but is more troublesome if gas has developed in other areas of the gastrointestinal tract. Thus exposure to altitude during a gastrointestinal disturbance can exacerbate symptoms. Inflammation of the ears or sinuses can be markedly exacerbated by ascent. Other gas pockets, such as may occur with a dental abscess, are also likely to become more troublesome at altitude.

Commercial aircraft commonly cruise at altitudes of around 38,000 ft, in order to avoid air turbulence and reduce drag on the aircraft, thereby improving fuel economy. Aircraft cabins must therefore be pressurised so that the effective altitude to which occupants are exposed is much lower than that at which they flying. Commercial aircraft are not pressurised to sea-level, but to a relatively modest intermediate cabin altitude. This is for reasons of weight and cost, and also because of concerns about shortening the working life of the aluminium airframe. Aircraft cabin altitudes can thus approach 8,000 ft (2438 m) while the aircraft is flying at 38,000 ft (11,582 m), and a pressure differential exists across the cabin wall, commonly of up to 9 pounds per square inch (psi) in aircraft currently in service. International aviation regulations[33] stipulate that at a plane's maximum cruising altitude, the cabin altitude should not

exceed 8000 ft (2438 m) except in an emergency. Thus almost all current commercial aircraft operate to maximum, although it may not be reached in all flights, especially short ones. One study of in-flight cabin altitudes on 204 scheduled commercial aircraft flights reported significant variations in cabin altitude.[34] In future, the Boeing 787 Dreamliner is expected to operate with a maximum cabin altitude of just 6000 ft (1829 m). The benefit of adopting a lower cabin altitude is supported by the results of a study sponsored by the aircraft manufacturer, which reported an increased incidence of subject discomfort after exposure to 7000-8000 ft over periods of 3-9 hours.[35]

In the event of cabin decompression at high altitude, all occupants require immediate supplemental oxygen to prevent dangerous hypoxia. Commercial aircraft are thus equipped with an emergency oxygen system for passengers, demonstrated before every flight in accordance with civil aviation regulations. The emergency oxygen supply is sufficient to protect a healthy individual from dangerous hypoxia for approximately 15 minutes. In that time the flight crew are expected to descend the aircraft to a less hazardous altitude. However, some passengers with impaired respiratory function may be unusually susceptible to the effects of ascent even to normal cabin altitudes. It is these problems that are addressed here. These recommendations apply only to larger, commercial aircraft and not to small, private or un-pressurised aircraft operating under general aviation regulations.

Clinical pre-flight assessment in adults

An audit of 109 applications for in-flight oxygen conducted by a major UK airline showed that they are rarely provided with objective information to assess risk, only 61% of requests including simple data such as oximetry or spirometry results (M Popplestone, personal communication, 2004). In the absence of such information, airlines traditionally favour the 50 metre walk test. Other procedures used to assess whether patients are fit to fly are predicting hypoxaemia from equations, and the hypoxic challenge test (HCT).

The 50 metre walk

The ability to walk 50 metres without distress has the merit of being simple, but is often the only subject of enquiry and not verified. There is no evidence validating this test. Although it may seem a crude assessment, the ability to increase minute ventilation and cardiac output in response to an exercise load is a good test of cardiorespiratory reserve. It is also a common-sense approach to simulating the

stress of the additional hypoxaemia patients will experience at rest during a flight. Respiratory physicians have experience of the value of walk tests in other contexts, including the six or 12 minute walk and the shuttle walk test.[36-38] Such tests are now commonly used when assessing patients for lung volume reduction surgery and lung transplantation.

If performed, the walk test should be that used in the laboratory where the assessment is performed. Failure to complete the task (whether distance or time), or moderate to severe respiratory distress as recorded on a Visual Analogue Scale, will alert physician and patient to a possible need for in-flight oxygen. Walk tests are clearly not suitable for those with significantly impaired mobility.

Predicting hypoxaemia from equations

Some centres use one of several equations predicting PaO₂ or SpO₂ from measurements at sea level.[39-43] The equations have been derived almost exclusively from patients with COPD who have had PaO₂ measurements made in a hypobaric chamber, or before and during exposure to simulated altitude while breathing 15% inspired oxygen from a reservoir bag. Measuring FEV₁ may improve the accuracy of predicted values.[40,41] One weakness is that the 90% confidence limits are ± 1 kPa ($\sim \pm 2-4\%$ SpO₂). However, the predictions are usually reliable enough to establish upper and lower thresholds for 'no in-flight oxygen required'. Flight duration and cabin conditions are obviously not reproduced.

Hypoxic challenge test (HCT)

The ideal test, which is to expose a subject to hypoxia in a hypobaric chamber, is not widely available. The HCT as described by Gong[42] is therefore often used. It assumes that breathing hypoxic gas mixtures at sea level (normobaric hypoxia) equates to the hypobaric hypoxia of altitude.[44] The maximum cabin altitude of 8000 ft (2438 m) can be simulated at sea level with a gas mixture containing 15% oxygen in nitrogen. Subjects are usually asked to breathe the hypoxic gas mixture for 20 minutes or until equilibration. Saturation is monitored throughout, and arterial blood gases (or SpO₂ if unavailable) measured before and on completion.

Fifteen percent oxygen can be administered in several ways. Oxygen and nitrogen can be mixed in the appropriate proportions in a Douglas bag, or cylinders of 15% oxygen in nitrogen can be purchased. The gas mixture can be given via a non-re-breathing valve, through either a mouthpiece or a tight-fitting face mask. It is also

possible to fill a modified body plethysmograph with a gas mixture containing 15% oxygen to provide the hypoxic environment without the need for either a face mask or mouthpiece.[45] This allows oxygen requirements to be titrated accurately using nasal prongs to supply oxygen to the patient within the body box. A similar but unpublished suggestion is to use a hood over the subject's head, which is filled with 15% oxygen. Finally, similar levels of hypoxic gas mixtures can be given with a commercial 40% venturi mask if 100% nitrogen is used as the driving gas. The entrained air dilutes the nitrogen, producing a 14-15% oxygen mixture under experimental conditions in subjects with a range of respiratory conditions.[46] Although probably inferior to a modified body plethysmograph, the venturi mask method is inexpensive and well tolerated.[47]

A subject is usually judged to require in-flight oxygen if the PaO_2 falls below 6.6 kPa (50 mmHg) or SpO_2 falls below 85%.[45] These figures appear arbitrary, with little supporting evidence, but many physicians have adopted them as a reasonable compromise. A study of 131 patients[48] has shown that for patients with a resting sea-level $\text{SpO}_2 >95\%$ there was no desaturation below 90% during HCT. The data suggested that all patients with sea-level $\text{SpO}_2 <95\%$ should undergo HCT as some patients without any existing predefined risk factors showed significant desaturation during hypoxic challenge. A recent study by Akerø *et al* [7] suggests that simple SpO_2 measurement is insufficient in COPD to identify patients who require in-flight oxygen. Kelly and colleagues[49] suggested that other measurements such as carbon monoxide transfer factor (TLCO) provide additional information which improve the ability to predict the response of COPD patients to altitude. As with prediction equations, flight duration and cabin conditions are not reproduced during HCT, but Akerø *et al* [50] showed that during a commercial flight lasting over 5 hours, 18 patients with COPD showed an initial reduction in PaO_2 which then remained stable throughout the flight. HCT is the pre-flight test of choice for patients with hypercapnia, but there are few published studies examining how hypercapnia influences fitness to fly.

Several studies published since 2004 have consistently confirmed previous data suggesting that neither resting sea level oxygen saturations nor FEV_1 reliably predict hypoxaemia or complications during or after air travel in patients with pulmonary disease.[3-7] There is thus no reliable threshold in these parameters which enables clinicians to determine with accuracy the safety of air travel or the need for in-flight oxygen. The original 2002 and 2004 recommendations were therefore in many cases

probably too conservative, although there may be situations where physicians may wish to assess patients more fully than previously advised, for instance patients with neuromuscular or interstitial lung disease.

In the absence of a better test, HCT is probably still the method of choice, but there is arguably a need for research to better define the role of walk tests. There is also a need for research to determine the potential value of a symptom-based approach, for example using the MRC dyspnoea scale.[24] There is no evidence to support changes to our original recommendations following the outcome of HCT.

Clinical pre-flight assessment in infants and children

The true incidence of in-flight paediatric respiratory emergencies is unknown as there is no national or international central registry. One study has reported over an eight-year period for a single US commercial airline 169 paediatric emergencies of which 22 were respiratory in origin.[51] The presence of pre-existing lung disease in these individuals was not reported. Since the first BTS recommendations in 2002 and 2004[1,2], evidence has accumulated to show that there is an increased risk of symptomatic hypoxia in very young infants, especially preterm infants, who fly.[52] Some of this evidence has contributed to recently revised guidelines published in the US[20] and Canada.[53]

The physiology of the child's lungs differs from that of adults. In particular, during early life compliance is lower, while residual volume and airway resistance are higher.[54] In the neonatal period regional lung perfusion may remain labile, with estimates of a persistent 10% right to left pulmonary shunt in healthy infants at one week of age.[55] Foetal haemoglobin is present in significant amounts up to three months of age. Its effect on the oxygen dissociation curve is to enhance oxygen loading in a hypoxic environment but possibly to decrease unloading in peripheral tissues.[56] Some of these factors may explain why the response to a hypoxic environment is less predictable in infants than it is in adults. There are few data on the SpO₂ in normal healthy infants and children exposed to cabin altitudes. A study by Lee et al [11] examined SpO₂ in 80 children 6 months to 14 years (43 boys) during prolonged commercial air travel. Saturation declined significantly during flight. Average sea level SpO₂ was 98.4%, falling to 95.7% after three hours and to 94.4% after seven hours. This was associated with reduced cabin partial pressure of oxygen (159 mmHg at sea level, 126 mmHg after three hours and 124 mmHg after seven hours), but the marked difference between SpO₂ at three and seven hours suggests

that flight duration may also contribute to worsened oxygen desaturation. However, no child became symptomatic.

The following key questions arise.

Should preterm infants who have not yet reached term have a fitness to fly test?

A recent study from Perth Australia has observed that in the preterm infant SpO₂ during flight may fall below 85% in the absence of any history of respiratory problems. In their study 16 out of 46 preterm infants (gestational age at time of flight 35 to 37 weeks) flying back to regional hospitals from a tertiary neonatal unit required supplementary oxygen.[25] Five of these 16 infants had no history of neonatal lung disease or requirement for oxygen. During the flight 7 of the 16 infants who required oxygen were symptomatic. Desaturation became evident during the sleep rather than wake state. The HCT employed in this study failed to predict those infants who became desaturated. The duration of HCT has been the subject of some debate. In one study investigating the effects of a prolonged HCT (mean duration 6.3 hours) on sleeping healthy infants aged between one and six months found that four out of the 34 infants studied had significant desaturation <80% at times between 1.9 and 5.2 hours. The relevance of these findings is uncertain.[57] It is important to realise that laboratory-simulated flight hypoxia may not necessarily be identical to that incurred when flying at altitude.[25,58,59,60] Factors such as humidity, noise, vibration and sleep/wake states may all influence the pattern of breathing during flight.

On the basis of current recent evidence it is recommended that infants born prematurely with or without a history of respiratory disease who have not yet reached their expected date of delivery do not require a fitness to fly test but should have oxygen available during the flight, delivered at 1-2 L/min in the event of becoming symptomatic or in-flight SpO₂ falling below 85%.

Should infants and young children with a history of chronic lung disease undergo a fitness to fly test?

One complication of preterm birth may be the development of chronic lung disease, which persists after the infant reaches their expected date of delivery. Some of these infants may require supplementary oxygen even at sea level for several months into the first or second year of life. When trying to predict the need for in-flight oxygen it is unclear what test is most appropriate for small children, and there has been debate

about whether to use 90% or 85% as the threshold value below which in-flight oxygen is recommended.[59] Studies evaluating the need for oxygen during flight in infants with lung disease have found that sea level SpO₂ is an unreliable predictor of SpO₂ in a hypoxic environment.[25,58,60,61,62]

Only one of these studies has also measured outcomes during flight;[25] they found that HCT was a poor predictor of in-flight desaturation. In a group of 35 infants with a past history of neonatal chronic lung disease, compared with 34 control infants in the first year of life, the Perth group found a cut-off of 85% more discriminating than 90%, using a face-mask to deliver 14% FiO₂. No child became symptomatic. However the study did not measure flight outcomes.[62] A subsequent study on 46 pre-term infants by the same group concluded that irrespective of whether 85% or 90% was used as the cut-off value, pre-flight testing using a face-mask could not accurately predict which pre-term infant would require in-flight oxygen. The authors suggested abandoning pre-flight tests in favour of monitoring high risk preterm infants during air travel with oxygen available if needed.[25]

Our 2004 statement advised exposing the infant or child to 15% FiO₂ while on the carer's lap in a whole body box. The advantage of this technique is that it is non-invasive. The Perth group have suggested that where a body box is not available a tight fitting non-re-breathing mask may be applied to the child's face, through which high 14% flow oxygen is administered.[63] This approach may be less well tolerated[62] and there has been no direct comparison of the two techniques.

Despite the lack of evidence it is suggested that infants with a history of chronic lung disease who have passed their expected date of delivery are discussed with a specialist respiratory paediatrician. The decision to perform HCT will depend on the child's current respiratory status and interval since they last needed oxygen. If it is less than six months, HCT is advised[64] Where HCT is performed it is recommended that the 85% cut-off is used as an indication for supplementary oxygen, delivered at 1-2L/min.

Should older children with a history of chronic lung disease including cystic fibrosis (CF) undergo a fitness to fly test?

Older children with chronic lung disease such as cystic fibrosis (CF) may be better adapted to a hypoxic environment, possibly through changes in haemoglobin oxygen dissociation characteristics. Two studies on young people with CF have evaluated

HCT as a predictor of the need for in-flight oxygen.[58,59] Both studies measured outcomes during flight. The latter study of 87 children with CF suggested that, in children old enough to do spirometry, FEV₁< 50% predicted is a better predictor of SpO₂ < 90% while flying than HCT.[60] In neither of these studies did children who desaturated <90% become symptomatic. With these authors we recommend that if a child with CF (or other chronic lung disease) has an FEV₁<50% predicted they should undergo HCT, and that if SpO₂ falls below 90%, in-flight oxygen should be available.

Is it safe for children with a history of asthma to fly?

There are no data enabling one to predict when it is safe to fly after an acute asthma attack. Providing a child is not suffering from an acute asthma attack it would be prudent for any child with a history of asthma to take their regular preventer and reliever medicines on board the aircraft.[52]

Is it safe for a child with a history of pneumothorax and/or cystic lung conditions to fly?

There is no evidence to suggest that a child with a recent history of pneumothorax is at a different risk from an adult.[52] Following pneumothorax it would seem prudent, as in adults, to ensure that a CXR is taken to check resolution before air travel, and then delaying travel for seven days after a spontaneous event and 14 days after a traumatic pneumothorax.

Intrapulmonary cysts connected to the airways should not present a problem during air travel since the pressure inside the cyst will equalise with that in the cabin. The situation for completely encysted air spaces, such as those found with some congenital malformations, is completely different. The risk in children should not differ from that in adults. Many cysts are asymptomatic and only detected during antenatal ultrasound scans; even if surgery is planned it is often delayed until the child is at least two years old. Although they do not generally seem to pose a problem, there is a case report of a 17 year old with a large congenital cyst, of which the patient was unaware, suffering a cerebral air embolus during flight, presumably due to its rupture.[65] The patient had previously flown without complications. It is thus difficult to give firm recommendations, but it would seem reasonable for parents to be made aware of the risk, albeit low, so that elective surgery can be considered.[52]

What about respiratory infection in infancy?

Infants, especially those born premature before 32 weeks gestation, who develop an acute viral respiratory infection, are known to be at risk of apnoea because they appear to revert to a more immature pattern of breathing.[66,67] Exposure to a hypoxic environment at this time may increase the risk of apnoea.[57] It is suggested that ex-premature infants should delay flying for six months after the expected date of delivery if developing signs of lower respiratory infection, for instance wheeze, cough or tachypnoea, or a significant upper respiratory tract infection.

Respiratory cross-infection risk

Although the potential risk of cross-infection would seem high in the closely confined space of the airline cabin, the evidence is that such cross-infection is minimal.[68] In modern aircraft cabin air is re-circulated through high efficiency air filters up to 20 times per hour and cabin flow of air is vertical rather than horizontal.[52] Tuberculosis (TB) and influenza cross-infection in the cabin environment have been reported.[69,70] In neither incident were children involved. Nevertheless a child with TB should delay flying until no longer infectious, and a child with influenza should not fly until fully recovered.

Middle ear barotrauma

This can result from failure to equilibrate the middle ear and atmospheric pressure difference, and tends to occur most often during descent. Children are especially at risk for several reasons.[52] They have narrower Eustachian tubes, are less able to regulate the pressure difference by performing a Valsalva manoeuvre, more likely to suffer from viral head colds, and more likely to have adenoidal tissue obstructing the Eustachian tube orifice. Parents should be advised to encourage their children to drink, chew, suck and blow their nose, particularly during descent, to prevent barotrauma. There is currently no evidence to support using pseudoephedrine pre-flight in children with ear pain or nasal congestion, or to prevent children with otitis media from flying.

Respiratory disorders with potential complications for air travellers

Asthma

The flight environment experienced by commercial passengers does not pose a problem for most patients with asthma. The main risk is that of bronchospasm induced by bronchial mucosal water loss resulting from the low cabin humidity.

Hypobaric hypoxia should not pose a significant risk and the effect of reduced cabin ambient pressure should not affect those patients with asthma without co-morbidities.

There are limited data on the physiological effect of the flight environment on travellers with asthma. In a study to examine the effect of reduced barometric pressure on exercise-induced broncho-constriction, Berntsen et al[71] subjected 20 asthmatics (13 male, age 10-45yrs) to exercise testing at sea level and 2500m in random order on separate days. They measured lung function, heart rate, oxygen uptake, SpO₂, respiratory gas exchange and minute ventilation. Mean SpO₂ fell from 94.4 (92.2-96.6) % to 85.6 (82.8-88.4) % but there was no increase in exercise-induced broncho-constriction. Other studies of the effect of altitude on asthma have been performed in travellers to high altitude destinations. These studies have demonstrated broncho-constriction as a result of exposure to heat loss and water loss from the bronchial mucosa.[72,73]

Several studies[74,75,76,77,78,29,79] have reported a frequency of in-flight respiratory medical events of around 10%. These studies do not specify asthma *per se* as the cause. Severe asthma appears rare although fatalities have been reported.[79] In a retrospective study from the Royal College of Surgeons in Edinburgh,[80] 65% of all events occurred in travellers with pre-existing medical conditions, of which 21% were respiratory. No respiratory events were reported in travellers without pre-existing conditions. One third of those suffering an asthma attack had forgotten their medication or left it in their hold baggage. Dowdall[29] has reported that asthma is the most common potentially life-threatening condition on British Airways flights, but that most episodes are minor and result from having left medication in the hold baggage. He notes that oxygen is available on board, as are an injectable bronchodilator and adrenaline in the aircraft medical kit. In the UK Flight Outcomes Study[6] 15% of the study population had asthma, all of whom were under specialist care. No deaths were reported in this group. While worsening breathlessness during flight and increased need for antibiotics after travel were reported, the study does not suggest that patients with asthma were particularly at risk. Overall it seems reasonable to conclude from these outcome studies that commercial air travel is safe for patients with well-controlled asthma and for those under specialist supervision.

COPD

The flight environment on commercial flights exposes passengers to the stresses of hypobaric hypoxaemia, low cabin air humidity and reduced atmospheric pressure.[32] Passengers with COPD may suffer adverse consequences from the reduced partial pressure of oxygen and expansion of gases within closed body cavities (bullae and pneumothoraces) as a result of Boyle's law. As outlined previously, humidified air contained within a closed body cavity expands as altitude increases, with volume expansion of up to 37% at a cabin altitude of 8000 ft.

The aircraft cabin is pressurised by outside air drawn into the cabin from the aircraft engine. This superheated air is cooled and subsequent pressure within the cabin determined by the rate of air intake and of air output through a regulated exhaust valve.[81] The precise cabin altitude achieved depends on the altitude of the aircraft and aircraft type. Cabin altitude therefore varies, not only according to the aircraft's actual altitude during flight, but also between different aircraft flying at the same altitude.[82] As noted previously, the maximum cabin altitude permitted is 8000 ft (2438 m)[33], but one study of in-flight cabin altitude on 204 commercial flights on 16 different aircraft found variable cabin altitudes, ranging from sea level to 8915 ft (2717 m) with a mean of 6214 ft (1894 m).[34]

Dalton's law of partial pressures states that the pressure exerted by a mixture of gases is equal to the sum of the pressures that each would exert if it occupied the space filled by the mixture alone.[19] This means that the composition of air is constant at any given altitude but the partial pressure of each component reduces with ascent to altitude. Thus at 8000 ft inspired oxygen tension is 108 mmHg, falling from 148 mmHg at sea level. This equates to breathing 15.1% oxygen at sea level.[19] In a normal healthy individual the reduction in inspired oxygen results in a fall in PaO_2 to 7.0 – 8.5 kPa (53-64mmHg, SpO_2 85-91%), which does not usually produce symptoms.

The normal physiological response to altitude hypoxaemia is well described.[19, 33,34,81,82,83,84] Hypoxia stimulates peripheral chemoreceptors within the carotid bodies producing hyperventilation, with an increase in tidal volume effected by increased minute ventilation to maximise PAO_2 and PaO_2 . The alveolar–arterial oxygen gradient falls. Hypoxic pulmonary vasoconstriction causes increased pulmonary arterial pressure and pulmonary vascular resistance which is benign and reversible. PaCO_2 falls as a result of hyperventilation, but the concomitant hypoxia overcomes the cerebral vasoconstrictor effect and maintains oxygen delivery to the

brain. Cardiac output increases due to tachycardia, thus maintaining blood flow and oxygen delivery to vital organs.

In a passenger with COPD the effect of a low inspired oxygen tension has potential for greater adverse effects. Several factors may affect the compensatory response to altitude-induced hypoxaemia, including potential causes of hypoxaemia within the particular individual (hypoventilation, ventilation-perfusion mismatching, impaired diffusion, low mixed venous oxygen saturation), rate of ascent, final cabin altitude and length of flight, airway resistance, the position on the oxygen dissociation curve, exercise at altitude and the presence of co-morbidities.[84]

Several studies have been performed in COPD patients examining the effect of altitude-induced hypoxaemia, performed either in the lung function laboratory using simulated altitude-induced hypoxaemia, or in a hypobaric chamber. Some authors have examined passengers with COPD during flight; while others have investigated flight outcomes in this group. The studies are generally small, making it difficult to draw firm conclusions.

Gong and colleagues, in their original publication of the hypoxia altitude simulation test (HAST)[42], studied 22 patients (13 men) with stable mild COPD ($FEV_1 < 80\%$ predicted), 17 of whom reported variable discomfort (chest tightness or exertional dyspnoea) on previous flights. They inhaled sequential gas mixtures of 20.9% (sea level baseline), 17.1 (simulating 1524m), 15.1 (simulating 2438m), 13.9 (simulating 3048m) and 20.9% O_2 (sea level recovery). With 15.1% inspired oxygen there was a mean fall in SpO_2 of 11% (94% to 83%). The lowest readings were 87% on 21% inspired oxygen and 74% on 15.1% inspired oxygen. Progressive hypoxia-induced mild hyperventilation caused small but significant falls in $PaCO_2$. Supplemental oxygen, given during inhalation of 15.1% oxygen in five subjects and 13.9% oxygen in 16, significantly increased PaO_2 . $PaCO_2$ returned to baseline with oxygen and in eight subjects rose slightly above baseline. Heart rate rose and asymptomatic cardiac dysrhythmias occurred in ten subjects. Blood pressure was unchanged. Eleven reported mild symptoms which did not correlate with hypoxia or hypoxaemia. Variable sleepiness noted by the investigators was partly reversed by supplemental oxygen.

Several authors have tried to identify factors measured at sea level which might predict hypoxia at altitude. Dillard[41] undertook a prospective study of 18 retired

servicemen exposed to an altitude of 8000ft (2438m) in a hypobaric chamber for 45 minutes. He demonstrated a correlation between PaO₂ at ground level with PaO₂ at altitude, and between FEV₁ at ground level and PaO₂ at altitude. However, Robson and colleagues,[47] in a small study of patients undergoing HCT using the method described by Vohre and Klocke[46] found that hypoxaemia at simulated altitude could not be predicted either by FEV₁ or pre-test SpO₂. Schwartz [85] studied 13 COPD patients during flight in an unpressurised aircraft, measuring arterial blood gases at 1650 and 2250 m. This study found no correlation with arterial blood gas measurements performed several weeks before the flight, but did find a correlation with PaO₂ measured two hours before the flight, whether breathing room air or a 17.2% oxygen mixture. Dillard and co-workers published a meta-analysis of hypoxemia during altitude exposure in COPD[40] looking at five studies including 71 subjects. This showed that the fall in PaO₂ per unit change in inspired oxygen pressure (PiO₂) correlated negatively with FEV₁ in all studies, such that the largest falls in PaO₂ per unit change in PiO₂ occurred in those with the lowest FEV₁. The authors concluded this provided evidence supporting FEV₁ as a predictor of PaO₂ at altitude in COPD patients.

Mortazavi and colleagues [87] have reviewed the acute response to hypoxia including the steps in oxygen transport from alveolus to the peripheral tissues. In COPD, hypoxia-induced pulmonary vasoconstriction at altitude may improve the ventilation-perfusion mismatch seen at sea level, thus limiting resulting hypoxaemia. Oxygen diffusion across the alveolar capillary membrane is limited by the lower PAO₂ at altitude, and this diffusion limitation is exacerbated by exercise as a result of shortened capillary transit time. This diffusion limitation contributes significantly to the risk of hypoxia in COPD. Dillard [88] tested the hypothesis that if studies of pulmonary function tests performed at sea level were predictive of poor tolerance to altitude hypoxaemia, then a further decrement in pulmonary function at altitude would be detrimental. This study reported a decline in FVC in six COPD and three healthy subjects at altitude which correlated with changes in maximum voluntary ventilation, but not with a worsening of arterial blood gases. Thus at altitude in this small number of subjects there was no worsening of the hypoxaemia as a result of worsening spirometric parameters. Berg [89] studied the effect of vasopressor responses to hypoxia in 18 severe COPD subjects undergoing hypobaric hypoxaemia in a chamber at 2438m for 45 minutes. This study found no evidence that vasopressor responses to hypoxia increase risk from altitude exposure.

Airline medical departments have traditionally used the un-validated 50m walk test.[23] However, Chetta et al[90] used the validated 6 minute walking test[36] to assess walking capacity as a predictor of altitude hypoxaemia measured using the HAST. They showed a significant relationship between mean 6 minute walk SpO₂ and mean HCT SpO₂.

One explanation for lack of consensus between many of the studies could be the use of different tests to simulate altitude-induced hypoxia. Dillard et al[44] compared the HAST with hypobaric chamber exposure at 8000 ft (2438 m) in COPD patients and healthy subjects. The two tests produced comparable changes in PaO₂. The authors also showed that spirometric measures FEV₁ and FVC predicted PaO₂ during hypoxic exposure where those with PaO₂<40mmHg had lower FEV₁ and higher pre-exposure CO₂. Martin et al[91] compared HCT with the four predictive equations provided in the 2002 BTS air travel recommendations[1] in 15 COPD subjects. With the exception of equation 3, they found poor agreement between PaO₂ values obtained during HCT and those calculated using predictive equations. Overall, using predictive equations would have led to more prescriptions for in-flight oxygen.

Use of supplemental oxygen at altitude has been evaluated by Berg et al.[92] They studied 18 patients with severe COPD in a hypobaric chamber at 2438 m with supplemental oxygen, and showed that oxygen reversed the hyperventilatory response to hypobaric hypoxaemia.

Earlier BTS advice[1] has been tested by Akerø and colleagues,[7] who stratified 100 subjects with COPD according to BTS guidance, using SpO₂ assessed against HCT. One third of subjects with sea level SpO₂>95% dropped their PaO₂ during HCT to <6.6kPa. Over two thirds of those with sea level SpO₂ of 92-95% with an additional risk factor also had PaO₂ values <6.6kPa. The authors concluded that sea level SpO₂ is not a reliable predictor of altitude PaO₂ ≥ 6.6kPa. In an earlier study by Christensen et al[5], the authors evaluated the guidance that a PaO₂>9.3kPa at sea level is adequate to avoid severe hypoxia at altitude.[42] Fifteen stable male COPD subjects (mean FEV₁ 30.3% predicted +/-11.6) were tested at sea level, 8000 ft (2438m) and 10,000 ft (3048 m). Many developed marked hypoxaemia at 8000 ft and on exercise at altitude. The authors concluded that a sea level PaO₂>9.3 did not preclude the risk of hypoxaemia at altitude, and that neither the resting nor exercise PaO₂ at sea level or the resting PaO₂ at 8000 ft (2438 m) predicted hypoxaemia at

altitude. However, sea level aerobic capacity (VO_{2max}) correlated positively with PaO_2 at 8000 ft.

Since the evidence base for advising on whether patients with COPD can safely undertake commercial air travel is inconclusive, it is important to consider the outcomes of air travel in this group.

Akerø [50] undertook in-flight assessment of 18 COPD patients on a flight lasting 5 hours 40 minutes with a mean cabin altitude of 6000 ft. They showed that stable patients with COPD were able to maintain stable arterial oxygen tensions. Kelly and colleagues[93] studied 13 COPD patients (7 female, mean FEV_1 1.39 \pm 20%). These patients underwent pre-flight pulmonary function tests (spirometry, static lung volumes and diffusion capacity) followed by in-flight measurement of SpO_2 , pulse rate and wrist altimeter, and finally a post flight HCT and six minute walk test (6MWT). During the flight there was significant hypoxaemia, worsened by exercise, but no adverse events. There was good correlation between HCT SpO_2 and mean in-flight SpO_2 , but no relationship between 6MWT and mean in-flight SpO_2 . There was a strong relationship between % predicted D_LCO and mean in-flight SpO_2 , confirming that diffusion limitation is an important determinant of altitude-induced hypoxaemia.[87] Kramer [94] published a series of 21 patients requiring either lung transplantation or pulmonary thrombo-endarterectomy who were transferred to a specialist centre for treatment by air with supplemental oxygen, demonstrating safety even at the most severe end of the spectrum.

The UK Flight outcomes Study[6] was a prospective, multi-centre observational study undertaken over two years (2003-2005), which examined the outcome of commercial air travel for patients with respiratory disease. Two hundred and forty three (39%) were COPD patients (mild 2%; moderate 29%; severe 43%; very severe 26% according to GOLD[95] criteria). There were no in-flight deaths, but one patient died within four weeks of returning. During flight 18% of the respiratory patients reported respiratory distress, usually mild and mostly manifest as worsening breathlessness. There was a relatively high need for antibiotics for respiratory tract infection within one month of travel. The conclusion was that commercial air travel appears generally safe for patients under specialist respiratory care. Dillard et al[96] studied 100 patients (76 male) with severe COPD (mean FEV_1 0.04 \pm 0.35L), of whom 44 underwent air travel. The 56 who did not fly had a lower FEV_1 and higher use of

home oxygen. Of the 44 who travelled, the median flight duration was three hours, and eight patients reported transient symptoms without adverse events.

Several studies report on the incidence of in-flight medical emergencies. In a one year prospective study of emergency medical responses to travellers at Seattle-Tacoma Airport, [74] respiratory causes represented 53 of 754 incidents (7%) with COPD and asthma being the most common (15/190 incidents or 8%). In a retrospective study by Delaune[75] respiratory events comprised 11% of all events and were responsible for 9/181 (5%) diversions. A study for QANTAS in 1993 showed that respiratory events comprised 9% of all in-flight medical incidents.[76] The Paris Emergency Medical service (SAMU) reported its experience of providing in-flight assistance to Air France[77] in 1989-1999, reporting 14/374 (3.7%) incidents of breathlessness with three requiring aircraft diversion.

Overall the available literature suggests that the frequency of severe adverse events in COPD patients travelling by air is very low. The evidence base has used a number of measured variables in order to try and predict for altitude-induced hypoxaemia. While studies undoubtedly show some correlation between these measured variables and altitude-induced hypoxaemia, there is insufficient evidence on which to base clear recommendations employing definitive cut-off levels of SpO₂, PaO₂, or FEV_{1.0}, 6 minute walking distance or other physiological variables. The lack of correlation between predicted levels of arterial hypoxaemia in COPD patients undertaking air travel and outcomes suggests that these patients tolerate hypoxaemia fairly well, as a result of physiological adaptations discussed above.

Cystic fibrosis

Patients with cystic fibrosis (CF) undertaking a commercial flight are exposed to the risk of cross-infection and hypoxia. In particular, patients are at risk of acquiring transmissible organisms from other CF patients on the same flight, and the CF Trust therefore strongly discourages group travel.

A number of studies have examined the risk of hypoxia during exposure to ambient hypoxia in CF, either in aircraft or at altitude, with or without exercise. One study in 22 children with CF[60] examined the incidence of hypoxia during hypoxic challenge testing in the laboratory, in the Alps and on commercial aircraft, and all desaturated at altitude. HCT was found to be the best predictor of hypoxaemia at altitude. An earlier study[59] of 87 patients with CF aged 7-19 who travelled on flights lasting

between eight and 13 hours had suggested, in contrast, that spirometry was a better predictor of desaturation. The discrepancy may reflect the longer interval between HCT and flight, or the fact that in-flight measurements included some made during sleep. More recent studies by Peckham et al[97] and Martin et al[91] concluded that HCT results in individual CF patients could not be predicted reliably from spirometry, clinical scores or sea level blood gases.

Fischer and colleagues[98] studied a group of 36 CF patients at rest and on exercise during a seven hour stay at an altitude of 2650 m. In these conditions, one third of patients had $pO_2 < 6.6$ kPa at rest, rising to 2/3 of patients with this level of hypoxia during mild exercise. The striking finding was that hypoxaemia was very well tolerated by patients; with none reporting dyspnoea and only the most hypoxic patient (pO_2 4.4 kPa) reporting some dizziness during exercise. Both spirometric measures and HCT predicted the majority of patients with altitude-induced hypoxaemia; however HCT yielded a high false positive rate. Studies by Rose [99] and Kamin[100] using both hypobaric chamber and flight-induced hypoxia also confirmed that CF patients do not usually report dyspnoea or other adverse symptoms, even when their pO_2 drops below 6.6 kPa.

In summary, patients with CF do become hypoxaemic at altitude, but rarely become symptomatic. Those with a low FEV_1 (<50%) appear to be at increased risk of hypoxaemia, and further information may be obtained by HCT. To date no study has demonstrated a completely reliable method of predicting which individuals will become hypoxaemic at altitude.

Non-CF bronchiectasis

There are no published studies examining specifically the issue of hypoxaemia associated with air travel in patients with bronchiectasis. Given the similar lung pathology, it is likely that the principles outlined above for cystic fibrosis will apply; however objective evidence to guide practice is currently lacking.

Cancer

This section considers primary thoracic cancers and cancers which have spread to lung, mediastinum or pleura; all disease stages from post-diagnosis to active anti-cancer treatment, progressive and terminal disease; and long-term survivors. Although there is no literature addressing specifically the challenges or outcome of air travel in patients in these circumstances, the UK Flight Outcomes Study[6]

included five patients with cancer, of whom one died within four weeks of returning home. Although the numbers are too small to draw firm conclusions, overall mortality in this study was just 1%, suggesting that cancer patients merit careful specialist review if considering air travel. In the absence of evidence we have formulated advice which takes into account the management of pain, dyspnoea and other key symptoms likely to impair patients' ability to undertake air travel, as well as the practicalities of travelling across borders with controlled drugs including opioids.

Patients are living longer with most forms of cancer, and with less intensive chemotherapy regimens and new targeted treatments are able to lead more 'normal' lives. This means that more cancer patients are able and keen to take overseas holidays, whether flying to European destinations or on long-haul flights. Some may be travelling abroad to seek medical, surgical or complementary treatments for their disease; often undertaken in advanced stages when all conventional treatments available at home have been tried and exhausted. Such patients will therefore be systemically more ill, as well as potentially having more serious pulmonary complications.

The issues the physician needs to consider include the effect of cancer on pulmonary function and reserve leading to dyspnoea, including thoracic muscle weakness, diaphragmatic weakness or paralysis; large airway obstruction; mediastinal lymphadenopathy; pleural disease and effusion and other forms of thoracic cage fixation. They also include cough and haemoptysis arising from cancer or as a result of anti-cancer interventions; pain arising from cancer or its surgical treatment; fatigue and reduced mobility caused by anaemia, biochemical abnormalities, cachexia and muscle de-conditioning following intensive treatment; seizures resulting from cerebral metastases, and special conditions relating to anti-cancer treatment, including neutropenic sepsis, bone marrow failure, pulmonary reactions, cardiac reactions. Co-morbidities such as COPD and cardiac disease are addressed in the relevant sections.

Few of these issues are specific to primary lung cancer or mesothelioma, so the primary specialist physician may be an oncologist or specialist in another field, such as gastroenterology. Even with primary thoracic cancers, the main medical specialist may be the oncologist rather than the chest physician. However, as the chest physician will be more familiar with respiratory physiology and appropriate investigations, communication between all relevant specialists and primary care is

important when planning for air travel. Owing to the pro-thrombotic tendency of many cancers, there is likely to be an increased risk of VTE in cancer patients. However, the magnitude of the increased risk is not quantified in the literature. Situations likely to impact on respiratory function and reserve are discussed below.

Patients with primary thoracic and secondary cancers are likely to suffer from dyspnoea. It is important to exclude correctable causes such as anaemia or reversible airflow disease. There is no published evidence to indicate the minimum haemoglobin (Hb) level with which it is safe to fly. However, major airlines recommend that Hb should ≥ 8.5 g/dl before flying.

Patients with major airway obstruction, including upper airway stridor, are likely to have received radiotherapy and, depending on cell type and general condition, chemotherapy. Some will have an airways stent *in situ*. None of these preclude air travel, but sufficient time should have elapsed since anti-cancer treatment or stent insertion to enable the physician to confirm that the patient's condition is stable.

Patients with lymphangitis carcinomatosa are likely to be very dyspnoeic on exertion. Air travel should only be undertaken if essential, and in-flight oxygen should be available. Patients with superior venal caval obstruction (SVCO) are likely to have a poor performance status and be heavily symptomatic. Several factors may contribute to dyspnoea, including micro-embolisation from thrombus in the SVC and concomitant mediastinal disease causing vascular and lymphatic obstruction. Air travel should only be undertaken if essential and in-flight oxygen should be available.

Patients may have pleural and chest wall infiltration, especially likely with mesothelioma but also arising with other primary or secondary cancers. The main consequence apart from pain (see below), is fixation of the thorax with reduced respiratory reserve. In-flight oxygen may need to be considered. Pleural effusion may co-exist; patients with large pleural effusions should ideally have them well drained before air travel.

Most patients with primary thoracic cancers have a degree of cough, but this may partly reflect co-morbidity such as COPD. The physician may wish to consider prescribing a cough suppressant for long flights. Productive cough should be treated appropriately with antibiotics and the patient may need to take more than one course

if staying overseas for a longer period, depending on the destination and medical cover available. Patients with major haemoptysis should not fly.

Management of cancer pain is a major topic beyond the scope of this document. Specific issues relevant for patients with thoracic malignancy planning air travel include the need for opiates, and in particular Schedule A controlled drugs. These are morphine (excepting oramorph solution), oxycodone, hydromorphone, fentanyl, buprenorphine and methadone. Patients travelling within the EU with such drugs should not experience difficulty, but the Home Office recommends a standard doctor's letter to allow easy exit from the UK with controlled drugs. This should contain the patient's name, address, date of birth, the outward and return dates of travel, the country to be visited and a list of drugs being carried, including doses and total amounts. Additionally, the Home Office advises those travelling abroad to contact the relevant Embassy/Consulate/High Commission regarding their policy on importing controlled drugs. The patient must understand that being able to take controlled drugs out of the UK does not automatically allow them to be taken into other countries. It is therefore advisable for the clinician to ascertain the local controlled drug importation rules before the patient leaves. Details are available on the Home Office website (www.homeoffice.gov.uk). Patients receiving opioid medication by patch delivery (fentanyl, buprenorphine) should have no particular difficulty during air travel. However, they should be made aware that in hot climates increased sweating may reduce patch adherence.

Some cancer patients receive analgesics and anti-emetics by continuous subcutaneous infusion through a battery-powered syringe driver. Ambulatory patients may have such a device fitted for several weeks. There are no published reports of the effects of reduced atmospheric pressure on the dynamics of the rather simple pump mechanism, but they should not present a contra-indication to air travel. Spinal drug delivery, either into the epidural or intrathecal space, using an external or preferably an implanted pump, may become more common for cancer pain control in the future. With a fully implanted pump, it is possible to top up the reservoir for several weeks. Despite an absence of data, it is not anticipated that reduced cabin pressure would have a significant effect on such devices if fully implanted. Patients with bone metastases may experience considerable discomfort from having to sit in one position for a prolonged time. Ideally, they should travel in seating which allows extra legroom.

Many cancer patients, even those apparently in remission, may suffer fatigue. Biochemical causes, such as hyponatremia, hypokalaemia and hypercalcaemia, should be corrected before flying. Frequently, patients are fatigued because of general debility and muscle de-conditioning. In general, corticosteroids have a poor evidence base for this purpose; ideally they should be avoided in patients travelling overseas because of the further risk of precipitating acute medical adverse effects.

Patients receiving chemotherapy should be aware of the increased risk of infection, and the peak timing after chemotherapy, and should ideally not fly until the likelihood of neutropenia has receded. Where there is doubt, the oncologist can advise. Patients with advanced malignancy and extensive bone metastases, where there is generalised bone marrow failure and pancytopenia, are likely to be very ill, and air travel may not be advisable.

There are no specific airline policies or IATA regulations regarding cerebral metastases and seizures. Most major airlines will not carry a passenger within 24 hours of a seizure, but do not otherwise place other restrictions on air travel in such circumstances. Although cerebral metastases should not themselves be affected by reduced pressure, moderate hypoxaemia at altitude could theoretically lower an already reduced seizure threshold. A commonsense judgement taking into account the patient's overall condition and the reason for flying is likely to be needed. The patient and carers should be aware that medical insurance is likely to be refused and that the costs of repatriation would be significant.

Cardiac disease

Exposure to acute hypoxia has multiple differential effects on the cardiovascular system.[101] In the systemic circulation, arterial hypoxaemia will induce vasodilatation, including the coronary arteries, thus reducing systemic vascular resistance. Sympathetic activation will increase cardiac output, due to an increase in heart rate and myocardial contraction velocity. The overall effect is either a decrease or no change in systemic blood pressure. Conversely, alveolar hypoxia induces pulmonary vasoconstriction. At cabin pressure, this effect will be mild in healthy passengers, but may cause clinically-relevant increases in pulmonary artery pressure in patients with existing pulmonary hypertension. Owing to common risk factors and disease prevalence, cardiac disease often co-exists with pulmonary diseases. Extra caution should be applied in this situation, as significant falls in oxygenation on board commercial aircraft may exacerbate cardiac disease. It is anticipated that the British

Cardiovascular Society will publish more detailed guidance on the safety of air travel in cardiac conditions in the near future. In the meantime we have produced advice based on a review of the current literature.

Coronary artery disease

The increased myocardial demand for oxygen on exposure to hypobaric hypoxia due to augmented myocardial work will increase the potential for myocardial ischaemia when coronary arterial flow is restricted. Atherosclerotic coronary arteries may constrict in response to sympathetic activation[102] and at 2500m patients with exercise-induced myocardial ischaemia show evidence of reduced coronary flow reserve by 18%.[103] Most data suggest that clinically-evident myocardial ischaemia will not develop at rest at barometric pressures experienced by passengers in commercial aircraft.[101]. One study demonstrated that ischaemic threshold was reduced by 5% in a group of 20 subjects (mean age 68 ± 3 years) taken acutely to an altitude of 2500m. Half of them had exercise-induced ischaemia at sea level.[30] Consequently, most passengers should be able to exercise close to their sea-level threshold for ischaemic symptoms during commercial air travel.

After an acute coronary syndrome, the risk of air travel should be based on the “sea-level” risk. Those at lowest risk are young patients in whom ST-elevation myocardial infarction (STEMI) has been treated early with percutaneous coronary intervention with good demonstration of restoration of coronary blood flow (TIMI 3), no clinical evidence of heart failure, normal ejection fraction and no arrhythmias.[104]. Non ST-elevation myocardial infarction (NSTEMI) has a risk of recurrence and death, and decisions regarding air travel need to be made following a full risk assessment.[105] Essentially, all patients without complications should be able to travel within by air within 10 days, unless further investigations are required.

Cyanotic congenital heart disease

In cyanotic congenital heart disease, an anatomical shunt exists whereby a proportion of deoxygenated mixed venous blood bypasses the pulmonary circulation, leading to systemic hypoxaemia that is uncorrectable even with 100% oxygen. Patients adapt to chronic hypoxaemia through increases in haematocrit and 2,3 diphosphoglycerate, to maintain oxygen delivery. For this reason, patients should be iron replete in order to facilitate increased red cell synthesis.[106] Given that not all mixed venous blood passes through the pulmonary circulation, the effect of hypobaric hypoxia on systemic oxygenation is less than in those with the same

degree of desaturation due to lung disease. Physiological studies and surveys of patients with cyanotic congenital heart disease show that air travel is safe,[107,108] but self-selection may have played a part in these studies and the results cannot be applied universally. Although not reported, it is likely that the majority of patients surveyed were in NYHA functional class I or II. A haemodynamic study in paediatric patients with congenital heart disease showed that a small number developed a pulmonary hypertensive crisis when 15% oxygen was administered.[109]

Heart failure, valvular disease and pulmonary hypertension

Patients with chronic heart failure may experience worsened symptoms in a hypobaric environment due to augmentation of underlying neuro-hormonal activation. Exercise capacity decreases at increasing levels of altitude, and the extent is dependent on baseline functional capacity.[110] In patients with severe heart failure, peak work rate falls by 11% for every 1000m ascended up to 3000 m. Chronically elevated left atrial pressure may result in “passive” pulmonary hypertension, where pulmonary vascular resistance is normal, or “reactive” pulmonary hypertension due to pulmonary vascular remodelling. In the latter case, alveolar hypoxia is likely to have a greater worsening effect on pulmonary hypertension and right ventricular function. Patients with other forms of pulmonary hypertension (pulmonary arterial hypertension, chronic thrombo-embolic disease and lung disease) may suffer clinically significant increases in pulmonary vascular resistance as a consequence of hypoxic pulmonary vasoconstriction, and if the right ventricle is unable to cope with the increase in afterload, significant deterioration may occur. Unlike other conditions dependent on the level of arterial oxygenation, because pulmonary vasoconstriction results from alveolar hypoxia, normal measures of peripheral oxygen saturation by oximetry are not helpful in predicting the response of the pulmonary circulation to hypobaric hypoxia. Recommendations are therefore made on saturations and/or NYHA functional class as an indication of ventricular function.

Rhythm disturbance

The increased sympathetic activity associated with hypobaric hypoxia may decrease the arrhythmia threshold.[111] Patients with severe underlying arrhythmias or high-grade premature ventricular contractions may therefore be at increased risk.

Hypertension

Patients with systemic hypertension at sea level display an exaggerated sympathetic response when exposed to isocapnic hypoxia.[112] There are no data to evaluate the

safety of patients with severe systemic hypertension travelling by commercial aviation, but it is possible that through this mechanism exposure to hypoxia may cause clinical changes of concern. Physicians should also bear in mind recommendations for VTE prophylaxis.

Hyperventilation and dysfunctional breathing

The literature is very incomplete and many studies are old. The symptoms of acute hyperventilation[113] are dominated by respiratory symptoms, particularly by acute breathlessness, and can cause great alarm and distress to individuals, observers and to flight crew in an in-flight situation.[114] Acute symptomatic hyperventilation may be triggered by emotion and by stressful situations including air travel. Symptomatic hyperventilation has been highlighted as a problem both in air crew[115] and passengers.[114] It is reported that a high proportion of aircrew under training exhibit hyperventilation in stressful flight situations.[116] Passengers subject to unusual stressors in flight such as unexpected emergencies may also hyperventilate.[117] Hyperventilation in response to stressful situations is particularly common in people with pre-existing anxiety and panic disorders.[118]

There is very limited literature on the prevalence and implications of functional breathing disorders in relation to air travel. Acute psychiatric emergencies have been reported to account for 3.5 to 5% of all in-flight medical emergencies;[119,120] 90% of these relate to acute anxiety episodes which may involve hyperventilation.[119] It has been suggested that a rapid-onset anxiolytic should be included in on-board medical kits.[120] It is also recommended that flight crews should receive training in recognition of acute hyperventilation[114,117] although distinguishing anxiety induced hyperventilation from life-threatening acute medical conditions can be problematic. The difficulties facing aircrew when faced with an acutely anxious and over-breathing patient are considerable, and the causes for rapid breathing and distress may include hypoxia, anxiety, hypoglycemia and acute cardiac disease.[114] Where any doubt exists, supplemental oxygen should be provided and medical assessment undertaken as soon as possible.[120] If hyperventilation and/or panic attack are confidently diagnosed, re-breathing[117] or the use of a rapid onset anxiolytic[120] have been advocated.

How to assess fitness to fly in patients with known dysfunctional breathing, hyperventilation or panic attacks has not been studied. Indeed, the diagnosis of 'hyperventilation syndrome'[121] or 'dysfunctional breathing'[122] can be taxing for

clinicians. Recognition of symptoms during a period of voluntary hyperventilation has been advocated as a simple test to demonstrate the link between abnormal breathing and somatic symptoms[121], some but not all of which relate to hypocapnia.[123] Breathing training exercises have been advocated as effective treatment for people with hyperventilation and panic,[124,125] and it seems advisable that patients should have been taught, and successfully used these techniques, before travelling by air. Where required, psychiatric assessment and treatment should be undertaken beforehand. It has been suggested that people who habitually suffer anxiety attacks and hyperventilation when flying should be prescribed a sedative or anxiolytic to take before travel.[117]

Airborne infection

The major concern for passengers with regards to the in-flight spread of respiratory infection is the recirculation of cabin air.[126] Air exchange rates on commercial airliners range from 20 to 30 changes per hour,[1127] and 30 to 55% of the air is re-circulated; in comparison, 80% of the air is re-circulated in commercial buildings.[128] The air that is mixed with the cabin air is taken from the external environment, which is effectively sterile at high altitude and is brought into the aircraft through the engines at very high pressures and temperatures.[129] Cabin air is routed through filters designed to extract droplet and particulate matter, known as high efficiency particulate air filters (HEPA).[129,130] The ventilation system is designed to provide laminar air flow; air is introduced from the ceiling and removed from the floor by the passengers' feet,[129,131,132] reducing longitudinal air flow along the cabin. Cabin humidity is kept low (5-15%) to prevent condensation on the aircraft's internal walls.

Respiratory pathogens usually spread by one of two routes; via large droplets or airborne tiny droplet nuclei. Large droplets quickly fall to the ground, whereas tiny airborne droplets may disperse widely. The normal microbiological composition of the air on domestic and international flights has been shown to be low [133,134] and less than that of normal city air.[135] HEPA filters are 99.9% effective at removing particles larger than 0.3 μ m; bacteria are generally larger than this. Viruses tend to clump into airborne droplets around 5 μ m. A study used an airborne tracer released into the passenger cabin of an aircraft cruising at altitude as a surrogate for the release of an infectious agent. It showed that maximum tracer concentrations were 500 times greater at 2 m from tracer release than at 30 m, where levels were at a maximum of just over 2 parts per billion volume.[136] HEPA filters were used on the flight, but would not have filtered out the gas. These studies were all performed

during “normal” situations; whether this corresponds to a lower level of microbiological transmission with a passenger with a highly infectious disease on board remains to be shown.

Tuberculosis

Active, smear positive tuberculosis (TB) is a highly infectious disease that is transmitted by airborne or (more frequently) large droplet routes.[137] TB is the most extensively investigated respiratory infection in the context of in-flight transmission of disease. The aircraft cabin is thought to be an area of low TB prevalence.[135] The rate of adults with active TB on long haul air flights is estimated at 0.05 per 100,000 long-haul passengers.[138] In total, of flights more than 8 hours in duration for the years 2000 to 2004 inclusive 34 cases of smear-positive TB were notified to airlines out of more than 68 million long-haul passengers. Five percent were classified as highly infectious and 12% possibly drug-resistant. Fifteen percent of these were known to be infectious or were under investigation before travel.

When restricting data to flights from endemic areas, TB notification rate was 0.35 per 100,000 long-haul passengers. However, this paper estimated under-reporting of at least 15%. A further paper looked at all TB air travel-related incidents reported to the UK Health Protection Agency between January 2007 and February 2008.[139] Twenty four cases were identified. Nineteen of these 19 were smear positive, 75% of whom flew on flights lasting over eight hours. Two patients were subsequently found to have multi-drug resistant tuberculosis (MDR-TB). For most cases further analysis was impossible owing to inadequate patient information.

There are few rigorous data on the transmission of TB on aircraft. The largest case series reported in a string of publications between 1992 and 1994 focussed on six cases of active, smear positive, highly infectious TB in five passengers and one member of the cabin crew.[140] Two of these cases had MDR-TB. Over 2,600 passenger and cabin crew contacts were identified over a number of different flights. Evidence of TB transmission was reported in two publications. In the first, the cabin crew contacts of a flight attendant with TB exposed over a five month period were given a tuberculin skin test (TST).[141] Twenty six percent of those exposed when the index case was more infectious developed a positive TST, compared with 4% of those exposed before the index case became infectious. Little evidence was found of transmission to passengers.

The second report detailed the results of contact tracing from a passenger with MDR-TB who had taken four long haul flights while infectious and symptomatic.[70] Seven hundred and sixty out of a possible 1042 passengers were contacted. Of the 11 contacts with a positive TST on the first two flights, all had other risk factors for TB. However, on the third flight there was one contact and on the fourth flight six contacts with a positive TST with no obvious risk factors for TB; four of these had a documented conversion on repeat TST. All these contacts had sat in the same cabin section as the index case, and four were seated within two rows. Using a similar contact tracing methodology, the other studies published in this series of infectious index cases on long haul air flights did not document any definitive evidence of transmission.[143]

In none of the above studies was transmission of clinically active TB reported. TB transmission was defined as a positive TST in the absence of any risk factors for TB. Associations with TB transmission included longer flights, and seating in close proximity to the index case. These data suggest that while in-flight TB transmission is possible, there is no greater risk of TB transmission with air travel compared with other modes of transport such as rail or bus,[145] or within office buildings.[146]

Following these initial studies, several case reports have been published, which provide little evidence for transmission of TB on aircraft. Laryngeal TB is thought to be more infectious than pulmonary TB. A report of an index case with laryngeal TB travelling on two short (under 2 hour) flights was published in 1996.[147] Of 161 possible in-flight contacts, only five were TST positive, and all had another risk factor for TB. In 1998 the pilot of a DC-9 aircraft was identified as having active TB.[148] In the preceding six months 48 pilots had flown with the index case, and none showed any evidence of transmission by chest radiograph or TST.

One study reported contact tracing from an index case with smear-positive, active TB on a 14 hour flight.[149] Eleven cases had documented TST conversions, of which three were not accounted for by other risk factors. However, these contacts were not, in contrast to previous case reports, seated in close proximity to the index case. A contact tracing study of a 21-year old with smear-positive active TB who travelled on two long-haul air flights whilst actively infectious reported 238 contacts on the two flights; serial TST results were available on 142.[150] Of 24 positive TST results, four were conversions (that is, they had an initial negative TST followed by a positive TST several weeks later), and all had other risk factors.

A patient with extensively drug resistant tuberculosis (XDR-TB) travelled on only a five hour flight from Beirut to Paris and died 10 days later.[151] The index case was smear positive with a productive cough. Contact tracing was initiated despite the flight duration being under 8 hours, because of the diagnosis of XDR-TB. Substantial obstacles to contact tracing were highlighted, including difficulty obtaining relevant contact details, poor international cooperation, and concerns over causing inappropriate anxiety. The 11 close contacts identified were distributed worldwide, and by the publication date only seven had been informed of their contact status. No active TB transmission was discovered.

The most recent (and most highly publicised) association of TB and air travel occurred in 2007.[152,153] A patient with presumed XDR-TB undertook several long-haul flights against medical advice. No cases of TB transmission were identified.

Mathematical models have been used to estimate infection risk to passengers from an index case with TB.[154,155] Infection risk depends on movement of the index case, effectiveness of ventilation, and the amount of mixing of cabin air. A figure of 1 in 1000 has been proposed as the risk of TB transmission for exposed passengers.

The evidence thus suggests that the risk of TB transmission during air travel is low, and certainly no higher than in any other confined spaces. Contact tracing is time and resource consuming,[156] and to date no cases of active TB transmission have been documented despite numerous contact tracing investigations. Risk factors appear to be infectious TB; productive cough and smear positive sputum, cavitating or laryngeal TB, flight duration (over eight hours), and proximity to the index case (within two rows).

Influenza

A large body of literature exists pertaining to international spread of influenza by air travel, particularly with reference to a pandemic. [157-162] In addition, several articles have examined whether restriction of air travel could mitigate pandemic influenza [163-167] or whether quarantine of suspected cases at airports or borders is a better approach.[168-170] Importation of influenza virus by air travel is well-described.[171,172] Discussion of such issues is beyond the remit of this document.

There are relatively few data on the in-flight transmission of influenza. In the first cases series, a Boeing 737 with 54 passengers was grounded for 3 hours in 1977 because of engine failure.[69] During this delay the normal ventilation system for the aeroplane was turned off. Most passengers remained on the aeroplane during the delay, and 38 (72%) subsequently developed an influenza-like illness (ILI) with a median duration of 38 hours after the event. The rate of illness increased depending on the length of time the passengers spent on the plane during the delay. The presumed index case was a symptomatic young woman who had a severe cough throughout the flight. Eight of 31 passengers tested had the same strain of influenza A as the index case. As some passengers left the plane and some remained in their seats, it was possible to show that the risk of ILI was significantly related to time spent in contact with the index case (53% attack rate for less than 1 hour on board compared with 86% for spending more than 3 hours on board). Twenty two of the symptomatic passengers had paired sera tested, with 20 showing a significant increase in antibody titres to the particular influenza strain.

The second case series involved an outbreak of influenza at a naval air base in 1986.[173] Sixty of 114 squadron members developed influenza over a short time period, of which 24 developed ILI on return from an assignment in Puerto Rico. Twenty three of 24 had travelled on a 2 ½ hour air flight on one of two DC-9 aircraft on which a squadron member who developed ILI prior to departure had also flown. Rates of infection were 4-fold different between the two aircraft, which the authors concluded was likely due to the infectivity of source patients and increased number of source cases on the second plane (three on the first and eight on the second).

A third case series was published in 2003.[174] A symptomatic index case with ILI boarded a 75-seat passenger aircraft on a 3 ½ hour flight. Over the subsequent three to four days, 15 people who also travelled on the same flight developed ILI, and a further six had acute upper respiratory tract symptoms. Those affected were more likely have sat within close proximity to the index case, both in front and behind.

Influenza outbreaks during air travel do occur with symptomatic patients, likely via airborne droplet transmission. In all of the above cases the aircraft were either old, or lacked functioning ventilation. This makes it difficult to generalise to modern, well ventilated aircraft, and accounts for the stark difference in attack rates.

Severe acute respiratory syndrome (SARS)

SARS is caused by coronavirus infection, and characterised by fever, cough and breathlessness.[17175,176] The two main concerns with regards to air travel are rapid dissemination of the disease geographically and in-flight transmission. There is substantial evidence that during the 2003 SARS outbreak, there was significant spread of the disease via air travel.[177-179] One paper describes six cases imported to Singapore in March and April 2003; four were rapidly identified and isolated on arrival, and no secondary cases developed as a result.[180] However the other two cases were imported before the disease was recognised, and substantial secondary spread was documented.

In-flight transmission of SARS does not appear to be common. An in-depth analysis of three flights on which a patient infected with SARS travelled occurred following the outbreak.[181] Three hundred and four (45%) travellers on the same planes were contacted and interviewed. Of these 16 developed SARS, and two probably developed SARS. Four of those not interviewed also developed SARS, with one other diagnosed as probable SARS. These 23 people were thought to subsequently spread SARS to at least 13 more people. Two of the three flights studied with five symptomatic patients resulted in only one additional patient becoming infected. However, one flight with one infected symptomatic patient resulted in infection in 22 (18%) other patients on the flight.

During this flight the risk of contracting SARS was greatest for the people on the same seating row or three rows in front of the index patient, although substantial numbers of patients who contracted SARS from that flight were seated further away or behind the index case, suggesting that spread may be airborne rather than large droplet. All patients infected were in the same section of the aircraft, indicating that the ventilation system was not responsible for transmission.

One study examined nine SARS cases on seven flights entering Singapore.[182] Of these, four patients on three flights were symptomatic, and only one case of in-flight transmission was reported. This patient had significant respiratory symptoms (cough), in contrast to some of the other cases who just had fever. Transmission was from an index case to a flight attendant; contact was minimal, with the attendant never coming within 1m. Transmission still occurred despite the patient being isolated at the back of the plane with suspected SARS.

One study examined the transmission of SARS by an index patient that had travelled on seven flights in Europe.[183] The patient was symptomatic during all but one of the flights. Two hundred and fifty patients were identified as contacts, but only 36 were included in the study. Of these, all were serologically negative for SARS. Ten described post-flight symptoms such as cough, headache and myalgia, but none developed proven disease. Finally, contact tracing studies of SARS patients flying to Canada [184] and the USA showed no evidence of SARS cases linked to in-flight transmission, even in symptomatic patients with contacts seated in close proximity.

In-flight transmission was thus probably low for most SARS patients. However, certain patients (“super-spreaders”) seem to have had high rates of transmission, predominantly those who were symptomatic, and particularly those with respiratory symptoms.

Common cold

Many air travellers complain of symptoms attributed to infection after air travel, such as dry eyes and throat, headache, fatigue and nasal stuffiness.[127,185,186] However, there are few convincing data indicating that these symptoms reflect infection. Robust data on the prevalence of respiratory viruses or bacteria in patients complaining of upper respiratory tract symptoms are not available. A study testing respiratory samples from 172 patients with suspected SARS following air travel found a broad range of respiratory viruses and atypical pathogens in 43% of subjects.[188] Pathogens included parainfluenza and influenza (most common), adenovirus, coronavirus, rhinovirus, metapneumovirus and respiratory syncytial virus, as well as bacteria such as *Legionella* and *Mycoplasma*.

Transmission was not identified between passengers, and “clumping” of cases with the same pathogen by seating pattern was also not evident. A study of patients attending airport medical facilities in Oman showed that 19.7% were diagnosed with upper respiratory tract infection, but the paper does not detail how the diagnoses were made.[187] None of the cases were subsequently hospitalised, and no cases of lower respiratory tract infection or pneumonia were reported. A further study compared the incidence of upper respiratory tract infection between passengers on flights where air is re-circulated and where air is fully imported from the external environment.[189] Similar levels of symptoms were reported in both groups, suggesting that air recirculation does not increase transmission of upper respiratory tract infection.

One study reported that by increasing in-flight humidification many of these symptoms can be alleviated.[186] Flight attendants are more likely to report work-related upper respiratory tract infections including colds and flu than the general population, but no more so than school teachers.[190] These data raise the possibility that upper respiratory symptoms experienced during air travel and attributed to infection may be due, at least in part, to a combination of the reduced partial pressure of oxygen, jet lag, noise, vibration, low humidity, and other stressors.[130]

Community-acquired pneumonia

Few data are available on the safety or airline travel for patients with community-acquired pneumonia (CAP). Data from emergency air medical transport cases show that despite the emergency repatriation of a number of patients with CAP, no deaths or adverse events were reported in-flight.[191] A study of cases for which medical assistance was required on British Airways flights between January and September 2000 found that around 5% were respiratory in origin and no cases of CAP were reported.[29] Furthermore, from a case series of nine patients returning by air from abroad with CAP who were symptomatic whilst in-flight, only one was as part of a medical evacuation, and in-flight adverse events were not reported in any of the others.[192] Other data have shown that around 6.9% of pre-flight oxygen assessments are made for patients who have had CAP in the preceding month.[193] Current guidelines state that patients should be afebrile and clinically stable enough to tolerate air travel and minimise transmission of communicable infection to other passengers.[20,194] Significant hypoxia would also preclude air travel given the relative hypoxia experienced in a cabin pressurised to between 5000 and 8000 ft.

Lung abscess

There are no published data on the effect of air travel on patients with lung abscess. Theoretically, in cases where the abscess communicates with other airways, equalisation of air pressures should occur and the risk of expansion of the abscess should be small. Where there is no communication with the airways, presumably the situation would be analogous with a non-communicating bulla, except that an abscess with thick walls might be expected to be less likely to collapse or expand due to pressure differences. The concerns should be as for CF / bronchiectasis: namely to maintain adequate hydration, access to medications, and adequate oxygenation prior to departure.

In summary, as regards the safety of air travel and respiratory infection, hypobaric hypoxia is the main risk to patients with chronic or acute respiratory infections. No additional risks specific to respiratory infections has been identified. In patients with cystic fibrosis, significant improvements in in-flight oxygen saturations and lung function can be gained by intensive physiotherapy in the four weeks prior to flying. Reports of patients with community acquired pneumonia (CAP) repatriated by air do not highlight any in-flight adverse events, suggesting that current guidelines are safe. There are no data relating to lung abscess and air travel.

Human immunodeficiency virus (HIV) infection

There is no literature specifically addressing the risk of air travel for patients with HIV, or who are at risk of other blood borne viruses. It is clearly vital to protect airline staff and other passengers from infection, and there is ample information on the risk of contracting HIV from body fluids. HIV is not present in urine, faeces, vomit and sweat. HIV is present in tiny but non-infectious quantities in saliva, tears and blister fluid. However, these fluids are potentially infectious if frankly blood stained. HIV is present in infectious quantities in blood and blood products, genital secretions including semen, and breast milk.

Although there are data to suggest that HIV positive patients with tuberculosis (TB) are less infectious than HIV negative patients,[195-198] this should not be assumed to be the case for air travel. The principles of preventing patients with infectious TB from travelling by air, and, if this fails, contact-tracing passengers sitting near the index case, should apply as usual. The HIV passenger who is exposed to a patient with sputum positive tuberculosis may if infected have a 50% greater risk of progressing to active disease (and greater lifetime risk) depending on their CD4 count.[199-201]

Interstitial lung disease

As in 2004, the data are limited. Kramer and colleagues reported on six patients with pulmonary fibrosis flown to specialist centres for single-lung transplantation.[94] Resting sea level PaO₂ ranged from 5.3 to 7.3 kPa and FEV₁ from 23 to 68% predicted. All patients flew with in-flight oxygen (4-8L/min), four had a medical escort and flight duration ranged from 4.5 to 20.5 hours. All arrived safely without complications. During a study of hypobaric hypoxia in patients with restrictive lung disease, Christensen [202] examined 10 patients with lung fibrosis (three with

sarcoidosis, two with fibrosing alveolitis and the remainder unspecified fibrosis). All had FEV₁ ~ 50% predicted and TLC <80% predicted. At simulated altitude PaO₂ fell significantly and fell further during light (20W) exercise, equivalent to slow walking along the aircraft aisle. Supplementary oxygen restored PaO₂ to acceptable levels.

More recently, Seccombe and colleagues[203] evaluated the effect of simulated cabin altitude on 15 patients with ILD (11 men) and 10 subjects with COPD at rest and during a limited (50m) walking test. They found that even with acceptable resting sea level arterial blood gas tensions, significant desaturation occurred in both groups (mean SpO₂ 87% and mean PaO₂ 6.8 kPa in ILD patients) which worsened with minimal exercise (mean SpO₂ 79.5% and PaO₂ 5.5 kPa in ILD). Furthermore, resting blood gas determinations at rest did not predict subsequent hypoxaemia. This finding is consistent with data from the UK Flight Outcomes Study, a prospective, observational study of 431 patients (including 186 with ILD)[6] which showed that neither FEV₁ nor resting SpO₂ predict desaturation at altitude. In this study, ILD patients were more likely to require unscheduled health care for respiratory events within four weeks of air travel than were other respiratory patients; there were no documented episodes of VTE in this period but 65% of all patients requiring unscheduled health care (irrespective of diagnosis) reported receiving antibiotics for lower respiratory tract infection.

Martin and colleagues[91] included 15 ILD patients in a study which compared hypoxic challenge testing with predictive equations; they found that predictive equations overestimated the need for in-flight oxygen in ILD patients as well as those with COPD and cystic fibrosis. Finally, in a study examining the effects of oxygen on sleep and breathing in ILD patients living at 2,240m of altitude in Mexico City (and thus acclimatized to moderate altitude), no difference in sleep efficiency or arousal index was observed between patients and controls.[204] Oxygen reduced heart rate and breathing frequency in ILD patients during sleep, but did not normalize breathing frequency.

In conclusion, patients with ILD should be evaluated as previously described, since at present there are insufficient data to justify changes to pre-flight evaluation. Patients staying at high altitude destinations will experience desaturation and tachypnoea; their significance is currently unclear but supplementary oxygen may need to be considered. ILD patients appear relatively likely to require emergency medical care after air travel. They should therefore be carefully assessed beforehand regarding

co-existing morbidities and their risk of respiratory tract infection, which may justify an emergency supply of antibiotics and appropriate medical advice.

Neuromuscular disease and kyphoscoliosis

Data remain sparse. There is one case report of cor pulmonale developing in a patient with congenital kyphoscoliosis after intercontinental air travel.[205] The patient was a 59 year old male with apparently stable cardio-respiratory function who developed a first episode of pulmonary hypertension and right heart failure after a long-haul flight. The authors concluded that this resulted from prolonged exposure to a reduced FiO_2 in the aircraft cabin.

A recent study[206] examined 21 patients (16 with idiopathic kyphoscoliosis and five with neuromuscular disease, including one with previous poliomyelitis). Thirteen were male and median age was 58 yrs (range 22-73yrs). Median FVC was 0.81 (0.3-1.2l) and median FEV1 0.66l (0.3-1.0). Median SpO_2 at sea level was 95% (range 92-99%). Fifteen patients were domiciliary NIV users. All patients underwent standard hypoxic challenge. In six patients with resting $\text{SpO}_2 >95\%$ on air, and in five with resting SpO_2 92-95%, PaO_2 fell to <6.6 kPa on hypoxic challenge testing.

Desaturation on hypoxic challenge was found to be likely if the FVC was below 1L, even where resting sea level SpO_2 exceeded 95%. There is still no evidence as to whether this level of hypoxaemia would have adverse effects, and no evidence exists as to whether NIV or supplemental oxygen is the best approach for such patients when travelling by air. The authors conclude that all patients with severe extra-pulmonary restriction should undergo hypoxic challenge testing before air travel, and that the decision to recommend in-flight oxygen and/or NIV for these patients must be made on an individual basis, taking into consideration the patient's previous travel history, overall clinical condition and the results of hypoxic challenge testing.

Obstructive sleep apnoea syndrome (OSAS)

Little is known about the effects of air travel on patients with OSAS. In general patients are advised to avoid alcohol before and during flight, based on the known adverse effects of alcohol on sleep and OSA.[207] Sleeping tablets and sedatives should also be avoided.[208] Flights may be scheduled overnight and many patients with OSAS report that if they allow themselves to sleep their snoring disturbs neighbouring passengers. Patients may wish to drive or work shortly after an overnight flight; evidence suggests that withdrawal of CPAP for just one day may

cause sleepiness.[209] Following trans-meridian flights patients may also have to contend with the effects of jet lag. For these reasons it would seem advisable for patients to use CPAP while sleeping in-flight (having notified the airline in advance) but this requires power either from a suitable battery or, when available, from the aircraft's power supply with suitable connecting equipment. Power supplies are not available on all flights, sockets may not be available at every seat, and even if available, not all airlines allow them to be used for such equipment. Airlines do not always provide an appropriate adaptor and older machines may not be compatible with the power supply. Some CPAP machines can be powered from a direct current while others may require an inverter. Dry batteries are heavy and will only power a CPAP machine for a limited time. Obtaining good advice from airlines can be difficult and may even result in the patient being barred from flying altogether.[210]

CPAP use in flight and at high altitude destinations requires a machine that will perform adequately at low ambient pressure. Calculations based on the collective fan laws and measurements made in a hypobaric chamber have shown that a fixed-pressure CPAP machine without pressure compensation set to deliver a pressure of 12 cm H₂O at sea level may deliver only 9 cm H₂O at 8000 ft. Machines with pressure sensors can deliver accurate pressures across a range of pressure-altitude combinations. Patients should use their CPAP machines at their destination as they do at home. Adaptors and extension cables may be necessary.

Obesity

The prevalence of obesity is increasing in all developed countries in response to lifestyle changes resulting from increasing prosperity. The association of OSAS with obesity is well known. Obesity may also cause dyspnoea, chronic hypoventilation (obesity hypoventilation syndrome), may complicate COPD (overlap syndrome) and is a risk factor for venous thrombosis and pulmonary embolism. Within the UK increasing numbers of patients are now making short flights to and from major centres for bariatric surgery. Whether or not this carries a risk is unknown. There are few data regarding the effects of air travel in the obese, but there is one case report of a morbidly obese woman who developed respiratory and cardiac failure at the end of a fortnight's tour involving two flights and a stay at altitude.[211]

Pneumothorax

Travel with an untreated current pneumothorax is a source of risk because of the potential pressure changes leading to expansion of the air contained in the pleural

space between the visceral and parietal pleura. The risk relates to ascent and descent, and there is no evidence to suggest that those at risk of developing a pneumothorax (rather than already having one) are more likely to do so as a result of air travel. Data from the British Thoracic Society UK Flight Outcomes Study[6] have given us more information regarding safety of air travel for those with lung disease, and despite a high proportion of patients flying with COPD there were no pneumothoraces reported. Nor were there any in a retrospective study of 10,189 cases of surgical and medical emergencies on board European aircraft.[12] A 'new' pneumothorax occurring at altitude may be hazardous because of absence of medical care, but air travel itself does not make a pneumothorax more likely.

The key issues to address are those regarding the likelihood of a pneumothorax occurring spontaneously in somebody with pre existing lung disease, and especially the likelihood of recurrence in somebody with a history of a pneumothorax. In order to determine an optimal time for air travel after a documented episode of pneumothorax the literature was reviewed to determine the recurrence rate without treatment or the recurrence rate after an attempted definitive procedure

In the 2002 British Thoracic Society air travel recommendations[1] it was noted that if the pneumothorax had been treated by thoracotomy and surgical pleurodesis or by talc insufflation (at thoracotomy), the recurrence rate should be so low that no subsequent restriction on travel is necessary. At that time a note of caution was inserted to the effect that similar interventions undertaken via thoracoscopy may not always carry the same certainty of success.[212-215] Subsequently a more recent systematic review of both randomised and non randomised trials has confirmed these earlier individual trials in showing a very high success rate with pleurodesis undertaken via open surgery but an up to four times higher rate of recurrence in those having a video assisted thoracoscopic procedure.[216] While there may be other reasons why video assisted thoracoscopic interventions have advantages in cases of recurrent pneumothorax, advice regarding future risk should be cognisant of the fact that the definitive nature of the intervention is more certain if the procedure was undertaken via open surgical procedure.

Chemical pleurodesis not using talc (for example with tetracycline) inserted without any form of direct vision (thoracoscopic or surgical) is associated with a much higher continued risk of recurrence: 16% in one study with 50% of the recurrences arising at 30 days,[217] and 13% in another.[214] The best figure was 9% rate of recurrence

after chemical pleurodesis[218]; these recurrence rates suggest that even after such an intervention the patient should still be subject to travel advice given to others having had a spontaneous pneumothorax.

For patients who have not had a definitive surgical pleurodesis via a thoracotomy, a risk of recurrence should therefore be expected. If they have had an intervention utilising video-assisted thoracoscopy the patients should be advised of a very low rate of recurrence. A definite risk of a recurrence should be expected in all other patients and whilst many studies have included details of the percentage of patients suffering a recurrence, very few have given much detail of the timing of these recurrences after the first episode, and few have characterised those most at risk. In one study a 54.2% recurrence rate was recorded with the majority occurring within one year of the first pneumothorax,[219] and in another study 72% of the recurrences occurred within two years of the first episode.[220]

Cumulative freedom from recurrence data have been published by Lippert[220] and stratified according to smoking history and underlying lung disease over a follow up period of up to 13 years. The shape of the curve (figure 2) does not imply that the biggest risk of recurrence is only in the first year. Furthermore, current advice does not take into account those with a higher risk of recurrence such as smokers, those with pre-existing lung disease, taller men, and possibly women.[220,221]

Thoracoscopic examination of the pleura does not improve prediction of those at greatest risk of recurrence.[222] Whether the same situation applies to those having had a traumatic pneumothorax is unclear. One study of 12 consecutive patients wishing to fly following recent traumatic pneumothorax showed that 10 waited at least two weeks following a radiological resolution and were asymptomatic during flight. One of the two patients who flew within 14 days developed distress during flight.[223]

A further situation is that of patients who appear to have residual small or loculated pneumothoraces which have been present for some time. Two case reports of investigations and outcomes in such patients have been reported. These were extensively investigated without problems, and/or tolerated HCT without adverse events. The authors concluded that some patients with a closed chronic pneumothorax can fly without adverse consequences. However, it should be made clear that these may not have been typical patients. They may have had spontaneous or surgically induced adhesions over much of the pleural surface, and

they only flew after extensive investigations had confirmed the stable nature of their condition.[224]

Patients with pulmonary lymphangio-leiomyomatosis (LAM) are prone to pneumothoraces, and a questionnaire survey of women listed on United States and UK LAM registries has recently been published.[225] Two hundred and seventy six respondents had travelled by air and ten had suffered a pneumothorax, of whom eight had the diagnosis confirmed by chest radiograph. These patients who reported a pneumothorax in association with air travel were asked for further information. Eight of the ten women had at least one prior pneumothorax; one respondent had developed a pneumothorax on two separate flights. The authors of this study estimate the risk of a pneumothorax in flight to be 2.2% (10 pneumothoraces during 454 flights), and the risk estimate of pneumothorax per woman flying was 4% (10 women with pneumothoraces among 276 women who flew). Half of those who suffered a pneumothorax had some symptoms to suggest that it might have been present before boarding the aeroplane, and in four symptoms began during flight or after landing. These authors, while acknowledging the limitations of their methodology, recommend that patients with LAM should be advised that the presence of any clinical symptoms such as unusual chest pain or shortness of breath before flight should preclude flying until fully evaluated. However, because a pneumothorax was a relatively uncommon occurrence in people with this disease, they did not believe that the disease by itself should preclude air travel.

Pulmonary arterio-venous malformations (PAVMs)

Pulmonary arteriovenous malformations (PAVMs) provide direct capillary-free communications between the pulmonary and systemic circulations.[226] Pulmonary arterial blood passing through these right-to-left shunts cannot be oxygenated, leading to hypoxaemia. Furthermore, the absence of a filtering capillary bed allows particular matter to reach the systemic circulation; embolic strokes are thus a common complication. The majority of PAVMs occur in individuals affected by the inherited vascular disorder hereditary haemorrhagic telangiectasia (HHT).[227]

From first principles, concern regarding in-flight exacerbation of hypoxaemia would appear justified, as well as concern regarding the increased risk of VTE, leading to the possibility of paradoxical embolic strokes. However, patients with PAVMs frequently tolerate severe hypoxaemia without ill-effect and there is no reliable threshold SpO₂ or PaO₂ which will predict the need for in-flight oxygen.

There are no published data on air travel and hypoxaemia. Anecdotal experience is that individuals with profound hypoxaemia (resting SpO₂ at sea level 60-70%) have flown without oxygen without first seeking medical advice and suffered no ill-effects. No data on flight-associated complications in PAVM or HHT patients were identified through a Medline search. However, one of a series of PAVM/HHT VTE cases,[228] and one of a series of PAVM/HHT paradoxical embolic strokes, [229] occurred immediately after transatlantic flights.

Sinus and middle ear disease

Sinus barotrauma occurs when pressure in the sinuses cannot equilibrate with the environment owing to occlusion of the sinus ostium.[230] It can occur on ascent (known as reverse squeeze) or descent (known as squeeze), but problems on descent are twice as common. Risk factors for squeeze are mucosal oedema, pus, thick mucin, extra-sinus polyps and tumours. Risk factors for reverse squeeze are similar but include intra-sinus pathology. Air that escapes via a non-physiological route with reverse squeeze can have serious consequences including subcutaneous or ocular emphysema, blindness, pneumocephalus, meningitis and trigeminal dysfunction.[231] Children are particularly at risk of barotrauma, as outlined previously.

The risk of sinus barotrauma is increased by a higher rate of change of altitude. Commercial air travel does not usually expose passengers to a faster descent than 100-120 metres per minute so where sinus barotrauma occurs it is unlikely to be severe. Sinus barotrauma has been classified by Weissman and Garges into Class 1, 2 and 3.(Table 2)[232] The more severe types are more likely to be seen in air force pilots.

Table 2 Classification of sinus barotraummas

Class	Symptoms	Radiography	Pathology
1	Transient discomfort	Normal	Slight swelling
2	Pain <24 hours	Mucosal thickening	Serosanguinous rhinorrhoea
3	Severe pain	Obliterated sinus	Haematoma, mucosal avulsion

Presentation in civilian passengers is usually with frontal sinus pain, but bloody discharge has been reported. More severe sinus barotrauma in aircrew also usually

presents with frontal pain but there may be malar pain and bloody rhinorrhoea. The mucosa may tear from the periosteum causing haematoma formation.[233]

There are no controlled trials in passengers at risk of sinus barotrauma, but there is evidence to support prophylactic treatment for adults at risk of middle ear barotrauma. An oral decongestant beforehand and a nasal decongestant spray during the flight just before descent are recommended in both situations.[230, 234] In contrast, a randomised controlled trial of pseudoephedrine given pre-flight to children with ear pain or nasal congestion did not show any benefit.[235] Patients in the first trimester of pregnancy may wish to avoid topical decongestants and take nasal steroids instead. A small study of air travel in children with otitis media did not find that air travel increased symptoms or subsequent complications[236], perhaps because the middle ear was filled with fluid and not air.

Treatment for sinus barotrauma after the flight is usually topical and oral decongestants, analgesics and oral steroids. Antibiotics are used if a bacterial sinusitis is thought to be the trigger and antihistamines if allergic rhinitis is suspected. All symptoms and signs of barotrauma should have resolved prior to flying again, and some recommend plain radiography to ensure that mucosal swelling has settled. This usually takes at least a week, and can take up to six weeks.[237]

Recurrent sinus barotrauma is usually only seen in military aircrew and has been shown to respond to functional endoscopic sinus surgery (FESS).[238]

In conclusion, there is limited evidence on which to base recommendations. However, mucosal oedema caused by upper respiratory tract infection or allergic rhinitis probably increases the risk of sinus barotrauma. Topical decongestants prior to the flight and nasal decongestant spray prior to descent are currently recommended for adults at risk but not for children. Severe barotrauma is unlikely in passengers due to the low pressure differentials and slow changes in cabin altitude.

Thoracic surgery

There is no direct evidence to guide recommendations for air travel in patients who have recently undergone thoracic surgery. Indirect evidence is largely extrapolated from small studies of pneumothorax and air travel, as reviewed above (see under Pneumothorax).

A “pneumothorax” is universal during intra-thoracic surgery, and the risk of persistence depends on a number of factors. With regards to the surgical procedure, procedures that breach the visceral pleura (for example pulmonary resection) have a higher risk of air leak compared to those that do not breach the visceral pleura (for instance resection of mediastinal tumours and pleural biopsies). Another potential for post-operative pneumothorax development is the introduction of air into the pleural space when the drains are removed. Owing to the lack of evidence to support decision-making after surgery, the BTS Air Travel Working Party has chosen to make recommendations consistent with those for pneumothorax.

Venous thrombo-embolism (VTE)

In 2001, a meeting held by the World Health Organisation (WHO) concluded that there was a likely association between air travel and increased risk of venous thromboembolism (VTE). It identified key areas for research, in particular to confirm and quantify the risk, determine the interactive effect of other underlying risk factors, and understand the underlying mechanisms. Lastly, there was a need to assess the impact of preventative strategies. Since then, many studies have been published in an attempt to address these questions. Most notable are those which comprised the WRIGHT project (WHO Research Into Global Hazards of Travel), commissioned by WHO in response to their conclusions.[239]

These studies have been reviewed in detail and also published in the WRIGHT project report.[239] They are divided into case-control studies, which provide an estimate of relative risk, and cohort studies, providing estimates of absolute risk. The data suggest an overall doubling of risk of VTE after long-haul air travel (over four hours). This risk can also be applied to other forms of travel, such as bus, train or car. Risk increases with duration of travel, with a four-fold increased risk with journeys over eight hours in duration. Multiple short journeys over a short period are also associated with increased risk. Using screening, the absolute risk of developing an asymptomatic VTE ranges from 0 to 10%.[240-244] The absolute risk of symptomatic VTE is much lower at approximately 1 in 4600, increasing to 1 in 1200 with journeys over 16 hours.

Pulmonary embolism following long-haul flights often presents earlier, on standing up or in the airport, and may be fatal. This probably explains why VTE has received so much attention in the media and raised concern among the flying public. The risk of presenting acutely with pulmonary embolism after a long-haul flight of under 8-9

hours remains very low (<0.5 per million), but increases to up to 5 cases per million in flights over 8-9 hours.[245] A recent study has shown that the risk of pulmonary embolism presenting up to two months after long-haul flight increases 17-fold from 0.03 to 0.5 cases per million when travel exceeds 5000km.[246] The reason for the discrepancy by an order of magnitude between these two studies is not clear, but nonetheless the absolute risk appears low.

Unpicking which aspects of air travel may be contributing to the increased risk of VTE has so far proven difficult. Hypobaric hypoxia itself does not seem to activate the coagulation system nor cause endothelial activation in healthy individuals.[247] A cross-over study in healthy volunteers comparing an eight hour flight with a movie marathon and regular activity did show increased thrombin generation following the flight in some individuals, especially those with Factor V Leiden mutation and/or taking the oral contraceptive pill.[248] This suggests that some flight-specific factors, such as hypobaric hypoxia and/or the type of seating, may be important in susceptible individuals.

Identifying individuals at higher risk is likely to be the first stage in a strategy to prevent VTE after prolonged air travel. The MEGA study was a case-control study of 1906 patients presenting with a first VTE and 1906 controls.[249] It showed that the risk of VTE was increased two-fold by travel (flight and non-flight) greater than four hours. Height greater than 1.90m increased risk when travelling on land by a factor of 4.7, Factor V Leiden mutation by 8.1 and those using oral contraceptives by greater than 20. These risks were greater with air travel. A body mass index over 30 kg/m² was associated with increased risk when travelling by land, but not air. Height under 1.60 m was however associated with increased risk during air travel, but not by land. The only thrombophilia testing undertaken was analysis for Factor V Leiden and prothrombin G20210A mutations and therefore no comment can be made about other acquired or heritable thrombophilic tendencies.

Another study which did not exclude patients with previous VTE found that the greatest risk factor present in patients with presumed flight-related VTE was previous VTE, with an odds ratio of 63, but the numbers in this study were small (46 patients and 92 controls).[250] Other risk factors included recent trauma, obesity, varicose veins, cardiac disease and immobility during the flight.

The recent study by Lehman[246] found that 40% of patients with travel-related VTE had evidence of thrombophilia, which compared with 48% in the group with no other cause identified, although testing was not performed on a systematic basis. This suggests that thrombophilia is no more a risk factor for air travel-associated VTE than it is for non-provoked VTE.

The World Health Organisation Research into Global Hazards of Travel (WRIGHT) Project has yet to produce data on prevention of VTE during flight. Several studies (under the acronym LONFLIT) have been published by a single research group from Italy, but their data using low molecular weight heparin[251] have not been replicated.

There are no data on use of aspirin for preventing air-travel associated VTE. It has been shown to reduce the rate of pulmonary embolism and deep venous thrombosis in post-surgical patients (PEP trial),[252], but has been superseded by low molecular weight heparin due to its efficacy and side-effect profile. Pneumatic compression devices appear to be no more effective than leg exercises, so may only be relevant in patients who are sedated or immobile.[253]

One trial has assessed the effect of below-knee graduated elastic compression stockings in passengers flying more than eight hours.[240] None of the 100 passengers in the group assigned to stockings developed asymptomatic VTE, whereas 12 out of the 100 control passengers did. Four patients developed superficial vein thrombosis in the stockings group; none did in the control group.

FUTURE DIRECTIONS

Research

There is a need for further research to identify which physiological variables can be used to predict arterial hypoxaemia with particular attention to outcome of air travel as measured by level of symptoms, functional ability and post flight respiratory status. The role of walk tests and use of symptom scores, such as the MRC dyspnoea scale, merits particular investigation. There is also a need for more data on infants and children with congenital heart disease.

APPENDICES (A1-7)

- Appendix 1 Reviewers
- Appendix 2 AHCPR grading scheme for recommendations
- Appendix 3 National referral centres with decompression centres
- Appendix 4 Major destinations exceeding 8000 ft (2438 m)
- Appendix 5 Sample MEDIF form
- Appendix 6 Figures 1-4
 - Figure 1. Relationship between atmospheric pressure (mmHg) and altitude (ft)
 - Figure 2. Cumulative freedom from pneumothorax recurrence in relation to pre-existing lung disease (adapted with permission from Lippert et al[220])
 - Figure 3. Conversion algorithm: saturations to kPa to mmHg
 - Figure 4. Conversion chart from feet to metres
- Appendix 7 Examples of equations for predicting hypoxaemia

Appendix 1 Reviewers (italics to be confirmed)

Dr Paulo Alves, Aviation Health, MedAire UK
Dr Ian Balfour-Lynn, President, British Paediatric Respiratory Society
Dr Simon Baudouin, Intensive Care Society
Dr Thomas Bettes, President, Airline Medical Directors Association
Mr Edward Black, Royal College of Surgeons of England
Dr Ian Cheng, Aviation Medical Services, Qantas Airways
Dr Chris Dyer, British Geriatrics Society
Mr Roland Furber, Chief Executive, British Paramedic Association
Dr Dhikan Ganguly, Respiratory Specialist, Kolkata, India
Group Captain David Gradwell, CAA Ireland
Dr Alastair Innes, Royal College of Physicians, Edinburgh
Dr Martin Johnson, Royal College of Physicians and Surgeons, Glasgow
Dr Ray Johnston, Civil Aviation Authority
Dr W S Lim, Royal College of Physicians, London
Dr Fiona Moore, Joint Royal Colleges Ambulance Liaison Committee
Dr Damian Muncaster, Chairman, Association for Respiratory Technology & Physiology
Mr D A Tolley, President, Royal College of Surgeons of Edinburgh
Dr John Shneerson, President, British Sleep Society
Dr Fiona Knight, Primary Care Respiratory Society UK
Ms Jenny Till, Association of Respiratory Nursing Specialists
Mr J Heyworth, President, College of Emergency Medicine
Dr Elizabeth Wilkinson, British Airways

Appendix 2 AHCPGR grading scheme for recommendations

Criteria for grading of recommendations are based on a paper by Petrie et al published on behalf of the Scottish Intercollegiate Guidelines Network.[254]

Table 1 **Levels of evidence**

Level	Type of evidence (based on AHCPGR 1992[254])
Ia	Evidence obtained from meta-analysis of randomised controlled trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well designed controlled study without randomisation
IIb	Evidence obtained from at least one other type of well designed quasi-experimental study
III	Evidence obtained from well designed non-experimental descriptive studies such as comparative studies, correlation studies and case controlled studies
IV	Evidence obtained from expert committee reports of opinions and/or clinical experience of respected authorities

Table 2 **Grading of recommendations**

Grade	Type of recommendations (based on AHCPGR 1992[255])
A (levels Ia, Ib)	<ul style="list-style-type: none">• Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation
B (levels IIa, IIb, III)	<ul style="list-style-type: none">• Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation
C (level IV)	<ul style="list-style-type: none">• Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality

Appendix 3 National referral centres with decompression chambers

1. RAF Centre for Aviation Medicine, RAF Henlow, Hitchin, Bedfordshire SG16 6DN.
Tel 01462 851 515

2. QinetiQ Centre for Human Sciences, A50 Building, Cody Technical Park,
Farnborough, Hampshire GU14 OLX. Tel 01252 392 600 (Facility Manager) or 01252
393 231

Appendix 4 Major destinations exceeding 800 ft (2438 m)

This is not an exhaustive list and passengers are recommended to contact the carrier if they suspect their destination may be at high altitude

Airport	Altitude (feet)
Bangda, Tibet	15,548
Bengdag, China	14,100
Bogota, Colombia	8,355
La Paz, Bolivia	13,310
Lhasa, Tibet	14,315
Quito, Ecuador	9,222
Telluride, USA	9,086

Appendix 5 Sample MEDIF form

Appendix 'E'

MEDIF

RESOLUTION 700 ATTACHMENT A

Information Sheet for Passengers Requiring Special Assistance

1. Last name / First name / Title

2. Passenger name record (PNR)

3. Proposed itinerary

Airline(s), flight number(s)

Class(es), date(s), segment(s)

4. Nature of disability

5. Stretcher needed onboard? Yes No

6. Intended escorts Yes No

Name

PNR if different

Medical qualification Yes No Language spoken

7. Wheelchair needed Yes No

Wheelchair categories WCHR WCHS WCHC Own wheelchair Yes No

Collapsible WCOB Yes No Wheelchair type WCBD WCBW WCMP

8. Ambulance needed (to be arranged by the Airline) Yes No

If yes, specify destination address

If no, specify ambulance company contact

9. Meet and assist Yes No

If designated person, specify contact

10. Other ground arrangements needed Yes No

If yes, specify

Departure airport

Transit airport

Arrival airport

11. Special inflight arrangements needed Yes No

If yes, specify type of arrangements (special meal, extra seat, leg rest, special seating)

Specify equipment (respirator, incubator, oxygen, etc)

Specify arranging company and at whose expense

12. Frequent traveller medical card (FREMEC) Yes No

If yes, specify FREMEC number, issued by, expiry date

Appendix 6 Figures 1-4

Figure 1 Relationship between atmospheric pressure (mmHg) and altitude (ft)

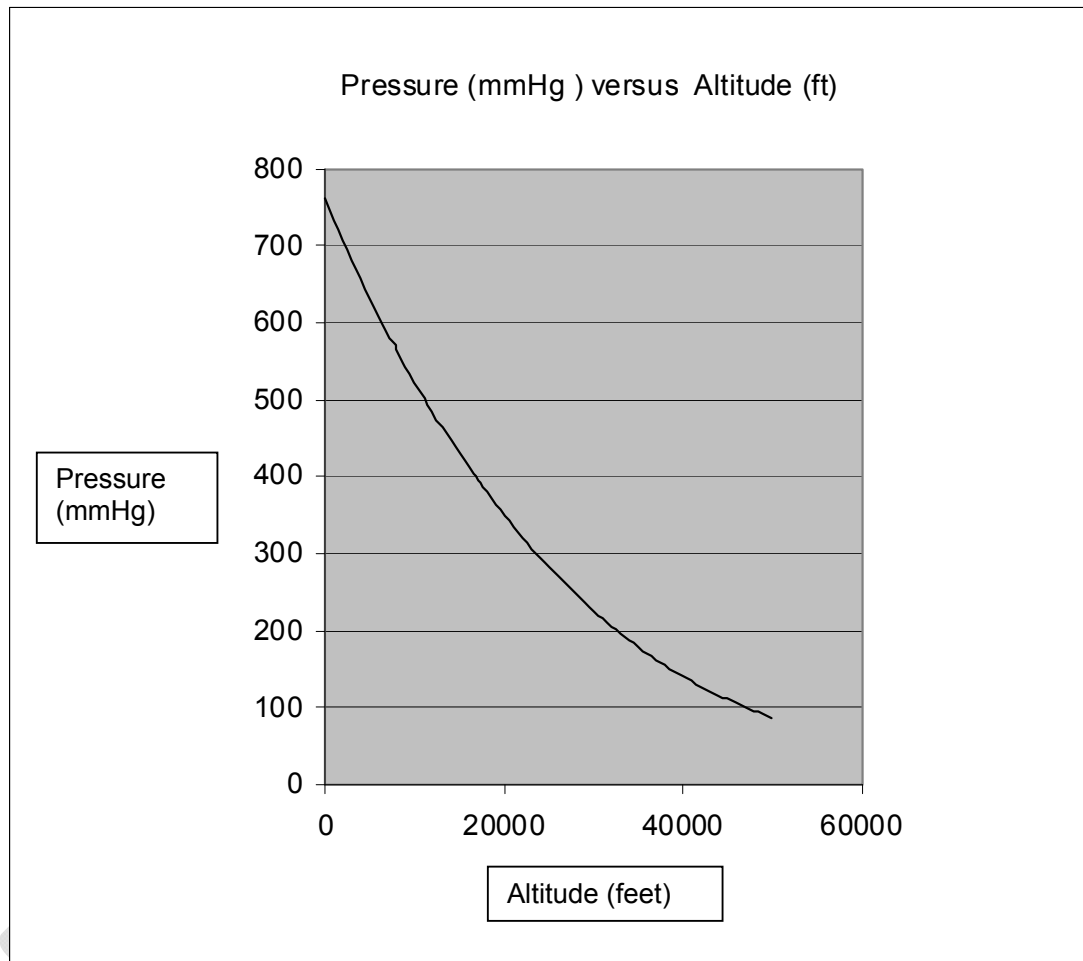


Figure 2 Cumulative freedom from pneumothorax recurrence in relation to pre-existing lung disease (adapted with permission from Lippert et al [220])

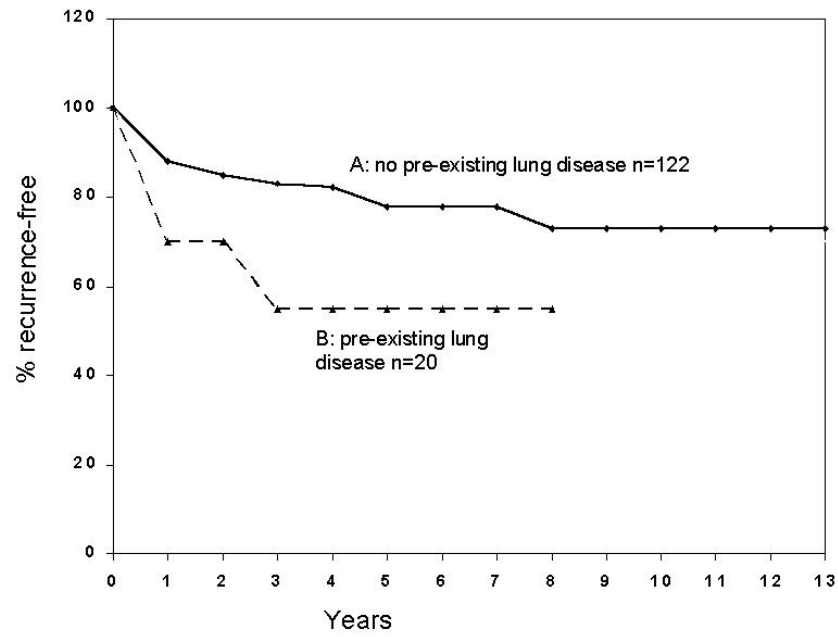


Figure 3 Conversion algorithm: saturations to kPa to mm Hg

SaO ₂ %	PaO ₂ kPa	PaO ₂ mmHg
97	12.7-14.0	95-105
94	9.3-10.0	70-75
92	8.9-9.7	67-73
90	7.7-8.3	58-62
87	6.9-7.7	52-58
84	6.1-6.9	46-52

Figure 4 Conversion chart from feet to metres

Feet	Metres	Feet	Metres
1000	305	26000	7925
2000	610	27000	8230
3000	914	28000	8534
4000	1219	29000	8839
5000	1525	30000	9144
6000	1829	31000	9449
7000	2134	32000	9754
8000	2438	33000	10058
9000	2743	34000	10363
10000	3048	35000	10668
11000	3353	36000	10973
12000	3658	37000	11278
13000	3962	38000	11582
14000	4267	39000	11887
15000	4572	40000	12192
16000	4879	41000	12497
17000	5182	42000	12802
18000	5486	43000	13107
19000	5791	44000	13411
20000	6096	45000	13716
21000	6401	46000	14021
22000	6706	47000	14326
23000	7010	48000	14630
24000	7315	49000	14935
25000	7620	50000	15240

Appendix 7 Examples of equations for predicting hypoxaemia

1. This relates PaO₂ at altitude (Alt) to PaO₂ at sea level (Ground) [42]:

$$\text{PaO}_2 \text{ Alt (mm Hg)} = 0.410 \times \text{PaO}_2 \text{ Ground (mmHg)} + 17.652$$

2. This relates PaO₂ Alt to PaO₂ Ground & includes FEV₁ in litres [42]:

$$\text{PaO}_2 \text{ Alt} = 0.519 \times \text{PaO}_2 \text{ Ground (mmHg)} + 11.855 \times \text{FEV}_1 \text{ (litres)} - 1.760$$

3. This relates PaO₂ Alt to PaO₂ Ground and includes FEV₁ as % predicted [42]:

$$\text{PaO}_2 \text{ Alt} = 0.453 \times \text{PaO}_2 \text{ Ground (mmHg)} + 0.386 \times (\text{FEV}_1 \% \text{ pred}) + 2.44$$

4. This relates PaO₂ Alt to PaO₂ Ground and includes flight or destination altitude [43]:

$$\text{PaO}_2 \text{ Alt} = 22.8 - (2.74 \times \text{altitude in thousands of feet}) + 0.68 \times \text{PaO}_2 \text{ Ground (mmHg)}$$

Notes:

a) thousands of feet should be entered as feet divided by 1000. 8000 feet would thus be entered in the equation as 8.0 not as 8000

b) Both papers use mmHg. One kPa = 7.5 mmHg

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