Aerospace Medicine: Part 3

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Abstract

ALTITUDE RELATED DISORDERS

Lung diseases may predispose to altitude illness. The term “high-altitude illness” is used to describe the cerebral and pulmonary syndromes that can develop in unacclimatized persons shortly after ascent to high altitude. Acute mountain sickness (AMS) and high-altitude cerebral edema (HACE) refer to the cerebral abnormalities, and high-altitude pulmonary edema (HAPE) to the pulmonary abnormalities. HAPE and HACE, though uncommon, are potentially fatal. Patients with known conditions and even without illness may consult pulmonary clinicians or generalists for counseling before participating. Other patients may present for consultations after complications have occurred. (76)

INCIDENCE AND RISK FACTORS

The incidence of AMS was 22%t at altitudes of 1850 to 2750 m (7000 to 9000 ft) and 42% at altitudes of 3000 m (10,000 ft). The incidence in children appears to be the same as that in adults. Women seem less susceptible to HAPE than men, but equally prone to AMS. (77,78)

The cause of AMS is not understood but is clearly related to hypoxia and factors such as exertion, air temperature, previous viral respiratory tract infection, and innate susceptibility. Other risk factors include a history of high-altitude illness, residence at an altitude below 900 m, and certain preexisting cardiopulmonary conditions. Persons over 50 years of age are somewhat less susceptible to AMS than younger persons. (76,78)

Physical fitness is not protective against high-altitude illness. Common conditions such as hypertension, coronary artery disease, mild COPD, diabetes, and pregnancy do not appear to affect the susceptibility to high-altitude illness. Diverse interactions between genetic factors and the environment most likely explain individual susceptibility or relative resistance to these hypoxia-induced illnesses (79)

Many studies suggest the hypothesis that the pathology of high altitude illness could be due to an early alteration of the hormones that regulate sodium homeostasis. The results show an early increase of plasma renin activity (PRA) and associated to a decrease of aldosterone plasma levels after exposure to hypoxia. This later returned to the baseline values at 180 min, whereas PRA remained increased throughout the exposure. Both arginine-vasopressin (ADH) and the atrial natriuretic peptide (ANP) significantly increased. These data demonstrate a specific sensitivity of the hormonal systems to hypoxia, which may be influenced by the time of the exposure. (80)

1) ACUTE MOUNTAIN SICKNESS

CLINICAL PRESENTATION AND DIAGNOSIS (81)

Acute mountain sickness is self-limiting and usually affects previously healthy individuals who go too rapidly to altitude. It is a syndrome of nonspecific symptoms and is therefore subjective. Headache is the early symptom of AMS in an unacclimatized person who has recently arrived at an altitude above 2500 m. Rarely, AMS occurs at altitudes as low as 2000 m.

Main symptoms of mild AMS are headache, nausea, dizziness, and fatigue during first 12 hr after rapid ascent to high altitude (>2500 m). The symptoms typically develop within 6 to 10 hours after ascent, but sometimes as early as 1 hour. There are no diagnostic physical findings except in the few cases that progress to cerebral edema.

Main symptoms of moderate AMS are moderate-to-severe headache with marked nausea, dizziness, lassitude, insomnia, mental confusion, ataxia, and fluid retention at high altitude for 12 hr or more. At altitudes above 9500 ft, AMS may be followed by the more serious conditions of HAPE and HACE, which frequently coexist.

PATHOPHYSIOLOGICAL PROCESS

In both the brain and the lungs, hypoxia elicits neurohumoral

and hemodynamic responses that result in overperfusion of microvascular beds, elevated hydrostatic capillary pressure, capillary leakage, and consequent edema. The exact process of AMS is unknown. The hypoxia-induced cerebral vasodilatation or its effectors, such as nitric oxide, most likely produce the headache, perhaps through the activation of the trigeminovascular system. The headache itself can cause other symptoms, such as nausea and malaise, and thereby account for mild AMS. An alternative hypothesis is that early AMS is due to mild cerebral edema. (82)

2) HIGH-ALTITUDE CEREBRAL EDEMA

CLINICAL PRESENTATION AND DIAGNOSIS

High-altitude cerebral edema is more malignant form of AMS. It is a potentially fatal neurologic syndrome that develops over hours or days in persons with AMS or HAPE. Clinically and pathophysiologically, HACE is the end-stage of AMS. This high-altitude illness typically presents with altered mental status, hallucinations, irritability, ataxia, altered consciousness and progressive neurologic deterioration. Associated findings of HACE may include papilledema, retinal hemorrhage (a common incidental finding), and occasionally, cranial-nerve palsy. Usually, the illness progresses over a period of hours or days. The cause of death is brain herniation. (83)

PATHOPHYSIOLOGICAL CHANGES

New evidence suggests that on ascent to high altitudes, all people have swelling of the brain. The magnetic resonance imaging techniques used for these studies, however, could not differentiate between vasodilatation-induced hyperemia and edema. An interesting hypothesis, supported by preliminary data, is that AMS might be related to a person's ability to compensate for the swelling of the brain. (82,84)

In those with moderate-to-severe AMS or HACE, neuroimaging demonstrates vasogenic edema. Hemodynamic factors such as sustained vasodilatation, cerebral autoregulation, and elevated cerebral capillary pressure most likely contribute to the formation of edema but cannot entirely explain the process. Hypoxia-induced biochemical alteration of the blood–brain barrier may also be important. Possible mediators, some triggered by endothelial activation, include vascular endothelial growth factor, inducible nitric oxide synthase, and bradykinin. (82-84)

TREATMENT AND PREVENTION

Management of AMS or HACE follows three axioms: further ascent should be avoided until the symptoms have resolved, patients with no response to medical treatment should descend to a lower altitude, and at the first sign of HACE, patients should descend to a lower altitude. Descent and supplementary O_2 are the treatments of choice, and for severe illness, the combination provides optimal therapy. HACE may require further descent. Antiemetics are indicated for nausea and vomiting. For insomnia requiring treatment, acetazolamide, which reduces periodic breathing and improves nocturnal oxygenation, is the safest agent. (78)

The symptoms of mild AMS is markedly improved by descend 500 m or more; or stop and rest; or speed acclimatization with acetazolamide (125 to 250 mg twice daily); or treat symptoms with analgesics. The preventive measurement includes ascend at a slow rate; spend a night at an intermediate altitude; avoid overexertion; avoid direct transport to an altitude of more than 2750 m; consider taking acetazolamide (125-250 mg twice daily) beginning 1 day before ascent and continuing for 2 days at altitude. (85)

AMS for 24 hr or more, with moderate-to-severe symptoms; Initiate immediate descent; if descent is not possible, use a portable hyperbaric chamber or administer O_2 (2-4 L/min); if descent is not possible and O_2 is not available, administer acetazolamide (250 mg twice daily), dexamethasone (8 mg orally or intramuscularly every 6 hr), or both until symptoms resolve; treat symptoms; or use a combination of these approaches. Same preventive measure as in mild AMS should be applied. (78,85,86) A single dose of 400 mg or 600 mg of ibuprofen may resolve high-altitude headaches. (87)

3) HIGH-ALTITUDE PULMONARY EDEMA

This is an unusual form of noncardiogenic pulmonary edema that develops after ascent to altitudes generally above 8000 feet. The ascent is often rapid, either by automobile or aircraft. Exposure to high altitude is for several hours, most commonly after an overnight stay. As is the case for AMS, the incidence of HAPE is related to the rate of ascent, the altitude reached, individual susceptibility, exertion and cold, which increases pulmonary artery pressure by means of sympathetic stimulation. (88)

This illness usually occurs only 2-5 days after acute exposure to altitudes above 2500-3000 m. Additional factors such as an inflammatory response and/or a decreased fluid clearance from the lung may, however, be necessary for the development of this noncardiogenic pulmonary edema. Bronchoalveolar lavage in patients with mostly advanced HAPE shows evidence of inflammatory response with

increased permeability. There are, however, no prospective data to decide whether the inflammatory response is a primary cause of HAPE or a consequence of edema formation. (89)

CLINICAL PICTURE

Early diagnosis is critical. In the proper setting, decreased performance, fatigue, dry cough and dyspnea should raise suspicion of HAPE. This life threatening condition may or may not be preceded by symptoms of AMS. Fever (up to 38.5°C) is common. Rales typically originate in the right axilla and become bilateral as the illness progresses. Upper respiratory tract infection or bronchitis may be precipitating factors. Late in the illness, dyspnea at rest, moist cough, severe weakness, drowsiness, cyanosis, tachycardia, tachypnea, rales, pink or bloody sputum and respiratory distress develop. Shock and death can result if symptoms are not recognized and treated. (88)

Abnormalities of cardiopulmonary circulation increase the risk of HAPE. High-altitude pulmonary edema commonly strikes the second night at a new altitude and rarely occurs after more than four days at a given altitude, owing to adaptive cellular and biochemical changes in pulmonary vessels. Cerebral signs and symptoms are common: 50% of those with HAPE have AMS, and 14% HACE. Of those whose condition deteriorates and who die, 50% have HACE at autopsy. (90)

Electrocardiography demonstrates sinus tachycardia and, often, right ventricular strain, right axis deviation, right bundle-branch block, and P-wave abnormalities. Chest X-ray typically reveals a normal-sized heart, full pulmonary arteries, and patchy infiltrates consistent with pulmonary edema, which are generally confined to the right middle and lower lobes in mild cases and are found in both lungs in severe cases. CT scans show a patchy predominantly peripheral distribution of edema. Measurements of ABG's reveal severe hypoxemia (PaO_2 of 30 - 40 mm Hg) and respiratory alkalosis. (88)

Wedge pressure is normal at rest, and there is rise in pulmonary artery pressure that precedes edema formation and appears to be a crucial pathophysiologic factor for HAPE. When the patient is removed to a lower altitude and treated with O_2, a dramatic improvement in symptoms and rapid clearing of chest X-ray findings occurs. (91)

PATHOPHYSIOLOGICAL PROCESS

High-altitude pulmonary edema is a noncardiogenic pulmonary edema associated with pulmonary hypertension and elevated capillary pressure. The usual pulmonary hypertension on ascent to high altitude is excessive in those with HAPE, as a result of exaggerated hypoxic pulmonary vasoconstriction. (91)

The mechanisms for this response include sympathetic overactivity, endothelial dysfunction, and greater hypoxemia resulting from a poor ventilatory response to hypoxia. In addition, the increased sympathetic activity probably raises capillary pressure as a result of pulmonary venous constriction. (91) Supporting this notion, a-adrenergic blockade improved hemodynamics and oxygenation in HAPE. (92)

Another possible explanation for elevated capillary pressure is uneven hypoxic pulmonary vasoconstriction. In addition, the dramatic increase in susceptibility to HAPE in persons with congenital or acquired pulmonary circulation abnormalities supports the idea that edema resulting from overperfusion in pulmonary vascular bed. (91,92)

The inflammation reported in HAPE is most likely a nonspecific response to stress-induced failure of capillaries and alveolar flooding, rather than part of the pathophysiological process. The dramatic response to O_2 can be explained by finding that the microcirculation rapidly returns to normal when capillary pressure drops. (91)

SUSCEPTIBILITY

Persons with a prior episode of HAPE may have a risk of recurrence as high as 60% if they abruptly ascend to an altitude of 4559 m. These persons are healthy but have a reduced ventilatory response to hypoxia and an exaggerated pulmonary pressor response to hypoxia and exercise. (93)

There is substantial overlap in the measured values between susceptible and nonsusceptible persons. However, it is not possible to predict exactly healthy persons who are at increased risk. In addition, in susceptible persons endothelial function might be impaired, with overexpression of constrictors such as endothelin-1 or underexpression of vasodilators such as nitric oxide (NO), or both, in response to hypoxia. (94)

Persons who are susceptible to HAPE have a genetic difference. Susceptible persons also have a higher incidence of HLA-DR6 and HLA-DQ4 antigens, suggesting that there may be an immunogenetic basis for susceptibility to HAPE. (95)

The concept that exaggerated hypoxic pulmonary vasoconstriction plays a central role in the pathogenesis of HAPE has led to several studies of pulmonary vascular pathophysiology in HAPE-susceptible (HAPE-s) individuals who previously experienced this condition. At 4559 m, HAPE-s subjects had an average pulmonary artery systolic pressure of 57 to 58 mm Hg by invasive and noninvasive means, compared with 37 mm Hg for normal subjects. (96)

Busch et al. (94) reported that NO excretion in expired lower respiratory gas decreased significantly during inhalation of hypoxic gas for 2 hours in HAPE-s subjects compared with normoxia. In contrast, the NO excretion rate of control subjects remained unchanged. The changes in Doppler pulmonary artery systolic pressure with hypoxia correlated with the percent changes in tract NO excretion ($P<0.05$).

An interesting study revealed that endothelin-1, a potent pulmonary vasoconstrictor peptide that also augments microvascular permeability, at low (580 m) and high (4559 m) altitudes, produced plasma levels about 33% higher at altitude in 16 HAPE-s mountaineers compared with 16 mountaineers resistant to HAPE. There was a statistical association between the changes from low to high altitude in endothelin-1 plasma levels and systolic pulmonary artery pressure ($P<0.01$). (97)

TREATMENT AND PREVENTION

Supplemental O_2 is the primary treatment in areas with medical facilities whereas the treatment of choice in remote mountain areas is immediate descent. Even susceptible individuals can avoid HAPE when they ascend slowly with an average gain of altitude not exceeding 300-350 m/day above an altitude of 2500 m. (88)

Administer oxygen (4 to 6 liters/min until condition improves, and then 2 to 4 liters/min to conserve supplies); descend as soon as possible, with minimal exertion, or use a portable hyperbaric chamber; if descent is not possible or oxygen is not available, administer nifedipine (10 mg orally initially and then 30 mg of extended release formulation orally every 12 to 24 hr); add Dexamethasone if neurologic deterioration occurs. Ascend at a slow, graded rate and avoid overexertion in persons with repeated episodes. In clinical studies, nifedipine reduced pulmonary artery pressure approximately 30% but barely increased the PaO_2. (78,85,86,98)

The Gamow bag is a portable hyperbaric chamber that allows the environmental pressure around the subject to be increased equivalent to a descent of up to 600 m. This can often improve symptoms considerably, but they will worsen once the subject is taken out of the bag to facilitate descent. (8)

Positive end-expiratory pressure delivered by means of a mask helps improve gas exchange and can be a temporizing measure. Antibiotics are indicated if there is evidence of infection. Endotracheal intubation, mechanical ventilation, and pulmonary-artery catheterization are rarely necessary. (76)

4) PERIODIC BREATHING DURING SLEEP

This phenomenon occurs commonly at high altitude even in normal climbers but also can become manifest at moderate altitude. Zielinski, (99) studied nine nonsmoking healthy men (mean age, 20 years) with full polysomnography at 760 m and at 3200 m. Periodic breathing appeared at altitude primarily during non–rapid eye movement sleep, ranging from 0.1% to 24% of total sleep time in different individuals. In addition, the number of arousals and awakenings doubled at high altitude, and episodes of central and obstructive apneas also increased ($P<0.001$). Mean pulse oximetry saturation was lower during the study nights at high altitude. Some ventilatory acclimatization was suggested by greater saturation during the sixth night compared with the first night at altitude ($P<0.001$).

Physicians treating patients with known sleep disorders should counsel patients to anticipate worsening during travel that involves exposure to moderate or high altitude. Adjustments to nasal continuous positive airway pressure devices may need to be considered to compensate for changes in ambient barometric pressure. (6)

PATIENTS WITH HEART AND LUNG DISEASE TRAVELING TO HIGH ALTITUDE AREAS (8)

Patients with well-controlled heart or lung disease may ask whether it is safe to travel at altitude. The evidence as far as heart disease is concerned is encouraging. Patients who have had a myocardial infarct or coronary artery bypass graft are probably safe to travel if they remain well three months after their operation or infarct. Patients with cardiac failure can travel providing they are capable of heavy exertion at SL without difficulty. Patients with systemic hypertension also seem to be safe at altitude. In a study of 935 patients there was no increase in incidence of stroke or cardiac failure in patients with systemic hypertension. Indeed, systemic blood pressure in patients with systemic hypertension falls up to altitudes of 3000 m. Patients with unclosed shunts should

not travel to altitude, as vasoconstriction will change the character of the shunt.

Patients with asthma usually do well. Allergen exposure is often less, but the cold, dry air of altitude may worsen asthma. Precautions for asthmatic patients include increase the prophylactic dose of steroids; carry a course of oral steroids and take a plentiful supply of inhalers. It is more difficult to advise patients with COPD. Ideally they should be fully assessed in a respiratory clinic before departure. In particular, gas exchange should be measured as this deteriorates with altitude.

ACCLIMATIZATION

Adequate acclimatization is essential for safe traveling in the mountains. The climber's adage is “climb high and sleep low.” Ideally acclimatization should be progressive. At altitudes above 3000 m individuals should climb no more than 300 m per day with a rest day every third day. Anyone suffering symptoms of AMS should stop, and if symptoms do not resolve within 24 hours descend at least 500 m. There can be a tendency, particularly on commercial expeditions, to push on at a rate that is too fast for weaker members of the group. This is dangerous, and the rate of ascent should be set to that of the slowest members of the party. (8)

FITNESS FOR FLIGHT DUTY

Medical illnesses that can cause sudden loss of consciousness or incapacitation in pilots create the greatest concerns for pilot and passenger safety. Conditions such as cardiac arrhythmias and other cardiac diseases, syncope, seizure disorders, and diabetes mellitus requiring hypoglycemic agents require immediate suspension of flight status for medical evaluation. (6)

Cardiovascular disease exceeds all other medical causes of premature termination for civilian airline pilots. There is a four-step screening algorithm to detect asymptomatic coronary artery disease in flight school candidates, cadets, and rated flyers of the United States Air Force. Risk factors for coronary disease, such as adequately treated hypertension, are not usually disqualifying. (100)

Clinicians who are not flight surgeons should be aware that many common self-limiting conditions, such as rhinitis, sinusitis, and otitis, and most prescription medications, have implications for temporary suspension of flight-duty status. Flight organizations may have a list of approved medications but even these usually require notification of the organization flight surgeon to continue on flight duty. (6)

Three common pulmonary disorders; chronic obstructive pulmonary disease (COPD), bronchial asthma and pneumothorax; frequently have implications for entry to or continuation on flight-duty status. The algorithm, for evaluating respiratory disorders, was based on history, physical examination, spirometry, post-bronchodilator and post exercise spirometry, methacholine challenge testing, diffusing capacity, radiography, and CT scanning in the evaluation of fitness for military flight duty. (7)

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

COPD is disqualifying for initial flight training, but may be waived for Flying Class II or III after careful evaluation if the aviator is asymptomatic or has only minimal symptoms, has no evidence of reactivity, and requires no medication. Smoking cessation is essential. Bullous emphysema is disqualifying because of the risk of rupture and pneumothorax at altitude. (6)

BRONCHIAL ASTHMA

Asthma or a prior history of asthma is disqualifying for flying training. It is also disqualifying as a new condition in rated aviators because it can be adversely affected by many stressors in the aviation environment such as cold dry air, smoke and fumes, pressure breathing, exertion, and possibly high +Gz. (7)

A personal history of asthma with an attack-free period greater than 5 years would not disqualify from flight training if further testing are normal. A negative personal history of asthma with a positive family history of asthma or atopy, especially among first-order relatives, requires further testing. Wheezing on unforced exhalation indicates asthma or localized airway obstruction, both are disqualifying factors. Prolonged exhalation without wheezing during quiet breathing requires further investigation. A recent respiratory infection should delay screening by at least 6 weeks. (7)

Some authors favor routine testing for nonspecific bronchial hyperresponsiveness (NBHR), with an agent such as methacholine, as a prerequisite for initial entry on military flight-duty status in circumstances of uncompromised lung function under all environmental conditions is considered essential. However, a study of US Army Reserve Officer Training Corps cadets raised concerns over false-positive test results when higher concentrations of methacholine are considered positive. (101)

An additional concern for military aircrew members consists

of prophylactic use of physostigmine during threats of chemical warfare with nerve agents. Physostigmine lowers the threshold for bronchoconstriction in individuals with latent NBHR. (26)

PNEUMOTHORAX

A history of spontaneous pneumothorax may qualify for a medical waiver if 5 years have passed since the last episode, provided chest CT scan gives no hint of subpleural blebs, localized overinflation, or generalized overinflation, and pulmonary testing function reveals no airways obstruction. In borderline cases, the candidate may be evaluated further by hypobaric chamber exposure under a carefully controlled protocol. Traumatic pneumothorax may qualify for a medical waiver after 1 year without recurrence if residual lung damage is minimal or absent. (7)

United States Army regulations differ somewhat from the previous recommendations. A single spontaneous pneumothorax disqualifies a candidate for selection to begin US Army pilot training. Before pilots or crew members already on flight status can return to aviation duties after a spontaneous pneumothorax, a 2-month waiting period and clinical evaluation that shows complete recovery, full expansion of the lung, normal lung function, and no lung pathology are recommended. (100)

After a recurrent spontaneous pneumothorax, pilots and crewmembers should not continue on flight-duty status. Waiver of this restriction may be requested after effective treatment by pleurodesis or pleurectomy, with complete recovery and successful completion of an altitude chamber exposure to 18,000 ft. Selection for free-fall parachute training in the US Army requires complete recovery, normal lung function, and a 3-year period without recurrence after a single spontaneous pneumothorax. (100)

Mass screening of all flight-duty applicants with chest x-rays may not be cost-effective. Keesling et al. (102) reviewed results of 3500 screening chest x-rays performed for flight duty to determine the rate of detection of significant abnormalities. Of 107 (3%) abnormal chest x-rays, 55 were found to be false- positive. Only two medically significant conditions were found in the screening population.

SARCOIDOSIS

The main aeromedical concern is possible cardiac granulomata, which have been associated with bundle branch blocks, AV dissociation, ectopy, paroxysmal tachyarrhythmias, coronary artery disease and sudden death. An aviator presenting with an abnormal chest x- ray or symptoms as above requires a thorough evaluation to rule out other disorders, and to rule out significant visceral involvement. If there is evidence of involvement of the myocardium or nervous system, or evidence of significant disease of any other viscera (e.g. restrictive lung disease, granulomatous hepatitis) the aviator is disqualified. (6)

CARDIOVASCULAR DISORDERS

The Aerospace Medical Association lists the following cardiovascular contraindications to commercial air travel: uncomplicated myocardial infarction occurring within 3 weeks of flight, complicated myocardial infarction occurring within 6 weeks of flight, unstable angina, severe decompensated congestive heart failure, uncontrolled hypertension, coronary artery bypass grafting performed within 2 weeks of flight, cardiovascular accident occurring within 2 weeks of flight, uncontrolled ventricular or supraventricular tachycardia, Eisenmenger's syndrome, and severe symptomatic valvular heart disease. (70)

DISORDERS ACQUIRED WHILE ON FLIGHT DUTY

Martin and colleagues (67) analyzed echocardiograms from military pilots (n = 46) who had flown at least 1000 hours in high-performance aircraft and from non-pilots (n=201) in a retrospective study. They found a greater incidence of pulmonary insufficiency and tricuspid regurgitation in the pilots. Possible explanations offered by the authors included a transient increase in right ventricular pressure caused by acceleration forces (+Gz) or straining maneuvers used to prevent or postpone g-LOC. This interesting question should be studied further for confirmation and attempts should be made to determine the mechanism.

Although the risk for cancer related to aerospace employment has been the subject of several studies, the incidence of lung cancer does not seem to be increased among aerospace employees. (103,104) Further study is required to establish the for risk cancers such as melanoma, other skin cancers, and other types of malignancy posed by aerospace employment. The US Federal Aviation Administration has developed computer programs that estimate the amount of galactic radiation received on a current or past flight back to January 1958. Published tables enable aircrew members to estimate possible health risks associated with their occupational exposure to radiation. (105)

POTENTIAL COMPLICATIONS FOR AIR TRAVELERS WITH RESPIRATORY DISORDERS

BRONCHIAL ASTHMA

Guidelines were identified relating to professional aircrew and potential recruits with asthma, but none were found relating to passengers. The flight environment experienced by commercial passengers should not pose a problem for most patients with asthma. In a review of all consecutive in-flight medical incidents reported for QANTAS airlines in 1993 there were 454 significant medical incidents, 9% of which were reported as respiratory tract infection or asthma. (106) A review of incidents on US commercial aircraft where an enhanced medical kit was used found that 10% of 362 episodes were due to asthma, lung disease or breathlessness. (107)

All airlines permit use of dry cell battery operated nebulisers, but there is usually a restriction during take off and landing because of the risk of electrical interference. Low cabin humidity may increase the risk of acute bronchospasm and retention of secretions that present a theoretical risk for asthmatic patients. (108) Precautions for asthmatic patients that arrange for air traveling in the form of increase the prophylactic dose of steroids and take a plentiful supply of inhalers. (8)

CHRONIC OBSTRUCTIVE PULMONARY DISORDERS

Data on patients with COPD are limited, and existing guidelines contain largely empirical advice based on relatively small studies. In addition to the risk of hypoxemia, patients with severe COPD may be put at risk from high levels of carboxyhemoglobin resulting from smoking. They may experience expansion of non-functioning emphysematous bullae and abdominal gases that could compromise lung function. (5)

Gong et al. (109) studied 22 patients with stable mild COPD (FEV_1 <80% predicted), 17 reported variable discomfort on previous flights. They inhaled sequential gas mixtures of 20.9% (SL baseline), 17.1% (simulating 1524 m), 15.1% (simulating 2438 m), 13.9% (simulating 3048 m), and 20.9% O_2 (SL recovery). With 15.1% inspired O_2 there was a mean fall in SaO_2 from 94% to 83%. The lowest recordings were 87% on 21% inspired O_2 and 74% on 15.1% inspired O_2. Progressive hypoxia induced mild hyperventilation resulting in small but significant falls in $PaCO_2$. Supplemental O_2 was given during inhalation of 15.1% O_2 in five subjects and 13.9% O_2 in 16. PaO_2 increased significantly with supplemental O_2 and $PaCO_2$ returned to baseline. Eleven subjects had no symptoms and 11 reported mild symptoms that did not correlate with hypoxemia. Variable sleepiness noted by the investigators was partly reversed by supplemental O_2.

Dillard et al. (110) examined 100 patients with severe COPD over a period of 28 months. Forty- four traveled on commercial flights, of which eight reported symptoms during air travel but reached their destination apparently without complications.

Christensen et al. (111) studied 15 patients with COPD with FEV_1 <50% predicted and SL SaO_2>94%, PaO_2>9.3 kPa. Arterial blood gas tensions were measured at SL, at 2438 m (8000 ft) and 3048 m (10,000 ft) in an altitude chamber at rest and during light exercise (20–30 watts). At 2438 m (8000 ft) PaO_2 fell below 6.7 kPa in three patients at rest and in 13 during exercise. None developed symptoms, probably because of existing acclimatization. Resting PaO_2 >9.3 kPa or SaO_2 >94% do not therefore exclude significant hypoxemia at altitude in patients with severe COPD. Light exercise may worsen hypoxemia.

The risk of recurrent pneumothorax will be discussed later on, but it should be noted here that COPD patients with large bullae are theoretically at increased risk of pneumothorax as a result of volume expansion at reduced cabin pressures. The volume of gas in a non-communicating bulla will increase by 30% on ascent from SL to 2438 m (8000 ft). There is one case report of fatal air embolism in a patient with a giant bronchogenic cyst. However, there are no data to state with any confidence what the maximum volume of a bulla should be before it reaches an unacceptable level of risk of rupture leading to tension pneumothorax, pneumomediastinum, or air embolism. (112)

Two studies (113,114) suggest that the best predictor of PaO_2 at altitude is pre-flight PaO_2 on the ground. In one study the authors measured PaO_2 and $PaCO_2$ in 13 patients with COPD at 1650 m and 2250 m. No symptoms attributable to hypoxia were recorded although PaO_2 fell from 68 mm Hg at SL to 51 mm Hg at 1650 m and 44 mm Hg at 2250 m. In the second study 18 patients with severe COPD were exposed to an altitude of 2438 m (8000 ft) in a hypobaric chamber. Mean PaO_2 fell from 9.6 kPa to 6.3 kPa after 45 minutes at steady state. The authors describe a predictive equation and recommend using the patient's pre-flight FEV_1 to limit variation in the PaO_2 at altitude.

On the other hand, Gong (69) recommended in-flight O_2 if the pre-flight PaO_2 breathing 15% oxygen at SL is <6.6 kPa. He concluded that equations do not accurately predict altitude PaO_2 and favor the hypoxia altitude test.

A study of eight patients with mild to moderate COPD (FEV_1 25–78% predicted) at SL and after ascent to 1920 m (6298 ft) revealed no significant complications at altitude. This was despite levels of hypoxemia similar to those observed in healthy mountaineers at altitudes of 4000–5000m (13,000–16,000 ft). The authors suggested that pre-existing hypoxemia resulting from disease might facilitate adaptation of patients to hypoxia and prevent symptoms of AMS. (115)

In summary, the clinical significance of temporary altitude induced hypoxemia in patients with COPD is unclear. The available controlled studies involve relatively small numbers of patients with stable disease and no co-existing medical problems. Simulated altitude exposure did not generally exceed 1 hour. These studies also largely excluded additional stressors such as exercise, dehydration, sleep, and active smoking. Therefore, the main recommendation is that patients with severe COPD must be assessed before air travel.

CYSTIC FIBROSIS (CF)

There are few data on the risks of air travel to patients with CF. In 1994 a study of 22 children with CF aged 11–16 years examined the value of hypoxic challenge testing. (116) They were assessed in the laboratory, and on commercial aircraft and all desaturated at altitude. Hypoxic challenge was found to be the best predictor of hypoxia. A more recent study of 87 children with CF aged 7–19 years who traveled on flights lasting 8–13 hours suggested that spirometric tests were a better predictor of desaturation. Low cabin humidity may increase the risk of acute bronchospasm and retention of secretions with possible lobar or segmental collapse. (117)

PULMONARY INFECTIONS

There is concern about the potential for transmission of infectious disease to other passengers on board commercial aircraft. The most important consideration is that of transmission of pulmonary tuberculosis, especially that of multiple drug resistant (MDR) tuberculosis. (118)

Seven cases of possible transmission of Mycobacterium tuberculosis on aircraft have been reported to the Center for Disease Control and Prevention (CDC), Atlanta, Georgia, USA. (118) The CDC concluded that the index case transmitted M tuberculosis to other flight crewmembers, but evidence of transmission to passengers was inconclusive. The CDC found no evidence of in-flight transmission of tuberculosis. (119) Other investigation considered that transmission of M tuberculosis had probably occurred. It was concluded that the likelihood of M tuberculosis transmission was low. The World Health Organization (WHO) concludes that air travel does not carry a greater risk of infection with M tuberculosis than other situations in which contact with infectious individuals may occur, such as traveling by rail, bus, or attending conferences. (120)

There are other studies of potential transmission of airborne infectious diseases on aircraft. An influenza outbreak occurred in 1979 among passengers on a flight with a 3-hour ground delay before take off. Seventy two percent of the 54 passengers developed symptoms; a similar virus was isolated from 8 of 31 cultures, and 20 of 22 patients had serological evidence of infection with the same virus. The high attack rate was attributed to the ventilation system being switched off during the ground delay. (121) Measles may be transmitted during international flights. (122) In a study of patients with recent lower respiratory tract infections, 23 patients traveling by air after acute respiratory infection suffered no adverse effects. (123)

NEUROMUSCULAR DISEASE AND KYPHOSCOLIOSIS

The data in this area are sparse, but there is one case report of cor pulmonale developing in a patient with congenital kyphoscoliosis after intercontinental air travel. The patient was a 59 years old man with apparently stable cardiorespiratory function who developed a first episode of pulmonary hypertension and right heart failure after a long haul flight. The authors conclude that this resulted from prolonged exposure to the low FiO_2 in the cabin. (124)

OBSTRUCTIVE SLEEP APNEA

Few data exist regarding the effects of air travel on patients with obstructive sleep apnea. There was a report of a morbidly obese woman who developed respiratory and cardiac failure after a 2 weeks tour involving two flights and a stay at altitude. (125)

It has been recognized since the 19th century that climbers to high altitude experience periodic breathing during sleep. Apneic periods arise with reductions in SaO_2 and are nearly universal above 2800 m. Periodic breathing can cause insomnia. It has also been speculated that the desaturations

may contribute to altitude sickness. Two studies have examined this phenomenon in greater detail but all the subjects were healthy volunteers. The apneas are thought to be central in origin. However, in the light of these observations they recommend that patients using CPAP should take their CPAP machine with them when visiting high altitude above 2438 m (8000 ft). (126,127)

PREVIOUS PNEUMOTHORAX

Airlines currently advise 6 weeks interval between having a pneumothorax and traveling by air. The rationale for this recommendation is not explicit, but it is assumed that it reflects the time period during which a recurrence of a pneumothorax is most likely. In fact, the risk for a patient with a pneumothorax relates to ascent and descent, and a "new" pneumothorax occurring at altitude may be hazardous because of absence of medical care. The "6 weeks rule" appears to have been arbitrarily applied with no account being taken of the type, if any, of underlying disease, or of any therapeutic intervention that has been undertaken, or of demographic factors. (5)

If the pneumothorax was treated by a thoracotomy and surgical pleurodesis or by insufflation of talc (at thoracotomy), the recurrence rate should be so low that no subsequent restriction on travel is necessary. Similarly, other interventions via a thoracoscopy may always carry the same certainty of success. (128,129)

Non-talc chemical pleurodesis (e.g. tetracycline) are associated with a more significant and continued risk of recurrence (16%) in one study (130) and 13% in another. (131) The best figure found was a 9% rate of recurrence after chemical pleurodesis. (132) These recurrence rates suggest that, even after such an intervention, the patient should still be subject to travel advice applied to others after pneumothorax.

For patients who have not had a definitive surgical pleurodesis via a thoracotomy, a risk of recurrence should therefore be expected. In one study a 54.2% recurrence rate was recorded with the majority occurring within 1 year of the first pneumothorax. (133) Cumulative freedom from recurrence data have been published by Lippert et al. (134) 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 does indeed imply that the biggest risk of recurrence is in the first year (72%).

In conclusion, the likelihood of recurrence during flight is low. Recurrence of a pneumothorax while flying is likely to have more serious effects than a first episode, and recurrence in passengers with pre-existing lung disease have serious consequences. A definitive surgical intervention makes the risk of recurrence of a pneumothorax negligible. Such patients may be able to fly 6 weeks after surgery and resolution of the pneumothorax in the absence of other contraindications. Careful medical assessment is required. For others the risk of a further pneumothorax is considerable for at least a year after the first episode. This strategy should be given special consideration by those who risk is greatest, smokers and/or have underlying lung disease.

VENOUS THROMBOEMBOLIC DISEASE (VTE)

The evidence of relationship between air travel and VTE is conflicting with many questions unanswered. BTS guidelines on suspected pulmonary thromboembolism list six major risk factors for VTE. Air travel is classified as one of several lesser risks. The evidence quoted in favor of an increased risk of air travel relates to long haul flights. (135) Such reports are supported by other surveys. (136-138) Hypotheses include immobility, seated position, dehydration, and alcohol ingestion. Owing to delayed onset of symptoms and rapid dispersal of patients after a flight, many current reports are likely to underestimate the size of the problem.

Evidence suggests that co-morbidity may increase the risk of VTE associated with air travel. Some studies suggest that previous VTE increases the risk of air travel associated recurrence. (137-139) Further research is needed to determine whether delay in travel for those at risk is beneficial. A recent study suggests that symptomless DVT may occur in up to 10% of airline passengers, and that during long haul flights, wearing elastic compression stockings is associated with a reduced incidence. (140)

The role of aspirin in this setting also requires investigation. A study of 13,356 patients undergoing surgery for hip fracture and 4088 patients undergoing elective arthroplasty showed that aspirin reduces the risk of pulmonary embolism and DVT by at least one third throughout a period of increased risk. (141)

THORACIC SURGERY

There are few data available. Postoperative complications such as sepsis or volume depletion should have resolved before patients undergo air travel. Severe headache precipitated by airline travel has been recorded 7 days after a

spinal anesthetic, presumed to be due to cabin pressure changes inducing a dural leak. North American guidelines highlight the fact that postoperative patients are in a state of increased O_2 consumption due to surgical trauma, possible sepsis, and increased adrenergic drive. Oxygen delivery may be reduced or fixed in patients who are elderly, volume depleted, anemic, or who have cardiopulmonary disease. (142)

DIFFUSE PARENCHYMAL LUNG DISEASE

There are no published data; clearly this is an area needing future research. However, patients with interstitial lung disease and their PaO_2 <70 must arrange for in-flight supplemental oxygen. (6)

CARDIAC DISEASES

Cardiac diseases is considered here briefly because it often co-exists with lung disease and may give rise to symptoms attributable to respiratory disease. Co-morbidity may present more of a risk to the passenger than the respiratory disease alone, although no data exist to support or refute this view. One study measured SaO_2 at simulated altitudes and on commercial flights in 12 patients with cyanotic congenital heart disease and acquired pulmonary hypertension and in 27 control subjects. At the simulated altitude (equivalent to FiO_2 15%) mean SaO_2 fell from 86% (range 69–98%) to 78% (range 56–90%) in the patients and from 98% to 90% in the controls. While, during air travel the mean in-flight SaO_2 in the patients was higher at 83% (range 78–94%). There were no changes in pH, or $PaCO_2$, and no clinical problems. (143)

The tolerance of patients with cardiorespiratory disease in a stable clinical condition to a moderate increase in hypoxemia is unremarkable since they are effectively “acclimatized” to hypoxia. As regard oxygen delivery to the tissues, a fall in SaO_2 of 10% is easily overcome by a similar percentage increase in cardiac output. Hypoxemia is a cardiac stimulant, and even patients in severe but stable heart failure can increase their cardiac output by 50% on mild exercise. (5)

See Aerospace Medicine: Part 4 for continuation

References

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