Study of possible effects on health of aircraft cabin environments - Stage 2

Contents

Foreword

The House of Lords Select Committee on Science and Technology published a report on 15 November 2000 entitled Air Travel and Health. As part of the Governments response to that report the DTLR, DH, HSE, and CAA jointly commissioned a study into The Possible Effects on Health of Aircraft Cabin Environments. This study was designed to reveal the main areas of concern, and to identify where there are significant gaps in the existing knowledge base, with a view to promoting or facilitating further, well-targeted research.

A report on the first phase of this study carried out by the Institute for Environmental Health, was published in January 2001. A second phase to this study was commissioned in March 2001 from the Building Research Establishment, following a competitive tender exercise. This stage 2 research project has investigated the current state of knowledge on each of the five issues identified in stage 1. A report on this second phase was submitted to the funding bodies at the end of June and was considered by the Aviation Health Working Group (AHWG) at their meeting on 27 July 2001. The AHWG welcomed the report as a helpful contribution towards consideration of research priorities and recommended that the report should be made publicly available as soon as possible as part of the wider consultation process.

The AHWG also agreed that the report should be subjected to an independent scientific peer-review. At the present time, therefore, the views expressed in the report do not necessarily represent the opinion or policy of any of the co-funding departments.

Views on any aspect of the report are welcome and should be sent to Dr W Maton-Howarth, Research and Development Division, Department of Health, Room 410ASkipton House, Elephant and Castle, London SE1 6LH.

Executive Summary

This literature study of aircraft cabin health has investigated the current state of knowledge on each of the five issues identified in Stage 1 of the DTLR research programme. A total of more than 2800 research papers were identified from the 17 databases and 20 Web sites that were searched. Current knowledge is deficient in each of the areas covered by this review, and the research needs are many. These have, therefore, been prioritised as below.

High Priority

Deep Vein Thrombosis

- Improved case-control studies (with particular attention to the selection of controls).
- Prospective studies, based on measurements prior to symptoms becoming apparent.
- Interaction of DVT risk with hypoxia and exercise.

Cabin air quality (CAQ)

- Investigate the key CAQ parameters in flight: the blood oxygen saturation of crewmembers and passengers, pressures and rates of change, temperature, air movement, humidity, ventilation rate and concentrations of common pollutants and organophosphates, self-reported health and comfort.

Jet lag

- Inclusion of jet lag as a confounding effect in studies of DVT, CAQ and infection risk.

Medium Priority

Deep Vein Thrombosis

- Experimental biomedical research, on the possible effects of decreased cabin pressure, low partial pressure of oxygen, stress.

Cabin air quality

- As for high priority recommendation, but for occupied aircraft on the ground.
- Laboratory/simulation studies of the CAQ parameters the effects of interactions.
- Intervention trials on the impact of altering parameters that correlate with health outcomes (e.g. humidification, gas phase air filters, reduced temperature).
- Measurement of exposure to insecticides and organophosphates.

Transmission of infection

- The incidence of the infectious agents of TB should be determined in the air, furnishings and filters on flights from countries where TB is endemic.

Cosmic radiation

- Exposure monitoring of cabin and flight crews.
- Further development of biological markers for cancer risk.

Low Priority

Deep Vein Thrombosis

- Co-ordinated case studies to clarify estimates of the incidence of recent travel in DVT patients (if possible, in association with case-control studies).

Cabin air quality

- A survey of air filter condition and maintenance (this would also be relevant to transmission of infection).

Transmission of infection

- The effect on the movement of pathogens of adjustable air supply nozzles. Cosmic radiation
- A large epidemiological study on the magnitude of risk, including discrimination of skin cancers risks from CR and UV exposure.

Jet lag

- Desk study of the short-term and long-term health and safety implications of jet lag, and the economic implications.

1. Aims

The issue of aircraft cabin health has become of major public and Government importance in recent years. The very rapid rise in air travel and the increasing distances travelled by the passengers has lead to concerns about their health whilst in travel. The House of Lords Science and Technology Sub-Committee Inquiry on *Air travel and health* investigated the matter and, as a consequence, the UK Government responded with a staged programme of research into the issues, funded through the Department of the Environment, Transport and the Regions (now Department of Transport, LocalGovernment and the Regions).

Stage 1 of the research programme was to identify the key areas of concern for aircraf tpassenger and crew health. This was carried out by the Institute for Environment and Health, with the aim of identifying the key issues for cabin health.

The project reported here is Stage 2 of the research programme. Its purpose was to identify and assess the research available on each of the issues identified in Stage 1 as being the main risks to health posed by the aircraft cabin environment. These are, in order of concern:

- deep vein thrombosis;
- aircraft cabin air quality (CAQ), including filtration, the effect of recirculated air, the risk and effect of organophosphate leakage, humidity, and the combined effect of aircraft cabin air and other stressors associated with flying;
- transmission of infection;
- cosmic radiation;
- jet lag and work patterns.

The DETR brief clearly outlined the requirements of the study. The objective of the work was to identify and assess the research available on each of the issues identified as being the main risks to health posed by the aircraft cabin environment. The specific tasks were as follows.

1. Locate the research available on the five key issues related to air travel and health that were identified by Stage 1.

2. For each of the issues, provide information on the quantity of research available, giving some indication as to whether there are any essential aspects of each issue which are not covered by existing research.

3. For each of the issues, provide an analysis of the quality of research available, pointing our areas where the research is scientifically invalid and/or contradictory.

4. Assess whether there is any research into the combined effects of these health issues, in the aircraft cabin environment.

5. Based on the quantity and quality of existing research on the health issues, provide detailed advice on research that should be commissioned to fill any gaps that have been identified. The advice should identify specific aspects contained within the issues listed above.

The following points were also made.

- Stage II work will need to build on Stage I work, and not take Stage I any further.

- The proposed study is to concentrate on the requirements above, and not provide details relating to the issues, e.g. the history of DVT.
- To discard anecdotal evidence (say, either those currently proliferating the Web and posted by self-interested groups, or from newspapers), and focus on peer-reviewed research.
- Not to focus on the guess of experts.
- Not just considering published literature, but reviewing the whole research process to get the right judgement, and provide robust and scientific answers.
- While noting the relevance of those items listed, to understand that the key issues of concern for the Department are those relating to DVT and CAQ.
- To understand that peripheral issues such as working practice of crew, operational aspects, and motion may also need to be considered.
- To consider two types of users passengers (including frequent flyers), and crew(both flight deck, and cabin).
- To provide sufficient levels of details on areas in which future work is required.

2. Description of the project

Introduction

This Stage 2 research study has investigated the current state of knowledge on each of the five issues identified in Stage 1. We conducted extensive search of medical and engineering databases, the Internet, and current research activities, and then reviewed the relevant material that was identified in the search. Together with the advice of experts in the field of aviation medicine, this review has been used to prepare guidance for the Department as to those areas of aircraft cabin health that most require further research.

A total of 17 databases and 20 Web sites were searched, the subject coverage of which included: medicine, occupational health and safety, psychology, biology, aviation, aerospace, aeronautics, engineering, science and technology, building services, US government publications, and transportation. The main databases searched, and the domains represented by these databases, are listed below.

Aerospace	
BIOSIS Previews	(Biological Sciences)
Ei Compendex	(Engineering)
Embase	(Medicine)
European Aerospace Database (EAD)	(Aerospace)
GPO Monthly Catalog	(US Government Publications)
IBSEDEX	(Building services)
Inspec	(Electrical Engineering)
JICST-EPLus	(Japanese Science & Technology)
NIOSHTIC	(Occupational Safety & Health)
MEDLINE	(Medicine)
NTIS	(US Government Publications)
OSH Plus	(Occupational Safety & Health)
PASCAL	(Science & Technology)
PsychINFO	(Psychology)
SciSearch	(Cited Reference Science)
Toxline	(Toxicology)

We also attended the following meetings:

- Cosmic Radiation Advisory Group
- Airline Medical Directors Association
- Aerospace Medical Association 72nd Conference
- Royal Society for the Promotion of Health conference on Healthy Flying.

The field of aircraft cabin health is extremely topical and more than a little controversial and fuelled by press speculation. This review is considered to be the most comprehensive and balanced possible at this time, in what is a very highly charged and fast moving research area.

The literature search was carried out by BRE s information scientists and library staff. The appropriate search strategies were agreed with the client prior to beginning, as far as was possible given the need to make rapid progress. Initial proposals were discussed with interested parties (DETR, HSE, DoH) and modified accordingly.

The search strategies and databases searched are given in Appendix 1. The bulk of the searches of the on-line databases were carried out between the 4 th and 12 th April 2001.Some Web-based searches continued beyond that point and an on-going search for new material has been maintained.

Quantity of research

The literature search returned more than 3500 abstract relating to the search topics. Within this total, however, are a number of repeat finds of the same paper from different databases. When these are taken into account, the total number of abstracts is approximately 2800. Having obtained the abstracts, all were reviewed by a team of health and environmental specialists who selected those suitable for inclusion in each of the categories of interest, as shown in Table 2.1.

Table 2.1 Number of abstracts on each issue

Issue	**No. of abstracts**
Deep vein thrombosis (DVT)	83
Cabin air quality (CAQ)	410
Transmission of infection	127
Cosmic radiation	212
Jet lag and work patterns	360

Quality of research

A number of procedures were used throughout the project to ensure that the quality of the research was maintained and that only relevant research material was considered.

The searches were carried out so that only reputable material would be located. The intention was to search established and credible databases comprised mostly of peer reviewed papers. Further Web-based searches were carried out and many other articles and documents located; as would be expected many of these were of little scientific value or credibility and therefore have not been used for this study. However, the number of these articles and their tone does reveal the degree of public and pressure group interest in a number of these topics, particularly DVT, air quality and cosmic radiation.

A further selection procedure followed, in which a BRE panel of experts selected from the abstracts those that fulfilled criteria of relevance and quality of research as determined by the journal or publication, author and quality of study. Following this, these papers were obtained for detailed review.

After analysing the material and making recommendations based on the research identified, the recommendations were submitted to established experts in the field for comment. The following external reviewers contributed:

- Professor Patrick Kesteven DVT
- Wing Commander David Gradwell Pressure and hypoxia
- Wing Commander Andrew Green Transmission of infection.

The findings of the literature search are reported below in the order of priority given in the brief. Because the literature search uncovered so many references across all the issues, and these were seen to relate to significant issues that are identifiable as subsets of the five main topics, they are reported in the following chapters:

- DVT
- CAQ: summary of literature search
- CAQ: pressure and oxygen
- CAQ: temperature
- CAQ: relative humidity
- CAQ: air pollutants
- Transmission of infection
- Cosmic radiation
- Jet lag and work patterns.

A final chapter draws together the conclusions and recommendations from the work.

3. Deep vein thrombosis

Introduction

Deep vein thrombosis (DVT) is a blood clot usually in the deep veins of the leg, although it can occur in other locations. It can be asymptomatic or can cause redness, swelling and pain; the danger, however, is that part of the clot can break off (embolise) and travel to the lung circulation, where it lodges in and blocks one of the pulmonary arteries pulmonary thromboembolism (PTE). This in turn can lead to low blood oxygen, circulatory failure, collapse and death.

An association between DVT and air travel was first suggested by Homans in 1954.Since then there have been two strands of evidence linking the two: (i) DVT cases and(ii) arguments from first principles. The DVT case evidence has built up as follows:

1954 First case report

1977 First case series looking at travel histories of DVT patients

1999 First case-control study comparing travel histories of DVT patients those of control (non-DVT) patients

2000 First prospective study of asymptomatic air travellers.

Working from first principles, the accepted predisposing factors for DVT slowing of the blood flow, increased blood coagulability and damage to or abnormality of the blood vessel wall can be argued to occur in the aircraft cabin environment.

Review of abstracts

Table 3.1 shows the breakdown of abstracts that were located by the search and by studying citations in the review and other papers. Generally, only English language papers have been consulted.

Note that abstracts listed in the column titled DVT/PTE in general are not the result of an exhaustive search: they represent some papers of more general interest for the understanding of DVT. Similarly, reference is made to two papers on diving medicine which are not counted in the table. They were both biomedical studies (there will be many other papers in the diving literature on decompression sickness).

The evidence from cases and from first principles will be considered in turn below, starting with three recent reviews of the evidence: those of the World Health Organisation (WHO), the Health and Safety Executive (HSE) and the Airline Medical Directors Association (AMDA).

Table 3.1Categories of reference on DVT

	Air travel-related DVT/PTE	DVT/PTE in general
Case reports	18	2
Case series	7	5
Case-control studies	3	0

Prospective randomised controlled trial	1	0
Survey/statistical analysis	0	9
Meta-analysis/clinical trials	0	3
Biomedical studies	5	13
Review	4	9
Editorial/opinion/short review	23	2
Letters	31	0
TOTAL	92	43

Analysis of three recent reviews

Three reviews of the literature on air travel related DVT were carried out earlier in 2001and the main features of each are summarised in Table 3.2. These have been taken as a starting point for the study of the recent experience and understanding. Each in turn was then examined for its approach to previous research and interpretation of the cited literature.

The WHO review is the most comprehensive of the three, discussing both biomedical and epidemiologic evidence and attempting to provide research recommendations and 'interim' advice for passengers until results from definitive epidemiological studies area vailable. However, it fails to state a definite conclusion on the risk of DVT associated with air travel and it does not actually provide advice for passengers - rather it summarises 'some of the recommendations [to passengers] which have been suggested'. It is not as critical of the evidence as the other two reviews.

The HSE review concentrates on epidemiological evidence, presenting a detailed critique of the three case-control studies. It also presents some unpublished data on PTE deaths at Ashford Hospital (which takes air side patients from Heathrow Airport). The conclusions on future research probably reflect the limited remit of the review: it did not examine the biomedical evidence and therefore did not reflect the existing studies that provide a 'biologically plausible' basis for an increased risk of DVT associated with air travel. The emphasis on 'evaluating' and 'giving fuller consideration to the biomedical evidence' contrasts with a recent article in the Lancet (Hirsch and O'Donnell 2001), which states: debate or further analysis of the published data is unlikely to clarify the situation.

Table 3.2 Summary of recent reviews of DVT and air travel			
	WHO	**HSE**	**AMDA**
Aims	1 Define the extent of the problem associated with air travel 2 If a problem exists, develop high priority research areas to identify possible solutions	Evaluate the epidemiological evidence base for the risk of DVT associated with travel as a whole	Provide an overview of current scientific evidence on DVT associated with air travel

	3 Recommend interim preventive measures based on currently available evidence		
Location of thromboses discussed	Leg/pulmonary Arm (subclavian) Cerebral	Leg/pulmonary	Leg/pulmonary
Biomedical evidence assessed?	Yes	No	Yes
Case-control studies discussed	Ferrari et al 1999 Kraaijenhagen et al 2000	Ferrari et al 1999 Kraaijenhagen et al 2000 Samama et al 2000	None
	WHO	**HSE**	**AMDA**
Conclusions re risk of DVT from air travel	None	Current epidemiological evidence in relation to DVT and air travel is limited and contradictory. Probably the best designed study demonstrates no risk, although its results may not be generalisable. Overall the epidemiology is probably able to exclude the possibility that travel is an independent and extremely strong risk factor for clinically significant DVT, although unable to provide a more precise	There is sufficient evidence accumulating to suggest that there may be an association, although not necessarily a causation. Current evidence indicates that any association between symptomatic deep vein thrombosis and travel by air is weak, and the incidence is less than the impression given by recent media publicity.

		consideration of risk, if any.	
Research recommendations	Need for a properly conducted prospective clinical trial that investigates prothrombotic markers and status of calf veins before and after air travel: - large numbers required - many logistical difficulties. Research studies are needed to answer the following questions. 1 Is air traveller's thrombosis a real entity? If so, what is the incidence? 2 Does this condition behave in a similar fashion to other better-researched forms of VT (e.g. post-operative)? 3 What are the predisposing factors of this condition? 4 What can be done to prevent it?	The difficulty of designing an appropriate epidemiological investigation and the time it would take to report indicates that initially consideration should be given to evaluating and developing other evidence. Fuller consideration of the biomedical evidence should be considered to investigate clinically significant travel related changes. This would identify whether there was a clear biologically plausible and medical coherent basis for any significantly increased risk of DVT with travel, and also help to inform the design of later epidemiology if necessary.	Supports the recommendations for future research of the House of Lords, the Australian multi-centre case-control study and the planned WHO study)
Interim advice to travellers	1 Possibly provide information on the potential risk of VT in advance with the flight tickets 2 Could give general	None	1 General advice to all passengers - stretching exercises particularly of the lower limbs, change

	advice to all passengers: - move and stretch feet and legs during prolonged travel - consume enough non-alcoholic drinks to avoid dehydration - avoid smoking. 3 Specific advice could be given to those with serious risk factors		position and walk about cabin 2 For those with risk factors, structured advice is given in the form of a table (adapted from Kesteven 2000): separate recommendations for low, medium and high risk passengers

The AMDA report, in contrast, focuses mainly on the biomedical evidence, although it also reviews the case series to date. As the AMDA report was published in 2001, and aims to be an overview of the current scientific evidence on DVT associated with air travel, its failure to discuss the three case-control studies (published in 1999 and 2000) is a surprising omission (the Ferrari et al 1999 study appears as an entry in a table simply giving the number of subjects and their mean age).

Interestingly, the three case-control studies were the only studies analysed by the HSE: only case-control studies (as opposed to case reports or case series) permit an assessment of the risk of travel in relation to DVT.

In all of the air travel-related DVT literature, the AMDA report is the only one to suggest that dehydration may be protective against DVT development.

Review of other research studies

Introduction

The key papers on which the reviews and current thinking depend are as list below.

Case-control.

1 Ferrari et al, 1999

2 Samama et al, 2000

3 Kraaijenhagen et al, 2000

Prospective randomised trial.

4 Scurr et al, 2001

Series of 86 air-travel related DVT analysing journey characteristics in detail combined with patient risk factors.

5 Kesteven and Robinson, 2001

Biomedical:

6 Wright and Osborne, 1951

7 Lanfgraf et al, 1994

8 Hamer et al, 1981

9 Bendz et al, 2000

These, and other papers that have been referred to, are listed in Table 3.3. These papers are discussed below in the category to which they belong so that a clear comparison can be made of their methods and findings. The biomedical evidence is discussed in a separate section on Evidence from fist principles.

Table 3.3 DVT References
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Case reports

Homans (1954) first reported cases of DVT linked to air travel. In a series of five cases of DVT, two followed air travel, two related to long car journeys and one occurred after an evening in a theatre. Many other cases have been reported since in the literature at least 14 reports of some 23 cases up to 1998; if we add the numbers from the case series (see next section) this gives a total of at least 312 cases. What general points can be made from these cases? One point is the variability in presentation. The DVT can be symptomatic or silent; it can appear during or after the flight. If it embolises, the PTE can appear spontaneously during the flight or can be precipitated by movement. For example, in the three cases reported by Ledermann and Keshavarzian (1983), the PTE developed as the passengers moved to get off the aircraft. In other cases, the PTE occurred days after the flight and was precipitated by more violent movement: in the case reported by Thomas et al (1981), the PTE occurred when the patient jumped suddenly to avoid a passing car; one of the cases reported by Cruikshank et al (1988)developed chest symptoms when he started to play tennis. Some cases are unusual in the combination of circumstances present: Beighton and Richards (1968) cite a death following air travel where part of a DVT embolised and passed through a hole in the heart to cause death from a cerebral embolus rather than the more usual PTE.

Although the mechanisms are different, it is interesting to note that arterial thromboses have also been associated with air travel: Collins et al (1979) and Teenan and Mackay(1992) each reported three cases, and Ashkan et al reported one case in 1998. Cerebral venous thromboses have been linked to travel: in a series of 15 consecutive cases, Pfausler et al (1996) found a history of recent air travel in five.

There is at least one report of PTE occurring in a pilot (Raboutet and Raboutet 1975).

As Homans commented in 1954, cases reveal a tendency rather than a proved relation of cause and effect . Without examining passengers before the flight, there is no certainty that the DVT has not already started before the flight. Indeed, the normal time course of DVT development (days, rather than hours to become symptomatic) would suggest otherwise.

Case series: travel history in DVT patients

In these studies, series of consecutive patients with hospital-diagnosed DVT/PTE have been analysed to find out what proportion have a history of recent travel. The subsidiary question is whether this proportion is large enough to propose recent travel as a risk factor for DVT. Some of these studies have looked at all modes of transport; others have focussed on air travel. They are summarised In Table 3.4.

The proportion of those with DVT who had recently travelled by air varies greatly in these studies from 1.6% to 50%. Part of the variation can be explained by different definitions of what constitutes long-distance travel and how recent it was. Another reason could be differences in the way medical records information is analysed. For example, Mercer and Brown (1998) reviewed the medical records of 134 patients with DVT/PTE and then only looked in detail at those patients (n=66) in whom the presence or absence of recent travel had been specifically documented. Others may have divided the number with a positive travel history by the total number of DVT/PTE patients (including those with no documentation of travel history), thus underestimating the true proportion.

Sarvesvaran (1986) studied 104 deaths at Heathrow airport reported to the coroner between 1979 and 1982, 12 of which were due to PTE. He classified the deaths into three groups: incoming passengers who died on the way to or on arrival at Heathrow, passengers waiting to depart Heathrow, and spectators/staff . Of the 12 PTE deaths, 11were of incoming passengers: 10 had been on 12-18 hour flights and one had been on a 6-12 hour flight. No statistically significant conclusions could be drawn, however, as the sizes of the three groups are not stated.

Table 3.4 Summary of case series reports on DVT and air travel

	Type of study[1]	**Total DVT/PTE patients**	**Travel: no of hours**	**Days between travel and DVT/PTE**	**No (%) with positive travel history**[2]	**No (%) who had travelled by air**
Symington & Stack 1977		182	>3		8 (4.4%)	3 (1.6%)
ODonnell 1988	Retro medical records	250	NI	NI	13 (3.2%)	8 (3.2 %)
Ekloff et al 1996		254			44 (17%)	
Mercer & Brown 1998	Retro medical records	66	>4	<31	NI	33 (50%)
Schmitt & Mihatsch 1992	Prospective	54			14 (25.9%)	
Ribier et al 1997		40				

Nissen 1997					5	
Rege et al 1999	Retro medical records	~375	>1	<35	NI	20 (5.3%)

[1] Retro = retrospective [2] Includes all modes of travel NI = no information

It is impossible to quantify risk from these studies without knowing the likelihood of air travel in the rest of the population from which these DVT/PTE cases are drawn. If long-distance/air travel is reasonably common in the population, there is a chance that anyone (including DVT/PTE patients) will have recently undertaken such a journey within the last month or so. This would particularly apply to studies in island locations (e.g.Mercer & Brown 1998).

Recently, three case series have been published looking specifically at patients diagnosed with air travel-related DVT/PTE. The purpose of these studies was to analyse the individual and journey factors to try understand how the DVT/PTE may have come about. In the first of these studies, Sinzinger et al (1999) analysed 19 cases of air travel-related DVT/PTE. The period between the flight and the onset of symptoms varied from immediately to 85 hours. None of their patients had coagulation defects; none had predisposing factors such as a past history of DVT/PTE or congestive heart failure, although one patient was under treatment for familial hypercholesterolaemia. The majority (84%) were not actively moving during the flight and window-seated passengers had the lowest prevalence. Flight duration was from 5-22 hours; most (68%) patients had one stopover. There were 17 males and 2 females with an average age of 50.2 yr; 79%were drinking alcohol during the flight.

Caillard and Clerel (2001) studied 109 patients with symptomatic PTE seen at the Aeroports de Paris emergency medical unit between 1990 and 2000; 95% had travelled for more than 6 hours, and 75% had travelled for more than 12 hours. Women represent35% of all passengers and yet 83 women and 24 men were affected. The mean age was 57.3 yr. Of the 109 passengers, 38 had no risk factors and no previous history of DVT/PTE and 80 did not move from their seats during the entire flight.

Kesteven and Robinson (2001) recruited 86 patients with air travel-related DVT/PTE via an article in a national newspaper. Inclusion criteria were that the DVT/PTE had occurred within 4 weeks of a journey greater than 100 miles. The mean age was 58.8 yr, 51.2%were male and 72% had at least one risk factor for venous thromboembolism (VTE). The length of the index flight ranged from 2 to 30 hours and over 90% developed symptoms immediately or within 48 hours. Of the 86 patients, 36 had window seats, 17 middle seats and 33 aisle seats. An important finding was that the VTE was initiated by the return flight in 57 (66%) of cases. Of the remaining 29 patients, 18 had had journeys involving sequential flights over a total duration of between 10 hours and several days. It was found that only two cases had either no risk factors for DVT or had not undertaken a recent flight prior to the index flight. The authors suggest, therefore, that multiple air trips may have a cumulative effect, which may persist for days or weeks.

Case-control studies

To date, three case-control studies have been carried out and these are described in detail below. These have been conveniently summarised by the HSE (2001), as shown in Appendix 2.

Ferrari et al (1999) investigated the history of recent travel in 160 patients attending their department with DVT/PTE. All journeys of 4 hours or more in the preceding 4 weeks were noted by whatever means of transport. The same travel questionnaire was submitted to 160 age-matched controls (consecutive patients admitted to the cardiology department for the first time and for a first event over the same time period as the cases). Patients with severe diseases that may have limited their mobility were excluded. Of the 39 patients who had recently completed a journey, 9 had travelled by air. A recent journey was found in 24.5% of cases and 7.5% of controls, a statistically significant difference ($p<0.0001$). Long-distance travel was associated with an increased risk of DVT/PTE (odds ratio 3.98 (95% CI 1.9 to 8.4)).

The HSE (2001) has criticised the selection of controls in this study because, since cardiovascular risk factors are inversely related with social class, and long-distance travel has the opposite relationship with social class, controls were less likely to have travelled than cases.

Samama et al (2000) studied 494 cases of non-hospitalised confirmed DVT. Cases were reported by GPs and the 494 controls were also selected by the GPs as the next patient after the DVT case who had influenza or rhinopharyngeal syndrome (matched on sex and age within +/- 10 years). Long-distance travel within the previous 3 weeks was enquired about although they do not specify what mode of travel or how long the journey was. Long-distance travel was associated with an increase in the risk of venous thrombosis: odds ratio (age/sex adjusted) was 2.35 (95% CI 1.45, 3.80): 62 cases(12.8%) and 31 controls (6.3%) met the criterion for previous long-distance travel.

This study was not specifically about air travel and can be criticised in that long-distance travel was not defined. The GPs asked about travel history knowing which patients were cases and which controls so could have been looking for a positive travel history more thoroughly in cases than in controls. The controls may have been sufficiently ill in the previous 3 weeks not to have been able to travel.

Kraaijenhagen et al (2000) obtained the travel history of 788 patients with suspected venous thrombosis, recent travel being defined as a journey of greater than 3 hours in the past 4 weeks. Participants were asked about this before they knew the results of objective diagnosis, eliminating recall bias and ensuring cases and controls were as similar as possible. Cases were defined as those who had a confirmed DVT on diagnostic testing (n=186) and controls were those in whom the tests were negative(n=602). Nine (5%) of the DVT patients and 43 (7%) of the controls had a history of recent travel, giving an odds ratio of 0.7 (95% CI 0.3 1.4). Four of the cases and 13 of the controls had recently travelled by air, giving an odds ratio of 1.0 (95% CI 0.3 3.0).They conclude therefore that there is no increased risk of DVT either among travellers as a whole or air travellers in particular.

If consideration of recent travel history formed any part of the clinical suspicion of DVT, then it is possible that recent long-distance travel is over-represented in the control group, relative to the general population (HSE 2001). Reele (2001) points out that patients who had travelled a few weeks before the study day and had a clot which had spontaneously lysed would have been assigned to the control group and not the DVT group, which would have confounded the results. Many of the passengers had flown for a relatively short time (Scurr et al 2001). On balance, these factors would tend to cause the risks of travel to be under-estimated.

Summing up, the first two of these case-control studies found a positive association of all long-distance travel with DVT/PTE but have the possibility of recall and referral bias. The third study avoided referral bias but did not find an association. Hirsch and O Donnell(2001) reconcile these differing results by pointing out that the numbers of events in the Kraaijenhagen et al (2000) study were small, as were the number of patients exposed to long-distance air travel. The upper limit of the 95% CI for relative risk of VTE with airt ravel was 3.0 and therefore not inconsistent with the other two studies.

Prospective study of symptomless DVT

Scurr et al (2001) carried out the first prospective study to determine the frequency of DVT associated with long-haul air travel, although the end point was symptomless DVT. Passengers were recruited via advertisements in local newspapers and travel shops. They had to be over 50 years of age and intending to travel economy class with two flight sectors of at least 8 hours duration within 6 weeks. Volunteers with serious illnesses and who had had previous episodes of venous thrombosis or were taking anticoagulants were excluded. Patients taking hormone replacement therapy were not excluded, however. Blood sampling and the assessment of the deep veins by duplex ultrasonography were carried out before and within 48 hr after travel. Passengers were randomly allocated to two groups one that wore class-1 below-knee graduated compression stockings during their flights and the control group who did not wear stockings. Out of 116 control passengers, 12 (10%) developed a symptomless DVT in the calf; none of the group wearing the stockings developed symptomless DVT although four who had varicose veins developed superficial thrombophlebitis.

Reported incidence of symptomless DVT was surprisingly high and it has been suggested it may be due to bias in the interpretation of the ultrasonography (Hirsch &O'Donnell 2001). The technicians were supposedly blinded to the treatment allocation of each patient (stockings/no stockings). However, no assurance was given that there had not been any communication between volunteers and technicians ideally, there should have been a third party present to check this. In addition, the D-dimer (a marker of recent thrombosis) blood test results were negative which suggests that either the thrombi were very small or were false positive findings. On the other hand, the very high thrombosis rates compared with the case-control studies may be due to the much longer criterion duration of air travel in this study. If these results were reproduced they would clearly establish lengthy air travel as a risk factor for thrombosis.

Evidence from first principles

Introduction

Virchow (1856) first postulated that there were three factors which predispose to the formation of DVT: slowing of the blood flow, increased blood coagulability and damage to or abnormality of the blood vessel wall. All individual and situational risk factors for DVT act via one or more of these three routes. Individual risk factors for DVT are well documented and include obesity, chronic heart disease, cancer, chronic renal failure, smoking, pregnancy, hormonal medication, previous DVT and recent trauma or surgery. The situational factors in aircraft cabins have been repeatedly argued to predispose to the development of DVT: for example, cramped seating positions, immobility, possible dehydration due to consumption of alcoholic drinks and other diuretics such as tea and coffee, and the low humidity of the aircraft cabin, relative hypoxia and reduced barometric pressure. These would apply to all passengers, whether or not they had individual risk factors for DVT. The biomedical evidence relevant to the aircraft cabin environment is reviewed below.

Dehydration

Most authors assume that dehydration will occur on aircraft and that this will increase the clotting tendency of the blood. The degree of dehydration that occurs during air travel is actually uncertain (see Cabin Air Quality: Humidity). It is also uncertain whether, if dehydration occurs, it does increase the risk of thrombosis. Most authors say it does, but without citing any evidence. The AMDA report takes a different line and proposes that dehydration may be protective against DVT. They cite a study by Janvrin et al (1980)looking at the effect of giving post-operative intravenous (IV) fluids on subsequent DVT development. Those given IV fluids were significantly more haemodilute and hypercoagulable than the controls, and had a significantly higher incidence of DVT. They concluded that dehydration may protect against DVT development. Alternatively, saline might itself create a risk of DVT.

AMDA also cite other work which had shown DVT incidence was lower in hot months in a country with a wide range of climate. This may, however, result from greater water intake in hot weather. No seasonal variation in DVT incidence was found in studies in Geneva (Bounameaux et al 1996) or Malmö (Nordstrom et al 1992).

It may be that, for the generation of DVT that overall dehydration is not important rather, it is the relative concentration of blood in the deep veins of the leg which matters. Moyses (1988) describes an experiment in seven seated volunteers in which blood samples were drawn from foot veins. There was a rise in haematocrit and in plasma protein concentration after one hour of quiet sitting, both of which would predispose to thrombosis.

Landgraf et al (1994), in their 12-hour simulated flight experiments designed to study pathological processes which might lead to DVT in long-distance air passengers, found a significant increase in plasma viscosity during daytime flights but not during night time ones. Haematocrit and albumin concentrations showed only circadian fluctuations. Blood samples were taken from arm veins and therefore do not reflect conditions in the deep leg veins in seated humans.

Seated posture

Simpson (1940) found that 21 of 24 PTE deaths in a 2-month period occurred either in air raid shelters or as people were leaving them. He concluded that these deaths were caused by people sitting for long periods in deck chairs, with the front edge of the seat compressing the veins in the legs. This compression could have damaged the lining of the veins and also slowed the blood flow, affecting two out of three of Virchow s triad of risk factors. Cases of fatal PTE decreased after the introduction of bunk beds for sleeping.

Wright and Osborne (1951) found that venous blood velocity in the seated position was two thirds of that in the supine position in normal volunteers.

Crossing one leg over the over such that there is a rhythmic, pulsatile motion of the foot shows that the popliteal artery of the crossed leg is likely to be compressed: the resultant decreased arterial flow may be an additional cause of venous stasis.

Lack of exercise

In the Wright and Osborne (1951) study on venous velocity, vigorous foot exercise for 2mins doubled the venous flow rate measured immediately afterwards but they did not investigate how long this increased flow lasted after the cessation of exercise.

Noddeland and Winkel (1988) looked at the effect of having one leg exercising and the other still on leg oedema during 8 hours of sitting at normal or reduced barometric pressure. The active leg could be moved freely and in addition the subjects did 10 plantar flexion movements with that leg every 15 min throughout the experiment. They found that leg activity had oedema promoting and preventive effects; the overall effect was to reduce oedema formation. Reduced barometric pressure made no difference to any of the experimental findings.

Landgraf et al (1994) in their 12-hour simulated flight study examined oedema formation in seated volunteers, who were divided into two groups exercising and non-exercising. The exercising group had to leave the seats and walk around the cabin for 5 min every hour. They found an increase in lower leg volume in both groups which was linear with respect to time. There were no significant differences in the leg volumes between the two groups. An average of 1150 ml fluid was retained which correlated with the average increase in body weight. This study did not simulate the cabin environment, however, as regards pressure, hypoxia and humidity.

They cite another study on the lower leg of sitting humans which found that calf muscle exercises instantly led to decreasing lower leg volume which, however, returned to the pre-exercise volume within minutes of ending the exercises. Between exercises the leg showed a continuous swelling process which was only interrupted but not delayed by the exercises.

Relative hypoxia

Two types of hypoxia may be important global due to decreased PO2 in inhaled cabin air and local in the leg due to decreased blood flow.

Bendz et al (2000) suddenly (within 10 min) exposed 20 male volunteers to a hypobaricenvironment similar to that of the aircraft cabin (76 kPa / 2400 m). They found thatmarkers of coagulation transiently increased by two- to eight-fold. They concluded that rapid exposure to hypobaric hypoxia may transiently activate coagulation. Others have criticised this study on the grounds that there were no controls, so it is difficult to know whether the changes were due to the pressure or hypoxic change, or to being placed in a hypobaric chamber for a week. Bartsch et al (2001) suggested a control experiment in normoxia to rule out any artificial activation of coagulation due to blood sampling or handling methods.

Gunga et al (1996) produced evidence that flying at 8000 ft (2438 m) creates hypoxic stress by measuring erythropoietin (EPO) concentrations in seven men during an 8-hourflight. EPO production in the renal cortex is regulated by the amount of oxygen available to the tissues involved in its production. It was found that the EPO concentrations increased significantly during the flight and returned to baseline values 8 hours after landing.

Local hypoxia can result from slowing of the blood flow due to immobility. Hamer et al(1981) examined leg veins in dogs and found that non-pulsatile blood flow led to stasis in valve pockets. Hypoxia in the static blood caused endothelial damage which then led to clotting. On the basis of their observations they proposed that the lining tissue of venous valves has no blood supply and so depends on oxygen diffusing directly from venous blood for its survival. If the blood flow is stagnant, oxygen in the layer of blood next to the vessel wall is used up and the resultant hypoxia can damage the valve lining. Early thrombus formation was seen on a valve cusp after only 2 hours of non-pulsatile flow.PO2 fell progressively towards zero in the valve pockets when the limbs were kept still but not if the limbs were moved. Vigorous passive movements of the limbs led to almost complete equalisation of the PO2 of blood in the valve pockets compared with that in the centre of the vein. The degree of hypoxaemia in the valve pockets is directly related to the PO2 in the vein lumen of which the valve pocket is a backwater any condition which causes venous hypoxaemia is likely to intensify the hypoxaemia in the valve pockets.

Malone and Morris (1977) carried out experiments on thrombus formation under different types of hypoxic conditions in rabbits. They concluded that a thrombus is a response to any physiological injury to the vessel wall, including hypoxic injury. This hypoxic damage can trigger thrombus formation just as surely as the physical or chemical injuries shown

to cause thrombus experimentally (Malone and Morris 1977).

Hypoxia also causes vasodilation and increased capillary permeability which would tend to worsen oedema (James 1996).

Reduced barometric pressure

One possible mechanism for an effect of reduced barometric pressure on blood clotting is via the formation of gas bubbles in the blood during decompression. Exposure of the blood to this gas surface may cause haematologic abnormalities. This phenomenon has been investigated in the context of decompression sickness after diving. For example, platelet behaviour was studied in rabbit decompression sickness by Tanoue et al (1987).Platelet counts significantly decreased after decompression, and platelet thrombi were found in the pulmonary arteries. They suggest that circulating air bubbles interact with platelets, causing the platelet release reaction, and these activated platelets participate in the formation of thrombi. Others (Philp et al 1972) have suggested that platelets recognise air bubbles in the blood as a foreign surface. Similar experiments in man during and after dives have produced conflicting results, leading some to suggest that activation of haemostatic mechanisms, platelet consumption and consumption of coagulation factors may be less significant in man than in animal models. For example, Goad et al (1976) found that white cell count was the only haematologic variable to correlate significantly with blood bubble count in decompression diving experiments.

Returning to the possibility of sub-atmospheric decompression effects, Macmillan (1999) points out that asymptomatic venous gas emboli have been detected by Doppler ultrasound at 10250 ft. It is possible, therefore, that gas emboli below the threshold size for ultrasound detection are present at lower altitudes. The rate of decompression would be particularly important in determining whether gas bubbles formed rather than the absolute pressure arrived at. This hypothesis may tie in with the Bendz et al (2000) study where there was transient activation of coagulation in the first few hours after exposure to hypobaric hypoxia, but this was not sustained 22-24 hours after the pressure change(Bendz et al 2001 - unpublished observations).

Noddeland and Winkel (1988) found no effect on oedema formation at reduced barometric pressure. Casley-Smith and Casley-Smith (1996) found that lymphoedema could be initiated or worsened by aircraft flights. They speculated that the mechanism had to do with decreased cabin pressure.

Issues

Case reports and case series

Case reports and case series accumulating over the last 50 years or so provide circumstantial evidence of an association between air travel and DVT. Studies of this type can never provide evidence of a causal relationship, however.

Case-control studies

Three case-control studies have been carried out to date, although that by Samama et al(2000) did not distinguish between different types of long-distance travel. The results of these studies have been debated in the medical press. Methodological criticisms have been levelled at them, particularly with regard to the selection of controls. Taken together, they provide weak evidence of a possible risk of long-distance travel for DVT. The HSE report (2001) concluded that: 'Overall the epidemiology is probably able to exclude the possibility that travel is an independent and extremely strong risk factor for clinically significant DVT, although unable to provide a more precise consideration of risk, if any.' This is echoed by Hirsch and O'Donnell (2001): 'From these three studies, a relation between long-distance travel and thrombosis is probable but unlikely to be strong.'

To put this another way, most of the risk arises from non-travel factors (e.g. age, pregnancy, prior occurrence of thrombosis and a range of medical conditions). While case-control studies permit estimation of relative risks, this is only one type of risk that is important. At population level, a low relative risk can be significant if a large number of people are exposed and/or the baseline risk is high. No doubt the individual passenger will be interested in his/her own absolute risk.

Prospective studies in asymptomatic passengers

Only one such study (Scurr et al 2001) has been carried out to date. The results were an apparent 10% risk of symptomless DVT in passengers not wearing compression stockings. This study has been criticised on methodological grounds, however.

Biomedical research

The biomedical research varies in quality. Some is generally well accepted, e.g. the early work by Wright and Osborne (1951) on the effects of posture on venous blood velocity. Other work is interesting and provocative - e.g. the recent study by Bendz et al (2000) on the possible relationship between exposure to hypobaric hypoxia and activation of coagulation - but lacks the necessary controls to reach a definitive conclusion.

Overall there is a fair amount of evidence that an immobile seated posture will affect all three parts of Virchow's triad and therefore predispose to DVT formation. The evidence on the presence/absence of dehydration in the aircraft cabin environment and its likely effects on DVT development is contradictory. Hamer et al's (1981) study in dogs showed that local hypoxia due to venous stasis led to damage to the valve linings and resultant thrombus formation. Local hypoxia due to venous stasis would be worsened by systemichypoxia due to low PO2.

Research needs

Further case reports and case series of consecutive patients diagnosed with DVT(looking for a history of recent travel) are unlikely to add much to the debate, except perhaps in clarifying the estimates of the incidence of recent travel in DVT patients, as this has varied widely in the case series to date. However, with modest extra effort, case reports can be generated from case-control studies.

There is a place for further series specifically of air travel-related DVT as the three carried out to date (Sinzinger et al 1999, Caillard and Clerel 2001 and Kesteven and Robinson 2001) had some contradictory findings, for example in the ratio of males:females and in the proportion of cases with DVT risk factors. These studies help to elucidate the factors which should be investigated in epidemiological studies. For example, Kesteven and Robinson (2001) found that only two out of their series of 86patients had either no risk factors for DVT or had not undertaken a recent flight prior to the index flight.

There is also a place for further case reports of thromboses at other locations (e.g. cerebral and arterial thromboses) in association with air travel. These are much rarer than DVT/PTE and were out with the scope of this review. They provide circumstantial evidence of a generalised 'thrombotic tendency' in association with the aircraft environment rather than necessarily a connection to the seated posture, immobility etc.

Further case-control studies may be useful provided they are adequately powered and methodologically rigorous, particularly regarding the selection of controls. Realistically, a sufficiently large sample is likely to be achieved only by multi-centre studies. At very least, it would be helpful to reach agreement between key parties as to what would constitute an acceptable control group.

There is definitely a place for further prospective studies as Scurr s but which are more rigorously designed and preferably independent (the Scurr et al study was partly funded by the stocking supplier). Interventions other than stocking should also be considered, and more needs to be understood about how the presumed precursors of DVT actually progress.

There is room for more biomedical research to clear up the contradictions in the work to date. As well as making the case from first principles that any particular factor will predispose to DVT formation, perhaps in future biomedical studies markers of clotting activation should be measured more often, as a surrogate for actual DVT formation.

Studies mimicking the aircraft cabin environment should have adequate controls, in order to separate out the possible effects of decreased cabin pressure, low PO2, the stress of being in an enclosed environment etc.

Adequate biomedical research is particularly important when it comes to giving advice to passengers on DVT prevention. Any suggested measures should be backed up by experimental evidence rather than based on 'common sense'. This is particularly well illustrated in the research on the effects of exercise. This research will need to take into account possible conflicts in recommendations. For example, exercise may reduce the risk of DVT but could increase the degree of hypoxia.

4. Cabin air quality: summary of literature search

The issue of CAQ was initially sub-divided into the relevant sections as shown in Table4.1. These topics are discussed in the chapters indicated in the table.

Table 4.1 Numbers of abstracts on cabin air quality topics		
Topic	**Number of abstracts**	**Chapter**
Cabin air pressure	139	5
Oxygen	89	
Temperature	29	6
Humidity	32	7
Carbon monoxide	18	8
Carbon dioxide	27	
Ozone	49	
Fuel gases	17	
Other chemicals	11	
ETS	34	

It must be borne in mind that many of these issues interact and act synergistically. Where this is known to be the case it is identified and discussed.

5. Cabin air quality: hypoxia and cabin pressure

It must be borne in mind that many of these issues interact and act synergistically. Where this is known to be the case it is identified and

Introduction

Virtually all commercial aircraft cabins are pressurised for the safety and health of the passengers and crew. There are two main reasons for the aircraft cabin to be pressurised:

- the effects of reduced oxygen partial pressure and the increased potential for hypoxia;
- the impact of reduced pressure on the physical responses of the body and its air-filled cavities.

In an unpressurised aircraft at normal cruising altitudes, the occupants would require supplementary oxygen for breathing, as the partial pressure of the oxygen in the atmosphere is too low to sustain human consciousness.

The standard set for pressurisation is SAE ARP1270. This standard sets down the guidelines for operation of the pressurisation systems of aircraft cabins and is the standard recognised by the FAA and JAA. The most important factor in this standard is that: the compartments to be occupied must be equipped to provide a cabin altitude pressure of not more than 8000 feet (2440 m) at the maximum operating altitude in normal conditions. This is inevitably a compromise between the ideal position (but not feasible in terms of cost and engineering) of maintaining sea level pressure while flying at over 30,000 ft and unacceptably risky exposures (Ernsting 1978). In practice, most passenger aircraft routinely operate at lower cabin altitudes.

It is worth noting that this maximum cabin altitude standard has been developed over the years based on data derived from the tests of hypoxia on healthy young males. This is obviously not a representative sample of the current travelling population and risks are greater for the elderly and those suffering from certain medical conditions, such aschronic obstructive pulmonary disease (COPD), in addition to anyone who has recently spent time diving to depth under water. The risk would also depend on the duration of the flight.

At 8000 ft, it is possible for some people to experience mild hypoxia, the symptoms of which include impaired mental performance, reduced exercise capacity, fatigue. Some individuals suffer mild hyperventilation, headache, insomnia or digestive dysfunction. The effects are not great, and would not necessarily be of significance in most cases, although accident risk could increase. It can also be speculated that fatigue resulting from hypoxia would discourage exercise and, therefore, increase the risk of DVT. Conversely, exercising to avoid DVT might increase the risk or effects of hypoxia.

The reduction of applied external pressure also leads to the air trapped in the body cavities to expand (by 38% at 8000 ft cabin altitude). The cavities of concern are the ears, sinuses, stomach, intestines and lungs (and, for some people, teeth and eyes).This gas expansion can cause discomfort for the occupant (for example, ears popping)but in some susceptible cases it can also present a health risk. Not only is the absolute pressure important but also the rate of change of pressure. This is particularly so for the ears, in which rapid changes in pressure can cause damage. This section of the report will deal with both aspects of reduced cabin pressure.

In addition to the maximum cabin altitude, the SAE standard also relates to the rates of change the aircraft cabin altitude as the aircraft ascends and descends. The rate of change of pressure is an important part of both comfort and safety, particularly for the ears. In practice, the rate of change in passenger aircraft should not be a problem except for some babies and young children. Susceptible individuals may experience discomfort on descent and need to clear their ears. There are some indications of a trend towards more rapid ascent/descent in newer aircraft, so that more time is spent a cruising altitude. The effects of any such trend should be monitored.

Analysis of abstracts

The total number of abstracts found in the search was more than 80 for issues predominantly to do with pressure and approximately 40 dealing with hypoxia and oxygen. These totals, however, include many topics of restricted relevance (e.g. Air transport of infants in Newfoundland and Labrador, Johnson et al 1978) and also there is a great deal of overlap between these two categories because they both derive from the reduced cabin pressure. The amount of actual relevant research is therefore rather less than the numbers of abstracts indicates.

The study of hypoxia and its effect on commercial aircraft dates back to the 1940s at least (Graybiel 1941) and continued at intervals up to the present day. As indicated above, a significant portion of the research has been carried out on healthy individuals and often in simulated conditions using oxygen reduced air. In recent times the focus has tended to be on at risk groups of passengers who may be suffering from a disorder that causes an earlier or greater hypoxic response.

Relevant review papers

For hypoxia and pressure effects the literature search did not find any papers that reviewed the subject in its entirety. Consequently, the review here is carried out on a paper by paper basis.

Review of key papers

The papers are listed in Table 5.1.

A key study in the work on hypoxia is that of Cottrell et al (1995). This was prospective study of pilots and flight deck crew and claimed to be the first to report saturation levels of aircraft personnel during modern commercial flights. The results showed quite low levels of arterial oxygen saturation under normal flight conditions. The individual differences were large and certain of the sample would be experiencing mild hypoxia. Given that the sample was of crew members it is likely that the average level of health and fitness would be greater than for the general travelling public.

Table 5.1 Key papers on cabin pressure and oxygen
Coker RK, Partridge MR (2000). Assessing the risk of hypoxia in flight: the need formore rational guidelines. European Respiratory Journal: 15: 128-130. Cottrell J, Lebovitz B, Fennell R, Kohn G (1995). Inflight arterial saturation continuousmonitoring by pulse oximetry. Aviation, Space and Environmental Medicine (Feb)126-130. Dillard T, Krishnan M, Rajagopal et al (1998). Lung function during moderatehypobaric hypoxia in normal subjects and patients with chronic obstructive pulmonarydisease. Aviation, space, and Environmental Medicine

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Flynn C, Thompson T (1990). Effects of acute increases in altitude on mental status.Psychosomatics V31: No 2.

Fatemain M, Kim D, Poulin M, Robbins P (2001). Very mild hypoxia for 8h can induceventilatory acclimatization in humans. European Journal of Physiology 441:840-843.

Gong H, Mark JA, Cowan MN (1993). Preflight screenings of patients, analysis ofhealth and flight characteristics. Chest 104 3 Sept 788-794.

Hale H.B, Goldzieher J.W, Storm W.F (1973). Physiological cost in 36- and 48-hoursimulated flights. Aerospace Medicine Aug: 871-881.

Hartzell WG, Newberry PD (1972). Effect of fasting on tolerance to moderate hypoxia.Aerospace Medicine Vol. 43 No. 8: 821-826.

Rose DM, Fleck B, Thews O, Kamin WE (2000). Blood gas-analyses in patients withcystic fibrosis to estimate hypoxemia during exposure to high altitudes in hypobaricchamber. European Journal of Medical Research 5: 9-12.

Simons M (1990). Environmental factors influencing flight crew performance. ICAOHuman factors seminar Leningrad April.

Stoller JK (2000). Oxygen and air travel Respiratory Care: 45; 2 214-221.

Westerman T, Fine M, Gilbert L (1990). Aerotitis: cause, prevention and treatment.JAOA Vol 90, No 10.

Simons and Krol (1996) found considerable individual differences in the response to lowered PO2. They measured arterial oxygen saturation (SpO2) 30 min after exposure of15 healthy individuals to 8000 ft the mean SpO2 was 90% but the range was from 85 93%. The body s response to hypoxia is to increase the rate and depth of breathing: this may be hindered in aircraft passengers by drowsiness, immobility, cramped seating conditions and gastrointestinal distension due to the decreased cabin pressure. For example, SpO2 fell as low as 80% in those who were dozing off.

Simon (1990) points out that mild hypoxia may be more of a threat to safety than previously believed but here he was quoting an anonymous report in Aviation Week and Space Technology.

Stoller (2000) suggests, from empirical studies, that short term exposure to cabin altitudes is well tolerated by travellers, even by those with chronic obstructive pulmonary disease. However, he does proceed to conclude that gaps exist in the current understanding of the risks of air travel and optimal ways of predicting the need for in-flight oxygen.

Coker and Partridge (2000) carried out a prospective observational study of physicians in England and Wales to determine if the advice currently given to potentially hypoxic patients is evidence based. Their questionnaire survey showed that advice is regularly given and that potential hypoxia on aircraft is well recognised by respiratory physicians in the UK. The tests administered and the advice given did not appear to be evidence based and the authors feel that better guidelines are needed.

The paper by Flynn deals mostly with altitude sickness as a consequence of mountains but also develops the ideas as they would relate to cabin aircraft altitudes. The authors contend that the mild levels of hypoxia that even cabin altitude can produce may be enough to bring about subtle changes in mental status, particularly in at-risk groups. These changes include cognitive impairment and may be accentuated by travellers who are drinking alcohol or smoking cigarettes. This can lead to erratic behaviour and loss of impulse control. It may be speculated that the current phenomenon of air-rage may notbe unrelated to this effect.

Fatemain et al (2000) used oxygen reduced gas in an experimental setting to show tha tthe ventilatory response of the subjects acclimatised to even mild levels of hypoxic exposure. The experimental conditions were set to mimic those found caused by short duration air travel.

The study by Hale et al (1973) considered the effect of a range of stressors on a group of young healthy men. From these laboratory simulations they concluded that there is a complex set of interactions between the stressors and the performance of a psychomotor task. However, they do state that The present study clearly shows that a common cabin altitude (8000 ft) is not as benign as it appears. There is some physiological cost which relates to altitude, and some of the physiological effects persist after rest.

Hartzell and Newberry (1978), in their investigation of the effect of fasting on the mean arterial pressure, indicates that it will be lower after fasting and exposure to low cabin altitude than either treatment alone. The example of one subject in their trial, and the reports of other studies, suggests that the combination of fasting and hypoxia can precipitate fainting and extend the time for which the symptoms remain.

Lung function in COPD and cystic fibrosis patients has been addressed by a number of papers. It is generally recognised that any problem with the uptake of oxygen may exacerbate problems when low cabin altitudes are experienced. However, the papers of Dillard et al (1998) and Rose et al (2000) would suggest that there is a small effect but not sufficient to warrant concern in all cases.

Gong et al (1993) have also researched the response of cardiopulmonary patients to hypoxic conditions. They tend to suggest that there are problems but that these may be addressed by suitable screening and medication. They also suggest that at any time there could be up to 5% of passengers in a risk category.

Thiebault (1997), in his general review, quotes the work of Cottrell et al (1995), and are view of altitude sickness in the Scientific American, that both suggest that for many more normal occupants of commercial aircraft even the moderate altitudes of 5000-8000feet may exhibit hypoxic symptoms.

The other aspect of pressure is the effect on the air trapped in the body cavities. Westerman et al (1990) point out that problems of the middle ear, resulting from changes in pressure when flying, are on the increase. The problems may be either temporary or permanent loss of hearing or other symptoms such as tinnitus and vertigo. An upper respiratory tract infection makes it more difficult for the sufferer to equalise pressures and is therefore increases the risk.

In general, gas expansion would cause only discomfort, although anyone close to ardiac failure could be at greater risk.

Gaps in knowledge indicated by research

It seems that the there is insufficient knowledge of the extent to which oxygen de-saturation is likely to be a problem among all groups of the travelling public. The current trend in aircraft operation is to fly at higher cabin altitudes (lower cabin pressure). The current guidelines suggest that 8000 feet should be the maximum sustained cabin altitude. The suitability of this figure may need to be re-examined.

Changes of cabin pressure as the flight progresses can be a problem for individuals at risk (e.g. owing to upper respiratory tract infections). The current operating practices for changes in flight levels, and the consequent changes in cabin pressure, are not known.

Research needs

An investigation should be conducted, into the in-flight oxygen saturation of a wide range of crew members and passengers, including those with risk factors such as COPD and cystic fibrosis. Non-invasive oximetry techniques could be used for this, allowing for the measurement error on individual measurements.

Interaction with DVT and exercise should be considered in any research on hypoxia.

It would be informative to carry out some monitoring of pressures and rates of change on commercial flights, particularly on descent from cruise to approach.

It should be possible to examine any risks due to gas expansion from in-flight medical reports.

6. Cabin air quality: temperature

Introduction

There is a large literature covering the area of thermal comfort in other environments, such as buildings, but relatively little research in aircraft. Extremes of temperature are highly unusual in normal aircraft cabin conditions. Temperature in aircraft therefore tends to be considered as a comfort issue rather than a health issue. However, the distinction between health and comfort is not always clear, especially since temperatures in the normal range still have an indirect effect on other health and air quality issues.

In general, the elderly and infants are most susceptible to temperature extremes but there is little evidence of this being a particular issue in aircraft. The environmental requirements of cabin crew and passengers are likely to differ because the crew will be more active that the passengers and more constrained in their choice of clothing.

Temperature will affect the rate of dehydration of passengers and crew. Also, the humidity will affect thermal comfort. In buildings, both high temperatures (within the comfort range) and low relative humidity have independently been associated with increased risk of sick building syndrome (SBS). The symptoms of SBS are acute non-specific symptoms such as fatigue, headache and irritation of the skin and mucous membranes.

Temperature also affects both perceived and objective air quality. Perceived air pollution is greater as the temperature increases (and also as humidity increases). Temperature will have an impact on generation of body odour and the rate of emission of VOCs from cabin materials, thereby affecting the pollutant concentration in the cabin air.

Hence, effects of temperature can easily be misattributed to other factors, especially air pollution. Thus, effort could be misdirected at other factors, missing out the relatively simple approach of reducing the temperature.

There are some issues of temperature that are more specific to the aircraft environment. One is the possible occurrence of steep temperature gradients throughout the cabin, and another is the sharp change in temperature that sometimes occurs between the aircraft cabin and the outside ambient air, when boarding or disembarking. There is also a suggestion that air velocities can occur in aircraft cabins than are greater than those normally encountered in buildings.

In principle, there could be other interactions involving temperature but these are poorly understood:

- the risk of DVT could be affected by cabin temperature, not so much because of its direct effect on the body but because people tend to be less active at higher temperatures;
- the combination of temperature and humidity could affect the viability of airborne pathogens and/or the ability of the body to resist infection;
- high temperature and jet lag could combine in causing some symptoms, such as fatigue and headache.

Review of abstracts by type

Studies	22

Guides	2
Reviews	2
Other/not known	3
Letters	-
General	-
Total	29

Relevant review papers

Two review papers dealt specifically with temperature in aircraft.

> Thibeault C, Cabin Air Quality, Aviation, Space and Environmental Medicine, Vol 68,No. 1, January 1997.
>
> Hartman BO, Storm WF, Vanderveen JE, Vanderveen E, Operational Aspects ofVariations in Alertness, Advisory Group for Aerospace Research and Development Paris (France), August 1974.

The paper by Thibeault is a Special Committee Report from the Aerospace Medical Association, which presents a short expert review on CAQ, and provides some simple, practical recommendations. The paper uses just eight references, but the information contained is based more on the experience and expertise of the committee experts, than on a literature review. This paper notes that temperature on aircraft is unlikely to cause more than discomfort, but in combination with low humidity, relative hypoxia and misuse of ventilation systems, could contribute to other problems. Cabin temperature is easily controlled, but thermal comfort for all passengers and crew is difficult to achieve. Their recommendation for temperature is that the flight and cabin crew should cooperate to maximise the thermal comfort in the cabin.

The paper by Hartman et al reviews the literature on the factors that influence pilot alertness, including thermal conditions, and the associated decrease in effectiveness. From this perspective, temperature is a safety issue.

In addition to these review papers, it is also worth noting the work being carried out on ASHRAE standard 161 Air quality within commercial aircraft. This work is ongoing, and covers many aspects of air quality on aircraft. The standard is likely to give suggested temperature ranges for majority thermal comfort, as well as addressing temperature non-uniformity issues, such as vertical temperature gradients, radiant temperature asymmetry and surface temperatures. The work is based on the ASHRAE guidelines for buildings, but recognises the particular constraints of design, activity, clothing and posture (among others) in aircraft. While this will partly account for the differences between aircraft and buildings, validation in field studies is essential since thermal comfort requirements vary, even between building types, after taking into account all these variables.

Review of other key papers

The other key papers identified from the review of abstracts are shown in Table 6.1.

Table 6.1 Key papers on temperature
Boettcher B (1991). Hot air in flight:. Medical Journal of Australia

(1824):154/8.

Haghighat F, Allard F, Megri A C (1998). Thermal comfort and indoor air quality inforty-three flights. EPIC (17) 2, 439-444.

Haghighat F, Allard F, Megri A C (1999). Measurement of thermal comfort and indoorair quality aboard 43 flights on commercial airlines. Indoor Built Environ, (8): 58-66.

Lindgren T, Norbäck D, Andersson K, Dammstrom BG (2000). Cabin environment andperception of cabin air quality among commercial aircrew. Aviation Space andEnvironmental Medicine 71,8: 774-782.

Nagda N, Fortmann R, Koontz M, Konheim A (1990). Investigation of cabin air qualityaboard commercial airlines. BIBINF Canada, Indoor Air '90, (2): 245-250.

O'Donnell A, Donnini G, Van Hiep Nguyen (1991). Air quality, ventilation, temperatureand humidity in aircraft. BIBINF USA, ASHRAE Journal (4): 42-46.

SAE Standard (1991). Air Conditioning Systems for Subsonic Airplanes (Reaffirmed,Jul 96): Society of Automotive Engineers.

Most of these papers present the results of studies in which temperature was one of many CAQ parameters investigated. In most cases, air temperature was measured, and the range and average reported. Lindgren et al (2000) used crew questionnaires as well as objective measurement. Complaints relating to temperature included temperature being too high and temperature variation being too great. This suggests the need for work on temperature variation, temperature asymmetry and measurement of air velocities. Haghihat et al (1998, 1999) estimated thermal comfort in aircraft from measurements of air temperature and relative humidity.

Gaps in knowledge indicated by research

Several studies on temperature in aircraft have been reported. However, most of these were carried out in a fairly ad hoc way. Temperature is usually included as one of several environmental factors being considered, rather than being the focus of research, and average air temperature as a broad metric for thermal comfort is the main parameter of interest in these studies.

There is a surprising lack of comprehensive measurement of air, radiant, surface and operative temperatures over time at different locations and heights, measurement of air velocities, and investigation of temperature non-uniformity.

The effect of temperature on emission of VOCs from cabin materials is not the subject of much work, but as the principles are reasonably well established in buildings, there is no particular need for fundamental work to be repeated in aircraft. Specific products could be tested for their suitability for use in aircraft.

Given the possibility of effects of temperature on risks of DVT, transmission of infection and jet lag, it is surprising that these interactions have not been explored.

Research needs

More comprehensive, detailed investigations on cabin temperature variation in time and space would be valuable. These investigations need to address both comfort and health issues; while there may be a case for reducing temperatures on grounds of health, this may conflict with expectations in relation to comfort. Hence, unless thermal comfort on aircraft is properly understood, it may be difficult to implement health-based recommendations.

The main health issues to be investigated in the context of cabin temperature are:

- DVT;
- transmission of infection;
- acute non-specific symptoms;
- jet lag;
- accident risk.

7. Cabin air quality: humidity

Introduction

There is a large amount of literature available on the effects of humidity on other air quality and health issues. However, unlike temperature, the levels of relative humidity(RH) that occur on aircraft are not typical of other indoor environments in most countries. Although the RH can be quite high while the aircraft is on ground (and the air flow is relatively low), once at cruise altitude, the cabin RH is generally much lower than in most buildings, and much lower than recommended by most standards and guidelines. Typically, RH would be between 5% and 15%, compared with recommended minima that range from 20% to 40% RH. However, guideline limits are set in buildings in the context that it is normally relatively straightforward to achieve 30% RH in buildings. Also, perceived humidity is dependent on temperature and air pollutants, and maintaining higher RH in buildings would possibly partly compensate for overheating and air pollution at ground level.

Low humidity can have direct effects on health and comfort, the range of effects depending on the humidity, the duration of exposure and other factors (e.g. temperature, water ingestion, wearing contact lenses, use of moisturiser). The main potential problems are:

- drying of the body surface (mucous membranes and skin);
- dehydration;
- perception of poor air quality at high RH;
- effects on thermal comfort (feeling cooler at lower RH, especially at higher temperatures).

In addition, humidity has many indirect effects, relating to several other factors that are addressed in this report:

- dehydration is a possible factor in DVT and jet lag (see also Chapter 3, on DVT);
- RH (in combination with temperature) affects the generation of body odour and emissions from materials;
- at altitude, humidification may cause condensation on surfaces, with associated risks of microbial growth;
- humidity affects the viability of some pathogens in the air, some being favoured by low RH and some by high RH;
- the effectiveness of the mucous membranes in defending against infection could also be compromised by low humidity.

Another potential problem in low RH environments is static electric shock.

Some of the factors affected by RH would be improved at higher RH, and others are improved at lower RH. A balance is therefore required between comfort, direct health consequences and indirect health consequences, although the principal concern is low RH. The relative merits of increasing the moisture content of the air and reducing the temperature also need to be considered. Much of the literature concerning RH on aircraft focuses on ocular discomfort and dryness of airways.

Review of abstracts by type

Studies	20
Guides	2
General	4
Letters	-
Reviews	4
Other/NK	1
Total	32

Relevant review papers

Four review papers dealt specifically with humidity in aircraft.

Simons M, Environmental Factors Influencing Flight Crew Performance Presented at Icao Human Factors Seminar, Leningrad, USSR, 3-7 Apr 1990. Govt Reports Announcements & Index (GRA&I), Issue 14, 1991.

Thibeault C, Cabin Air Quality, Aviation, Space and Environmental Medicine, Vol68, No. 1, January 1997.

Hartman BO, Storm WF, Vanderveen JE, Vanderveen E, Operational Aspects ofVariations in Alertness, Advisory Group for Aerospace Research and DevelopmentParis (France), August 1974.

Owe JO, Christensen CC, Medical problems among airline passengers, TidsskrNor Laegeforen 1998 Sep 30;118(23):3623-7.

The Simons paper discusses the combination of environmental factors that affect pilotsperformance, including low humidity. The paper recommends controlled studies of multiple factors under cockpit environmental conditions.

The paper by Thibeault is a Special Committee Report from the Aerospace Medical Association, which presents a short expert review on CAQ, and provides some simple, practical recommendations. The paper uses just eight references, but the information contained is based more on the experience and expertise of the committee experts, than on a literature review. This paper notes the low RH, but considers only the direct effects such as nasal dryness, and suggests that the common recommendation of increased fluid intake is adequate to control these mild side effects. The indirect effects of RH are not dealt with.

The paper by Hartman et al reviews the literature on the factors that influence pilot alertness, including hygrothermal conditions, and the associated decrease ineffectiveness. The paper by Owe and Christensen describes the environmental and physiological stresses of air travel, including the effects of low humidity, and gives some practical recommendations, and a review of reported illnesses on two airlines.

In addition to these review papers, it is also worth noting the work being carried out on ASHRAE standard 161 Air quality within commercial aircraft. This work is ongoing, and covers many aspects of air quality on aircraft. The standard is likely to suggest a*maximum* RH, and notes the need to compromise comfort to some extent, in order to avoid adverse indirect health effects.

Review of other key papers

The other key papers identified from the review of abstracts are shown in Table 7.1.

Table 7.1 Key papers on humidity in aircraft
Backman H, Haghighat F (2000). Air quality and ocular discomfort aboardcommercial aircraft. Optometry Oct;71(10):653-6.
Bagshaw M (1996). Jet leg, pulmonary embolism and hypoxia. Lancet 348: 415.
Carruthers M, Arguelles A E & Mosovich A (1976). Man in transit: biochemical andphysiological changes during intercontinental flights. Lancet 8:977-980.
Haghighat F, Allard F, Megri A C (1999). Measurement of thermal comfort and indoorair quality aboard 43 flights on commercial airlines. Indoor and Built Environment (16)8: 58-66.
Landgraf H, Vanselow B, Schulte-Huermann D, Mulmann M V & Bergau L (1994).Economy class syndrome: rheology, fluid balance, and lower leg edema during asimulated 12-hour long distance flight. Aviat Space Environ Med 65(10 Pt1): 930-5.
Ledermann J A & Keshavarzian A (1983). Acute pulmonary embolism following airtravel. Postgrad Med J 59(688): 104-5.
Lee SC, Poon CS, Li XD, Luk F (1999). Indoor air quality investigation on commercialaircraft. Indoor Air Sep;9(3):180-7.
Lindgren T, Norbäck D, Andersson K, Dammstrom BG (2000). Cabin environmentand perception of cabin air quality among commercial aircrew. Aviat Space EnvironMed;71(8):774-82.
O'Donnell A, Donnini G, Van Hiep Nguyen (1991). Air quality, ventilation,temperature and humidity in aircraft. BIBINF USA, Ashrae Journal (4) 42-46.
Simons R & Krol J (1996). Jet leg, pulmonary embolism and hypoxia. Lancet 348:416.

O'Donnell et al (1991) measured humidity and other cabin environment factors in 45aircraft but conclusions about health are based on building guidelines rather that data from the flights. Haghighat et al (1999) estimated thermal comfort from measurements of air temperature and RH. Backman & Haghighat (2000) describe a study measuring temperature, RH and carbon dioxide to estimate ocular discomfort. This paper suggests that airlines should aim for RH levels of 40-60% but other sources suggest that, at altitude, those levels would be too high. Lindgren et al (2000) describe a study using questionnaires for air crew, as well as objective measurements. Mean RH was low, and complaints included dry air and static electric shocks. The authors suggest that air humidification may be a solution, but note the possible problems of microbial growth in air-conditioning units, condensation problems and corrosion. The authors suggest the need for epidemiological studies on air humidification at very low humidity levels. Lee etal (1999) also used crew questionnaires and measurement of RH. Again, mean RH during cruise was very low, and complaints of low humidity, associated discomfort and dry eyes, airways and skin, were common. The paper notes that ASHRAE Standard 62suggests a minimum of 20% RH in buildings.

Most authors assume that dehydration will occur on aircraft but it is not clear whether the degree of dehydration would be significant. Landgraf et al (1994) cite a study during an intercontinental flight which found insensible fluid losses of 84 ml/hour. However, Bagshaw (1996) quotes a RAF Institute of Aviation Medicine study which showed that the maximum possible increase in body water loss at 0% humidity (compared with the normal day-to-day environment) over 8 hours was ~100 ml.

Simons and Krol (1996) describe a pilot study in which they exposed people to a simulated altitude of 8000 ft for 8 h at 8-10% humidity, and instructed them to drink 2 l in that time. Compared to the control condition (sea level; 30-40% RH), they found an increased plasma osmolality, urine osmolality and urine specific gravity, indicating dehydration. Carruthers et al (1976) studied 13 crew and two passengers during a 20-hour flight from Buenos Aires. Compared to the five non-flying controls, they found decreased urine volume and increased urine concentration in the subjects, and attributed these findings to the combined dehydrating effects of a hot Argentinian summer and the low humidity during the flight. Ledermann and Keshavarzian (1983) report on a patient with air travel-related PTE who had an elevated blood urea on admission, evidence of possible dehydration.

The degree of dehydration that occurs during air travel is therefore uncertain. This maybe because of differences between real world and theoretical or laboratory settings. For example, passengers might experience a sensation of thirst or dry mouth because of superficial drying of the body surface. They might respond to this by drinking alcoholic or caffeine-containing drinks, which have a diuretic effect. There are also uncertainties over the effects of a low-RH environment on water distribution in the body, as distinct from overall water loss.

Gaps in knowledge indicated by the research

Although there is a large amount of literature on RH in buildings, the accumulated knowledge cannot be directly applied to aircraft. This is partly because of the effect of lower air pressure, partly because of the particular constraints of the aircraft environment, and partly because of the much lower RH levels being considered.

While there are several potential health problems with low humidity in aircraft, there is little evidence on the actual situation. Neither is it clear to what extent passengers can self-manage their health, for example through water intake, use of moisturisers or taking out contact lenses.

There is a need for research to bridge the gap between the measured RH levels on aircraft, and the established knowledge of RH in buildings and other environments. The needs are to establish typical cabin conditions, investigate the effects of these conditions(singly and in combination), and investigate solutions and improvements.

Research needs

- In-depth analysis of literature on direct and indirect health effects of very low RH levels in other environments.

- The effect of altitude (and therefore reduced air pressure) on recommended levels of RH.
- Experimental work, with robust methodology, to measure RH on aircraft, and to investigate physical, chemical, biological and physiological effects of lower RH, in controlled / simulated cabin environment.
- Epidemiological study of health outcomes related to air humidification at very low RH in aircraft.

As RH is an important cross-cutting issue, affecting many other aspects of health on aircraft, it is recommended that research is carried out in this area, as detailed above. Without a proper understanding of the effects of low humidity, other areas of work will not be fully informed.

8. Cabin air quality: air pollutants

Introduction

This section refers to the literature on the main pollutants found in aircraft cabin air. Mostpapers discuss more than one pollutant. Much of the relevant literature considers the pollutants in the context of comfort, rather than health. There are obvious interactions between pollutants, and with other issues covered by this report, particularly temperature and relative humidity, but also infectivity, jet lag and pressure/oxygen.

Research and review papers on environmental tobacco smoke (ETS) are plentiful, but are excluded here, as most flights are already, or will soon become, non-smoking.

Carbon dioxide (CO_2) is a useful indicator for ventilation rate in a space occupied by a constant number of people, and concentrations in aircraft cabins have been measured often. Most studies show that, although concentrations often exceed the 1000 ppm level recommended for comfort in buildings, the levels were always within health recommendations, and would not be expected to have significant adverse effects on health (except possibly in combination with other cabin conditions). The highest concentrations of CO_2 generally occur while power to the ventilation system is reduced, for example while the aircraft is on the ground, during take-off and during landing. Sublimation of dry ice (used for chilling food) can cause transient high levels.

Carbon monoxide (CO) concentrations are recorded in many papers. Levels are generally well within recommended guidelines on non-smoking flights.

Ozone (O_3) has also been measured in many studies, because of the relatively high levels found in the outdoor air at altitude. O_3 has an irritant effect on the lungs at low concentrations, and can also react with other pollutants to produce new irritant compounds. Some O_3 is lost by high temperatures and pressures, and by reaction with surfaces before air reaches the cabin, and catalytic deozonisers are commonly now provided on the supply air stream to control O_3 as a pollutant. Most studies show that measured levels are within health guidelines. However, one review (Nagda et al, 2000)suggests that the existing measurement techniques are not adequate, and development of a reliable and practical method of continuous measurement of O_3 is necessary before firm conclusions can be drawn.

Respirable particles have been measured in many studies, and a wide range of results have been obtained. For non-smoking flights, levels are generally lower than or similar to levels in buildings, and within recommended guidelines, but a few studies have reported higher levels. The wide range in measurement results may be due to selection of measurement technique, rather than genuine variation in levels of particles. Particle matter in the air increases during boarding and disembarking, and it is not always clear whether studies have included these phases, or just the cruise phase. Generally, use of HEPA (high efficiency particulate air) filters in aircraft ventilation systems reduces the level of airborne particles.

Levels of bacteria and fungi in aircraft cabin air are consistently reported as lower than would generally be found in buildings. As with non-viable particles, HEPA filters should keep these at an acceptable level, if they are correctly installed and maintained. Within the cabin, the low humidity during flight would mitigate against colonisation by the fungi and mites that are common sources of allergens in buildings. However, allergens(especially cat allergen, Fel d1) have a tendency to adhere to clothing and would collect on aircraft seats if they are not adequately cleaned.

There are many sources of organic chemicals in aircraft cabins, including the aircraft fabric and furnishings, cleaning materials, fuels, lubricants and pesticides. Hence, there may be hundreds of chemicals present in the air at low concentrations in aircraft, as in other indoor environments. Measurements of total or individual volatile organic compounds (VOCs), are sometimes made in air quality studies, using a variety of techniques. Measurement of semi-volatile organic compounds (SVOCs) is less common. Individual chemicals of particular interest include formaldehyde and acrolein.

Some chemicals are from sources within the cabin, and some find their way into cockpit and cabin due to, for example, oil leaks or hydraulic seal failures. For these, consideration must be given to the chemicals themselves, and also the products of thermal decomposition, due to the high temperatures and pressures they are subject to.

Disinsection is used on some routes to minimise the risk of insects carrying diseases(such as malaria and dengue fever) being carried on the flight. Depending on the procedure used, disinsection is sometimes carried out with passengers on board, and sometimes with crew only on board. The pesticides generally used have not been shown to have adverse human effects, but the long-term health effects of repeated exposure to possibly fairly high levels of the pesticides needs to be evaluated.

Organophosphates (OPs) are present in minute quantities in some aviation jet fuels and hydraulic fluids. These are chemicals of high toxicity, capable of producing serious adverse neurological and other effects. In normal cabin conditions, exposure to these chemicals is minimal. However, there is some concern that low concentrations entering the cockpit and cabin due to oil or lubricant leaks could cause both short-term and long-term health risks. There is strong concern about this issue, but little substantial evidence to support the perceived risk.

Papers on thermal degradation of aero engine lubricants do not provide any evidence of generation of toxic chemicals at levels that could give rise to the symptoms sometimes attributed to them by flight crew. However the symptoms reported might be explained by a reaction to odour exacerbated by the internal cockpit environment and motion (some chemicals reported would be pungent at very low concentration and cause nausea because of the odour).

Review of abstracts by type

Studies	108
Guides	4
General	35
Letters	-
Reviews	23
Other/NK	32
Total	202

Relevant review papers

The main review papers are:

- Thibeault C, Cabin Air Quality, Aviation Space and Environmental Medicine, January 1997, Vol 68, No. 1, pp 80-82.
- Rayman RB, Passenger safety, health and comfort: a review, Aviation Space and Environmental Medicine, May 1997, Vol 68, No. 5, pp 432-440.
- Nagda NL, Rector HE, Zhidong L, Space DR, Aircraft cabin air quality: a critical review of past monitoring studies, Air Quality and Comfort in Airliner Cabins, ASTMSTP 1393, N L Nagda Ed. ASTM, West Conshohocken, PS, 2000.
- Brundrett G, Comfort and health in commercial aircraft: a literature review, Journal of the Royal Society for the Promotion of Health, March 2001, 121(1), pp 29-37.

The paper by Thibeault (1997) is a Special Committee Report from the Aerospace Medical Association, which presents a short expert review on CAQ, and provides some simple, practical recommendations. The paper uses just eight references, but the information contained is based more on the experience and expertise of the committee experts, than on a literature review. The paper reports that recorded levels of CO, CO_2,O_3 and VOCs in aircraft cabins met relevant standards for health. For biologicalcontaminants, the paper notes that recorded levels of airborne micro-organisms remained well below health recommendation levels, but recommends use of HEPA filters to avoid spread of contaminants in recirculated air.

Rayman (1997) is a wide-ranging review of passenger health, safety and comfort, with recommendations on these issues, including a section on CAQ. This section draws primarily from two large studies of CAQ (Nagda/DOT et al and ATA) and concludes that recorded levels of CO, O_3, respirable particles, and micro-organisms are within recommended limits, and in many cases lower than those found in public buildings. CO_2concentration is acknowledged to be higher than comfort recommendations, but still within health recommendations. Rayman recommends that although these air pollutants do not appear to be a cause of the adverse physical symptoms experienced by crew and passengers, the issue of CAQ in general should be studied further defining the problems and recommending research to resolve them. He also recommends that all commercial aircraft should have HEPA filters installed and properly maintained.

Nagda et al (2000) is a detailed review and comparison of monitoring studies of CAQ, concentrating on the measurement parameters, evaluation of measurement techniques and results from 9 studies between 1985 and 1998. Nagda reports that average concentrations of bioaerosols, particulate matter and CO were lower than or similar to those in ground-level environments. CO_2 levels routinely exceeded 1000 ppm (the level used for judging acceptability in buildings, which may be inappropriate for the cabin environment). Formaldehyde, O_3 and VOCs were measured in fewer studies, and the lack of data or inadequacies in measurement technique precludes definitive conclusions. No measurements of SVOCs were identified in the published literature. The authors recommend that measurement studies should give high priority to parameters such asaldehydes, O_3, SVOCs and VOCs, using reliable and appropriate methods. The paper also recommends that quality assurance is as important as choosing right parameters and methods, and comprehensive reporting of methodologies used is also important.

The paper by Brundrett (2001) reviews the literature on many aspects of comfort and health in commercial aircraft. The section on ventilation provision discusses concentrations of CO_2 in aircraft cabins. He notes that in measurement studies, CO_2concentration is often above recommended levels for comfort, but within health guidelines. He notes that CO_2 levels can be particularly high during take-off and landing when power requirements reduce the amount of ventilation available. He suggests that the minimum fresh air rate of 2.5 l/s/p (litres/second/person) proposed in the draftASHRAE standard for aircraft would result in a level of 2200 ppm CO_2. However, manufacturers may well exceed this level to achieve other criteria. On the subject of O_3,Brundrett notes that aircraft expecting to fly through areas with significant O3 content are fitted with a catalytic deozoniser, to reduce the O_3 entering the cabin.

Review of other key papers

The other key papers identified from the review of abstracts is shown in Table 8.1. There have been many studies of air pollutants on aircraft, but many of them describe fairly ad-hoc measurements. There are relatively few significant studies with comprehensive and robust measurement methodologies.

For most air pollutants, the general consensus from the literature is that, where we have reliable measurements of pollutants, the levels are similar to, or lower than, those found in most buildings. Levels are generally within health guidelines (where guidelines exist) although occasionally exceed comfort guidelines (e.g. for carbon dioxide). In the latter case, the guidelines are based on the perception of body odour by visitors to a space; occupants would adapt to the background level of body odour, probably more rapidly than it could build up. Aircraft in flight typically do not receive visitors.

Control of these pollutants is primarily achieved by ventilation and filtration. ASHRAE is preparing a draft standard for air quality on commercial aircraft (161P), and may recommend a minimum fresh air ventilation rate of 5 cfm/person (2.5 l/s/person).However, the additional criteria for CO, CO_2, O_3 and respirable particles may well require a higher fresh air rate. Filtration is clearly very important, and HEPA filters, when correctly installed and maintained, can minimise levels of particles. As the filters get older, the pore size becomes smaller, thus trapping smaller particles. However, they may themselves become sources of odours or even biological contamination.

Table 8.1 Key papers on cabin air pollutants
Dechow, M. Sohn, H. Steinhanses, J. (1997). Concentrations of selected contaminants in cabin air of airbus aircrafts. Chemosphere (35); No.1/2, 21-31.
Hocking M B (1998). Indoor Air Quality: Recommendations Relevant to Aircraft Passenger Cabins. American Industrial Hygiene Association Journal, 59; No 7, 446-454.
Hocking M B (2000). Passenger aircraft cabin air quality: trends, effects, societal costs, proposals. Environmental Science & Pollution Research International (7): Part 3: 173.
House of Lords Select Committee on Science and Technology (2000). Fifth Report.
Kelso A G, Charlesworth J M, Mcvea G G (1988). Contamination of environmental control systems in Hercules aircraft. Materials Research Labs. (Melbourne, Australia).
Lee SC, Poon CS, Li XD, Luk F (1999). Indoor air quality investigation on commercial aircraft. Indoor Air. 9(3):180-7.
Lindgren T, Norbäck D, Andersson K, Dammstrom B G (2000). Cabin environment and perception of cabin air quality among commercial aircrew.

Aviat Space EnvironMed;71(8):774-82.

Lindgren T, Norbäck D, Andersson K, Dammstroem B G (1999). Subjective air quality, cabin air quality (CAQ) and medical symptoms in aircraft crew. Indoor Air 99, Vol 4:1001-1006.

Martinac I (1996). Cabin air quality (CAQ) onboard commercial jet aircraft. International Society of Biometeorology. Vol./Issue/Part No. CONF 14; No. 2; Vol 3: 349-360.

Nagda N L, Koontz M D, Fortmann R C (1993). Cabin Air Quality Aboard Commercial Airliners. Air & Waste Management Association; Vol./Issue/Part No. Vol 34: 243-248.

Nagda N L, Rankin W L, Space D R (2000). Passenger Comfort and the Effect of Air Quality. ASTM Special Technical Publication 1393: 269-290.

O'Donnell A, Donnini G, Van Hiep Nguyen (1991). Air quality, ventilation, temperature and humidity in aircraft. BIBINF USA, ASHRAE Journal 42-46.

Pierce W M, Janczewski J N, Roethlisberger B, Janczewski M G (1999). Air quality oncommercial aircraft . USA, ASHRAE Journal, 26-34.

Porter HO (1990). Aviators intoxicated by inhalation of JP-5 fuel vapors. Aviat SpaceEnviron Med;61(7):654-6.

Van Netten C (1998). Air quality and health effects associated with the operation ofBAE 146-200 aircraft. Applied Occupational & Environmental Hygiene 13; No 10, 733-739.

Van Netten C, Leung V (2000). Comparison of the constituents of two jet engine lubricating oils and their volatile pyrolytic degradation products. Appl Occup EnvironHyg;15(3):277-83.

Wick RL Jr, Irvine LA (1995). The microbiological composition of airliner cabin air. Aviat Space Environ Med Mar;66(3):220-4.

For organic chemicals and fuel gases, the general conclusion from the literature is that the concentrations measured should not be sufficient to cause adverse health effects. The typical symptoms experienced (e.g. nausea, dizziness etc) are typical of reaction to odours, and some of the chemicals present would be pungent at low concentrations. It is possible that, because of the specific environment in the aircraft, the reaction to odour is more extreme than normal. This could be because of combinations of chemicals, or because of the physical environment (e.g. mild hypoxia, vibration and motion, higher temperatures, low humidity) or purely for psychological reasons.

It is worth making a particular note on organophosphates, as they are the subject of much interest at present. Of particular interest is the presence of tri-ortho-cresylphosphate (TOCP) in some aviation fuels. There is significant concern about the risks of low concentrations of OPs entering the cockpit and cabin, with much semi-anecdotal evidence and incident reporting available, as well as web-based information sites, such as the Aviation Organophosphate Information Site. Kelso et al (1988) found small traces of OP in air filter bags, following a fuel leak, and suggests the use of carbon cloth filters for absorption. However, there is no clear consensus on this issue. The US Naval Flight

Surgeon Handbook s chapter (1998) on toxicology suggests that a large quantity of TOCP would need to be ingested before a toxic dose was reached.

After considering the available evidence on the issue, the House of Lords report (2000)concludes that the absence of confirmed cases of TOCP poisoning from cabin air and the very low levels of TOCP that would be found in even the highly unlikely worst case of contamination from oil leaking into the air supply lead us to conclude that the concerns about significant risk to the health of airline passengers and crew are not substantiated. We have found nothing to contradict this view, but it will be important to research this subject further, either to allay the concerns, or to confirm them.

The other issue that is not clear is the effect of exposure to multiple chemicals. Most studies of indoor air quality consider health risk and exposure to chemicals by comparing concentrations of individual chemicals with their threshold limit values. However, with a large number of chemicals present, the combined effect of the chemicals may take the equivalent exposure above suggested thresholds. Some authors believe that toxic effects are fully additive, others seem less certain. There may be additive, synergistic or masking effects in different chemical mixtures. A demonstration of combined toxicity of multiple chemicals could have a significant effect on the risk assessment of chemicals in the air, and is an important issue to investigate further.

Gaps in knowledge indicated by research

There are many papers on this subject, but relatively few significant measurement studies. There is a need to benchmark air pollutants in aircraft, with a comprehensive set of measured parameters and an agreed methodology. In particular, robust data for formaldehyde, VOCs and SVOCs in aircraft cabins is scarce, and with so many potential sources, could be very important. This would need to include measurement of OPs. Continuous measurement of ozone by a reliable and practical method would be valuable.

There is general agreement that the level of most pollutants in aircraft cabins is similar to or lower than levels found in most buildings, but passengers and crew still report adverse health effects that they attribute to air quality. It is important that the health effects of pollutants in the specific aircraft cabin environment is investigated, in combination with other physical and environmental factors that can cause perception of poor air quality, such as temperature, humidity and cabin motion. Research on the reaction to odours generated by thermally degraded engine oils might explain some of the reported symptoms.

The effects of low concentrations of many chemicals in the cabin air may be having a cumulative effect that the individual chemicals would not cause. Some argue that multiple chemical concentrations are additive in their toxicological effect, others disagree. Clearly, this is an important issue to address for aircraft. This leads into the need for amore general investigation of the toxicity of chemicals in the cabin environment, including the effects of pyrolysis (by-products of thermal degradation and decomposition).

There is little information on the levels of insecticides in aircraft cabins following disinsection, the personal exposures of crew (especially) and passengers. Long-term and short-term health effects of repeated exposure to low levels of pesticides in dry environments, and repeated exposure to fairly high levels of pesticides during disinsection, should be considered.

Controlling the levels of many pollutants relies on correct installation and maintenance of HEPA filters, but there are some reports of poor maintenance. It is not clear how widespread a problem this is. It would be useful to look further at this, perhaps with a survey of airlines on their maintenance procedures and even spot checks on the condition of filters. The potential for using carbon filters to remove pollutants in the vapour phase (especially while aircraft are on the ground) could be investigated.

Research needs

The overriding research need is to benchmark the air quality in current aircraft. This should involve a comprehensive set of measurements, using agreed methodologies, made on a sufficiently large number of flights to be typical, if not fully representative. These measurements would obviously need to include parameters other than air pollutants as well. This should be done alongside crew and passenger questionnaires, and even physiological tests.

Having characterised as far as possible the normal level of CAQ, the next research need is to investigate the physiological and subjective responses of people in simulated cabin conditions to combinations of environmental, chemical and physical parameters.

There is a lack of strong evidence behind two contentious issues exposure to OPs in cabin air, and the additivity or otherwise of effects of multiple chemical exposure. These areas should be investigated further, keeping in mind the need to consider interactions with other cabin conditions. Part of the problem is that investigations into suspected incidents are, by their nature, retrospective, which means there is little evidence about the composition of the air when the problem occurred. Perhaps a portable kit could be developed that the crew could use to sample the air when fuel or other odours are noticed. This would provide more pertinent data to support this subject area.

Passengers often express a preference for adjustable air supply nozzles (gaspers).The pros and cons of these should be clarified, in relation to air supply to the individual passenger, drying of the body surface, air distribution in the cabin and movement of pathogens.

9. Transmission of Infection

Introduction

The transmission of infection by the agency of aircraft has become of increased interest in recent years. The greater number of flights, to a wider range of destinations, has increased the potential for disease to be transmitted from areas of the world where it is endemic to passengers on aircraft and to regions where the disease has a lower incidence. There are a number of serious diseases that fall into this category, such as malaria, cholera, tuberculosis, dengue and ebola. Each of these has been addressed in the research revealed by the literature search, together with more common infections such as influenza and *Salmonella* food poisoning.

The transmission of disease in aircraft cabins can occur by a number of means:

- contaminated water or food (e.g. cholera, food poisoning);
- toilets (e.g. *Shigella* dysentery);
- direct contact or body fluids (AIDS, hepatitis);
- insect vectors (e.g. malaria, dengue);
- airborne person-to-person spread.

While each of these may be important, this review is concerned only with airborne transmission of infection between people while they are on board aircraft. For such illnesses, the means of control is not obvious and close proximity of passengers for extended periods cannot be avoided. The model for understanding such spread appears to be tuberculosis (TB), which is caused by airborne transmission of *Mycobacteriumtuberculosis* from an infected person to an uninfected person (not withstanding the fact that, in many countries, persons infected with TB are not allowed to travel by air).

While other diseases may be spread in a similar way, from colds, influenza and Norwalk virus gastroenteritis to more serious illnesses, TB is more persistent once acquired, without being rapidly fatal. It is also a disease with which approximately one third of the world s population is infected, most being unsymptomatic at any one time. TB is also readily diagnosed with certainty and creates sufficient public concern to generate research funding. All these factors make it an good model.

Abstracts Analysis

The search found more than 120 papers that broadly fall into the category of transmission of infection. Much of the literature deals with transmission of diseases such as malaria (13 papers) and cholera (7 papers), neither of which is transmittable by the air within the cabin, and other food-borne infections (11 papers) such as *Salmonella* food poisoning. Influenza is the subject of a further 7 papers. Of those dealing with a specific infection, TB is the most researched issue with approximately 20 documents. A significant number deal with general non-specific issues or transmission away from the aircraft environment, malaria in airport workers for example. Other infections identified in the search include ebola, dengue, HIV, meningitis, smallpox, plague and hepatitis.

The topic of disease transmission by aircraft was raised in 1965 and papers on the incidence of infections from food are reported as early as 1974 and continue until the present. However, the work on TB has begun rather later and most of the interest has been in the later part of the 1990s.

Review papers

There is one paper that reviews in detail the transmission of TB, published by the World Health Organisation (Tuberculosis and Air Travel: Guidelines for Prevention and Control). This paper reviews the research relating to the incidence of TB transmission on aircraft, citing literature up to 1998. In all, seven cases are reviewed, each of which deals with the air travel of an infected person and the subsequent follow-up for infection of fellow travellers.

There are a number of very clear observations made by this document:

- TB can be transmitted during air travel but none of the infected persons has developed active TB to date;
- there is no evidence that air recirculation facilitates transmission of M. tuberculosis aboard;
- in case of ground delays of more than 30 minutes, provisions must be made to supply adequate ventilation on board;
- risk of TB among cabin crew is similar to that of the general population (the review states that no mandatory routine or periodic TB screening is indicated for flight crew, but presumably there is a greater risk of onward transmission from cabin crew than from passengers or flight crew);
- airborne transmission of infectious diseases in aircraft appears to be limited to person-to-person spread within close proximity.

Therefore, the general conclusion of the report is that the likelihood of transmission of TB is low and is limited to people in close proximity on an aircraft for an extended period of time. From the perspective of future research needs, the report is quite clear that given the scale of infection world-wide, the routine use of BCG vaccination, and the numbers of people travelling that Further epidemiological studies on TB transmission in aircraft would be time and resource consuming. In case of exposure to *M. tuberculosis* infection during air travel, tracing and information of passengers and crew may be warranted.

In reaching their conclusions the authors of the WHO report cite a number of key papers, including:

- McFarland JW, Hickman C, Osterholm M, MacDonald KL. Exposure to Mycobacterium tuberculosis during air travel. Lancet 1993;342:112-3
- Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multi drug-resistant Mycobacterium tuberculosis during a long airplane flight. N EnglJ Med 1996;334:933-8
- Moser MR, Bender TR, Margolis HS, Noble GR, Kendal AP, Ritter DG. An outbreak of influenza aboard a commercial airliner. Am J Epidemiol 1979;110:1-6
- Miller MA, Valway S, Onorato IM. Tuberculosis risk after exposure on airplanes. Tubercle and Lung Dis 1996;77:414-9.

The WHO review accurately interprets these papers in reaching its conclusions. We have further researched more recent papers dealing with the transmission of infectious diseases and TB in particular.

Review of other papers

Further papers published after 1998 have been studied to ascertain if the view expressed in the WHO review is still appropriate. The papers are listed in Table 9.1.None of these papers indicates that the WHO findings should be changed.

Table 9.1 Key papers on transmission of infection
Gillen PB (1999). Ebola and the filo viruses; reducing the threat by improving Third World medical care and education of aircrew members. Air Medical Journal18:4;156-9. Ormerod P (2000). Tuberculosis and travel. Hospital Medicine, Vol 61, No3. Parmet AJ (1999). Tuberculosis on the flight deck. Aviation, Space, and Environmental Medicine. Vol 70, No 8. United States CDC (2001). Exposure to patients with meningococcal disease onaircraft United States 1999-2000. MMMR, 50(23), 485-9. Wang PD (2000). Two-step tuberculin testing of passengers and crew on a commercial airplane. American Journal of infection Control, Vol 28(3): 233-238.

The case reported by Parmet (1999) concerned an infectious pilot who had flown for six months with a total of 48 other pilots, none of whom had become infected. Ormerod(2000) repeated the analysis of the WHO review and added the observation that most cases of TB were acquired on prolonged visits to regions where it is endemic. Wang(2000) deals mostly with testing methodology, taking it as read that transmission could occur on aircraft, but also other crowded settings such as school buses, ships, bars and hospitals.

The paper on ebola, Gillen (1999), serves to reinforce the potential dangers of transmission of infection by aircraft and the role of health care workers and airline personnel in containing the problem.

NIOSH announced in 1999 a peer review meeting entitled Study protocol peer review meeting: Evaluation of factors affecting disease transmission in commercial aircraft cabins as yet there is no known publication to come from this review meeting.

Issues

There are few papers that relate specifically to the airborne transmission of diseases within the aircraft cabin, other than those dealing with the specific cases of TB. Therefore, this chapter has concentrated on the transmission of TB as this is perceived to be the greatest risk and a model for other infections.

For most diseases, and TB in particular, the perceived risk is most probably far greater than the real risk. This perceived risk has been fuelled by the introduction of recirculated air within the aircraft, giving the impression that airborne infections are distributed throughout the cabin by the ventilation system. The actual arrangement of the ventilation in aircraft cabins is designed with the intention that this will not happen and filtration is put in place to extract any likely pathogen. Consequently, the reality is that the engineering of the ventilation system suggests that there is a reduced risk of transmission by comparison with other means of transport given similar long-term and dense occupancy patterns.

In addition to TB there is a wide range of infectious diseases that may be transmitted as a consequence of the conditions on or surrounding aircraft and air travel. The various diseases have different mechanisms of transmission and this means different approaches to the investigations. Each of these warrants some concern and a possible outbreak of malaria caused by the carriage of mosquitoes is potentially serious as are cholera infections transferred by unhygienic practices both on board and off the aircraft.

Gaps in knowledge indicated by research

In general, the microbiological loading of aircraft cabins has not been widely researched. Only a small number of studies have been carried out and these have adopted a range of methods and procedures. A more clear understanding of the level of infectious agents within cabin air would be useful.

For TB, there are issues that have not yet been addressed by research. For example, the occurrence of *M. tuberculosis* in the air on flights is not clearly known and would provide useful evidence of the ventilation system s capability to remove it from the air. The greatest risk may be under conditions of reduced ventilation, when the aircraft is on the ground or in climb.

The significance of the cabin environment in airborne transmission of infection is unclear. Temperature and humidity may have only a small effect on the viability of airborne pathogens, over the distances involved in person-to-person spread, but their effect on resistance to infection should be explored (see Chapters 6 and 7). The role of poor local ventilation effectiveness, which may increase the risk of transmission local to the infected passenger, should also be investigated.

Research needs

To establish a greater level of knowledge of the microbiological loading of aircraft by a standardised and accepted methodology would be a valuable contribution to the understanding of the potential for infection transmission.

In the case of TB in particular the incidence of the bacterium in the air, furnishings and filters on flights from countries where TB is endemic would provide evidence on the likelihood of infection. For example, the in-service performance of the HEPA filters that extract the *M. tuberculosis* from the recycled air could be confirmed by suitable monitoring and testing. Where *M. tuberculosis* is identified on a flight, passengers on that flight could be followed up to determine whether the illness has spread.

As part of the understanding of the incidence of the bacterium in the aircraft, a study of cabin cleaning procedures and effectiveness would be valuable.

There is a potential benefit for cabin health if there were more knowledge of the role of local and individual ventilation control in avoiding person to person transmission of infection. Similarly, the impact of low ventilation rates while aircraft are on the ground is not fully understood.

The overall risks of acquiring TB on aircraft could be assessed by comparison of aircraft carrying larger or smaller numbers of infected passengers, although the follow-up would be difficult. Follow up of flights known (retrospectively) to have carried a highly infectious person is more realistic but less useful for estimating risk.

In addition to the studies relating solely to the transmission of TB, the effectiveness of disinsection practice, and the interaction between disinsection and air quality, needs to be considered in the context of removing other vectors for other diseases. Toilets and aircraft food should be reviewed separately as possible causes of disease.

10. Cosmic radiation

Introduction

Active interest in the exposure of air travellers to cosmic radiation (CR), or more strictly cosmic galactic radiation, began some 30 years ago. Exposure to CR is not an issue of great concern on the earth s surface because the atmosphere serves as a protective layer, but it may become important when travelling by air, especially at high altitude and/or high latitude. CR is ionising radiation, and it is known from the effects of other sources of ionising radiation to be carcinogenic and teratogenic. Since the crew and passengers in aircraft are exposed to CR in flight the question is naturally asked is there a finite cancer risk.

It is generally considered that the three main types of health risk associated with in-flight exposure to CR are radiation-induced cancers, genetic damage that might be passed on by parents to offspring, and direct radiation damage to the foetus. The two main issues which have developed from this problem up to the present day are (a) accurate measurement of radiation dose and (b) the difficulty in proving the connection with cancer in retrospective studies. It has become more obvious that measurement of the strength and quality of CR is a complex issue in spite of a battery of techniques. The connection with carcinogenesis and teratogenesis is difficult to prove by current methods and epidemiological studies are subject to many confounding factors.

Review of Abstracts

Key papers are listed in Table 10.1.

The literature material consisted of 86 abstracts dated between 1972 and 2001, of which24 were followed up as full papers or reviews. Fifty percent of the documents, including most of the full papers, were dated between 1996 and 2001 with the mode at 1999/2000.The abstracts were classified as research studies (42), reviews (17), case studies (3),guides (8) and general papers including Internet information (16).

All of the abstracts and papers had some connection with health aspects of CR in aircraft. The main thrust of the sub-divisions included: CR measurement (28), aircrew(40), supersonic aircraft (21) and regulations (16).

Most of the key original papers have been found in *Health Physics, Aviation Space and Environmental Medicine and Radiation Protection Dosimetry*.

Table 10.1 Key papers on cosmic radiation
Bagshaw M, Irvine D, Davies DM (1996). Exposure to cosmic radiation of BritishAirways flying crew on ultralonghaul. Occupational Environmental Medicine, 53: 495-498. Band PR, Le ND, Fang R, Deschamps M, Coldman AJ, Gallagher RP, Moody J (1996).Cohort study of Air Canada pilots: mortality, cancer incidence, and leukemia. AmericanJournal of Epidemiology, 143: 137-143. Butler GC, Nicholas J, Lackland DT, Friedberg W (2000). Perspectives of thoseimpacted: airline pilot's perspective. Health Physics, 79: 602-607. Goldhagen P (2000). Overview of aircraft radiation exposure and recent ER-

2measurements. Health Physics, 79: 526-544.

Grayson J K, Lyons T J (1996). Cancer incidence in United States Air Force aircrew,1975-89. Aviation Space and Environmental Medicine, 67: 101-104.

Friedberg W, Copeland K, Duke FE, O'Brien K 3rd, Darden EB Jr (2000). Radiationexposure during air travel: Radiation Protection Dosimetry, 1993, 48: 21-25; HealthPhysics, 79: 591-595; 602-607).

Irvine D, Davies D M (1999). British Airways flightdeck mortality study, 1950-1992.Aviation Space and Environmental Medicine;70(6):548-55.

Nicholas J, Copeland K, Duke F, Friedberg W, O'Brien K, (2000). Galactic cosmicradiation exposure of pregnant aircrew members II. (Aviation Space and Environmental Medicine, 71: 647-648.

Pukkala E, Auvinen A, Wahlberg G (1995). Incidence of cancer among Finnish airlinecabin attendants, 1967-92. Abstracts, British Medical Journal, 1995, 311: 649-652).

Rafnsson V, Tulinius H, Jonasson JG, Hrafnkelsson J (2001). Risk of breast cancer infemale flight attendants: a population-based study. Cancer Causes and Control, 12:95-101.

Romano, E. Ferrucci, L. Nicolai, F. Derme, V. De Stefano, G. F. (1997). Increase ofchromosomal aberrations induced by ionising radiation in peripheral blood lymphocytesof civil aviation pilots and crew members. Mutation Research, 377: 89-93.

Schrewe U.J (2000). Global measurements of the radiation exposure of civil air crewfrom 1997. Radiological Protection Dosimetry, 91: 347-364.

Waters M; Bloom T F; Grajewski B (2000). The NIOSH/FAA working women's healthstudy: Evaluation of the cosmic-radiation exposures of flight attendants. HealthPhysics, 79: 553-559.

Relevant review papers

Measurement

From a number of review papers it is clear that there is no shortage of effort directed at present in North America, Europe and other countries to improve the accuracy of estimating CR doses. Computer programmes (e.g. CARI) have been established and improved, and large-scale in-flight measurements have been made and are under way. There is a general consensus on what constitutes the CR exposure cumulative dose regarded as a risk (e.g. of developing cancer) which is 6 mSv/year (0.3 of the occupational dose limit recommended by the International Commission on Radiological Protection). Concorde is perhaps the commercial aircraft that is most vulnerable to CR,because of the height and latitude at which it flies. Nevertheless, studies on suggest that less than 4% of Concorde cabin crew flying between London and Tokyo could reach or exceed the 6 mSv/year level (Bagshaw et al, 1996).

A seminal paper by Schrew (2000) calibrates CR monitors in-flight against a tissue-equivalent proportional counter, a technique favoured by many similar studies. It is noted that the exposure of aircrew to the increased CR at normal flight altitudes will soon be treated in the EU as an occupational risk and that radiation exposure of aircrew must therefore be determined.

An equivalent paper from the USA by Goldhagen (2000) argues that at present, calculations of CR exposure in aircraft are uncertain because knowledge of important components of the radiation field come primarily from theoretical predictions (e.g. for calculations of dose equivalent rates a ± 20 to 50 % uncertainty).

Cancer

There is also considerable uncertainty about radiation-induced health risks for air crew on whom most of the current attention is focussed. Presumably the thinking is that passengers generally receive far less cumulative exposure and, therefore, if crew are protected then so are passengers. The papers reveal an apparent difference in emphasis between North America and Europe.

In North America, studies from both military and commercial sectors have suggested that aviators may have elevated risks of colon, skin, testis, brain and lymphatic cancers, which possibly arise from exposure to CR. The conclusions reached from a major survey of US Air Force aircrew (1975-1989) indicated a notable excess of testis, bladder and all sites cancers, using an intrinsic control group of non-flying officers for comparison (Grayson and Lyons, 1996). In contrast, a cohort study of Air Canada pilots (1950-1992) found standard incidence ratios significantly increased for prostate cancer and acute myeloid leukaemia but decreased ratios for rectal, lung, bladder and all cause cancers(Band et al, 1996).

The perspective adopted by Friedberg and his associates in giving guidance for the US Federal Aviation Administration is that in the absence of other occupational exposure to ionising radiation, a crew member working 700 block hours / year for 30 years would incur a lifetime risk of developing CR induced fatal cancer of 1 in 190, while in the general population of USA 1 in 4 adults will eventually die of cancer. Although it is conceded that the possibility of harm from exposure to CR in flying cannot be excluded, it would be impossible to establish that an abnormality or disease in a particular individual resulted from such exposures (Friedberg et al, 1993, 2000).

The main review papers and studies from the UK and particularly a large body of work from the Nordic countries on this topic take a more optimistic view, emphasising the confounding factors in linking cancer incidence to CR exposure in aircrew (e.g. Rafnsson et al, 2001). Pukkala et al (1995) conclude from a large study based on most reliable and unbiased retrospective follow-up data that there is no marked cancer risk attributable to CR, and that the highly elevated risk of skin cancer among pilots is probably associated with solar (UV) exposure. From the British Airways Flight Deck Mortality Study 1950-1992, Irvine and Davis (1999) claim that there is no evidence, from epidemiological studies of flight crew, of any increase in the incidence of cancers linked to CR.

Subsidiary papers

A number of related topics were revealed by the literature search, which are, or may become, important for further consideration and research.

Pregnancy

One of the most sensitive issues involving possible CR damage in flying is its effect on human reproduction in genetic damage to (possibly both) parents before conception, damage to the foetus during pregnancy, and to the infant who may be more susceptible to radiation effects. Estimates of CR exposure indicate that frequent air travel mayexpose pregnant flight attendants to ionising radiation that exceeds recommended limits(Waters et al, 2000). In recommending the occupational dose limit of ionising radiation for pregnant women, the assumption made by the International Commission for Radiological Protection was that there is significant shielding of the conceptus, provided by the mother s body. According to the FAA computer programme CARI-LF2, this is incorrect (Nicholas et al, 2000). In European legislation, once pregnancy is declared, therequirement is that the CR exposure is kept as low as is achievable such that the dose to the foetus is unlikely to exceed 1 mSv during the remainder of the pregnancy. The policy of British Airways is to ground flight crew when pregnancy is declared.

Synergism

The issue of synergistic effects of both ionising and non-ionising (magnetic fields) as well as other physical properties of the cabin environment has been raised (Butler et al,2000). Airline pilots are exposed to magnetic fields by the aircraft s electrical system, and it has been suggested that this may increase the risk of CR-induced cancers. There is laboratory evidence of enhanced chromosomal aberrations in human lymphocytes (Romano et al, 1997) when there is exposure to both ionising radiation and 60 Hzmagnetic fields. In other studies there is found a potentiating effect of magnetic fields onionising damage in cultured cells.

Biological markers

In order to develop a better understanding of the potential biological hazards in aircrew exposed to low doses of ionising radiation proposals have been made to investigate biological markers of radiation damage in humans (Butler et al, 2000) by assessing total DNA oxidative damage. Other studies of such markers on aircrew and non-flight personnel claim to be able to show increased chromosomal aberration of a type similar to that in workers exposed to low doses of ionising radiation (Romano et al, 1997). DNA damage is apparently greater with acute rather than chronic CR exposure and repair greater in chronic exposure. This suggests that DNA damage may be subject to biological adaptation.

Issues

Physical dosimetry of CR is not yet on solid ground and may result in large errors in the estimation of dose. Keeping track of CR exposure should be possible by self monitoring, aircraft monitors (perhaps including a monitor alarm for worst-case solar particle events),and ground-based computer monitors.

There remain a number of major concerns:

- the need for a monitoring campaign;
- the desirability of providing more information on board aircraft;
- solar flares and related high levels of exposure;
- pregnancy -related issues;
- causes of cancer;
- social (passenger) protection.

Can CR exposure be controlled? CR shielding is not an option in aircraft and neither aircrew nor passengers can easily reduce flying hours or transfer to low altitude or low latitude flights. Neither can airlines or pilots easily co-ordinate flights with solar activity. Hence, any serious risk management strategy is likely to have a high cost. As a consequence, very strong epidemiological evidence is likely to be needed before significant new action is taken.

Epidemiological studies on aircrew have suffered from a low statistical power with confounding factors of other noxious agents and lifestyle. The considerable funds often spent on epidemiological studies are sometimes regarded as questionable, but it may be that more money must be spent on a major project, so that definitive data can be generated.

Gaps in knowledge indicated by research

The biological incidence of highest energy particles and heavy ions is not well documented. There is still no single device that is capable of measuring the whole range of particle type.

DNA damage is apparently greater with acute rather than chronic CR exposure and this requires further investigation with regard to use of biological markers and exploration of possible adaptive responses.

More information is required on limits of exposure for passengers. Special groups include pregnant women, frequent fliers and private jet pilots and their passengers.

There is a need to discriminate the cause of cases of cancer that are suspected of arising from CR exposure. In particular, there needs to be good control of the possibility that skin cancers have been caused by UV exposure rather than CR.

Research needs

The present aim should be to try to reduce the uncertainties about CR exposure risks. Judgement about the possible risks from CR for flying personnel as far as higher incidences of malignant skin tumours has yet to be made.

Attention should be paid to special groups who may be at greater risk than healthy aircrew, e.g. infants, children and the elderly.

There should be further monitoring of exposures involving the use of biological markers.

Though the incidence of all cancers among pilots does not deviate noticeably from the general population according to present knowledge, the case for excess skin cancers is still open for discussion. The carcinogenic potential for radiation risks is still focussed on the fundamental problems of threshold and small radiation doses.

11. Jet lag

Introduction

Unlike the other topics reviewed in this report, the issue with jet lag is not whether air travel causes it or how likely it is to occur. In the technical literature, as among travellers, it is taken as read that jet lag is a normal consequence of transmeridian flight. Although the effects of jet lag are widely thought of as minor and transitory, the number of people adversely affected is much greater than for the other issues dealt with in this report. Hence, at population level, its overall impact may be greater.

The questions of concern are as follows.

- Effects: are there consequences of jet lag that present an unacceptable risk, either in the population in general or in specific groups of people?
- Causes: are there aspects of air travel that avoidably exacerbate jet lag?
- Management: how can travellers reduce the severity or the consequences of jet lag (without adverse side effects)?

The search on jet lag and work patterns identified papers almost exclusively on jet lag. Of the 360 abstracts that were identified in the search, the issues covered were as follows.

- Effects of jet lag 83 (23%)
- Causes 63 (18%)
- Management 180 (50%)
- Research methods 31 (9%)
- General description of jet lag/shift work 44 (12%)
- General aviation medicine, including jet lag 21 (6%)

The figures do not add up to 100% because some papers fall into more than one category.

Abstracts Analysis

The types of papers break down as follows.

Study	146
Review	108
Guide	9
Letter	15
Not clear/opinion	82

Most of the Not clear/opinion papers were in the style of review papers but the scale or originality of the work was not clear from the abstract. Hence, original studies are clearly outnumbered by reviews, opinions, letters and guides; this reflects the relative lack of good original research that underpins the mass of comment on the subject.

Key papers

There has been such a diversity of opinion that a number of reviews need to be consulted in order to get a balanced picture. The following are probably among the most significant reviews.

Table 11.1 Key papers on jet lag
Arendt J, Deacon S (1997). Treatment of circadian rhythm disorders--melatonin. Chronobiol Int Mar;14(2):185-204.
Arendt J, Skene DJ, Middleton B, Lockley SW, Deacon S (1997). Efficacy of melatonin treatment in jet lag, shift work, and blindness. J Biol Rhythms Dec;12(6):604-17.
Avery D, Lenz M, Landis C (1998). Guidelines for prescribing melatonin. Ann Med1998 Feb;30(1):122-30.
Copinschi G, Spiegel K, Leproult R, Van Cauter E (2000). Pathophysiology of human circadian rhythms. Novartis Found Symp 2000;227:143-57; discussion 157-62.
Price WJ, Holley DC (1990). Shiftwork and safety in aviation. Occup Med 1990 Apr-Jun;5(2):343-77.
Redfern P, Minors D, Waterhouse J (1994). Circadian rhythms, jet lag, and chronobiotics: an overview. Chronobiol Int Aug;11(4):253-65.
Samel A, Wegmann HM, Vejvoda M (1995). Jet lag and sleepiness in aircrew. Journal of Sleep Research 4 (SUPPL. 2):p30-36.
Samel A, Wegmann HM (1997). Bright light: a countermeasure for jet lag? Chronobiol Int Mar;14(2):173-83.
Samel A (1999). Melatonin and jet-lag. Eur J Med Res 1999 Sep 9;4(9):385-8.
Wagner DR (1996). Disorders of the circadian sleep-wake cycle. Neurol ClinAug;14(3):651-70.
Youngstedt SD, O'Connor PJ (1999). The influence of air travel on athletic performance. Sports Medicine (SPORTS MED.) (New Zealand) 1999, 28/3 (197-207).

Issues

Effects

Papers on the effects of jet lag can be divided into those that deal with the consequences in general and those that focus on a particular group of people. A further distinction can be drawn between the direct effect of jet lag on people and the possible consequences of jet lag for vulnerability to other hazards, either during the flight or after disembarking.

The primary consequences of jet lag include, by definition, desynchronisation of circadian rhythms from the local day/night hours and, consequently, difficulties in getting to sleep and/or remaining asleep or awake at times consistent with local norms. The time course of desynchronisation and resynchronisation has been reasonably well studied and modelled but is not entirely predictable. Resynchronisation can take up to 10 days. Other direct effects have been listed as:

- fatigue;
- reduced alertness/concentration;
- impairment of mental performance, including memory;
- reduced motivation;
- irritability;
- nausea/digestive problems.

Findings on mental performance have not been entirely consistent and it is not clear why results vary from study to study, for example whether it is related to the motivation of the subjects or to some other confounders in the study design.

There have also been suggestions that jet lag directly causes stress/anxiety, largely based on cortisol measurements. The research to date does not seem adequate to exclude the possibility that stress is due to other flight-related factors, or to difficulties in functioning with impaired mental performance.

In addition to these effects, a number of physiological indices have been used to track changes in circadian rhythm, e.g. heart rate, hormone levels, body temperature. The indices themselves are not necessarily indicative of adverse health effects.

Not surprisingly, of those papers that focus on a particular group of people, the most common target is aircraft crews (both flight crew and cabin crew), including some work on military crews that is potentially of relevance to civil aviation. In this context, it seems to be implicit that crews suffering from jet lag (or fatigue for any other reason) is a health and safety issue on the aircraft. One paper (in 1996) concluded that EU flight-duty and rest times for pilots need to be reviewed since subjective and objective fatigue measures suggest risks under current rules. However, overall there is not definitive evidence of the magnitude of the accident risk due to jet lag, either for air accidents, accidents on board or accidents after disembarking.

The only other professional group that appears to have been studied is sportsmen/women. Hence, one industry has shown significant concern over the impact that jet lag could have on performance following the flight. Perhaps ironically, the evidence is not convincing that sports performance is affected, so long as motivation is intact. The risks for other groups do not appear to have been specifically researched, whether the risks be to health, safety (e.g. when driving or operating equipment) or work performance (e.g. making important decisions while mentally below par).

While the consequences to individuals are usually minor, they are not desirable, as evidenced by the body of work on management of jet lag. At population level, the consequences may be significant in terms of the costs of accidents (e.g. when driving or operating machinery), medical treatment, impaired performance at work and days of work missed.

Causes

The factors that exacerbate jet lag can be categorised as either inherent to the individual person, related to environment or behaviour, or due to the characteristics of the flight.

Groups identified as possibly at greater risk are:

- the elderly;
- people suffering from other conditions that involve disruption of melatonin metabolism and/or circadian rhythms (i.e. mania, anorexia/starvation, chronic fatigue syndrome, or depression, especially seasonal affective disorder);
- people suffering from psychiatric disorders generally;
- those suffering from other pre-existing illness;
- introverts (morning types).

A number of interactions have been identified, whereby jet lag may increase the risks from other causes, or other factors might exacerbate jet lag. In each case, the evidence comes from only one study but the following could be of interest when considering further research:

- transmeridian flight causes changes in lymphocytes and related cells (could affect susceptibility to infection but both positive and negative changes were observed);
- measures of risk for DVT were affected by circadian rhythm;
- interaction between jet lag and temperature/humidity (possibly confounded by the use of melatonin to manage jet lag, since another paper suggests that melatonin acts by suppressing core body temperature);
- interaction with exposure to elevated carbon dioxide concentration (paper in Russian,English abstract unclear about the nature of the effects);
- an interaction between circadian rhythms and radiation (again, a Russian paper with an unclear English abstract the radiation referred to could be visible light or cosmicradiation);
- shifting the circadian rhythm increased alcohol consumption by rats (while this is some way from a valid conclusion about humans, anything that increased the tendency to drink during or after flights would have the potential to interact with other risks).

Also, consumption of alcohol can exacerbate jet lag.

Flight characteristics that increase jet lag are:

- number of time zones crossed;
- eastbound travel, i.e. a shortening of the day (the human diurnal cycle tends to belonger than 24 hours in the absence of day/night cues).

Management

The strategies offered for reducing the impact of jet lag can be broadly classified as:

- schedule management (e.g. adapting activities to the time zone rather than the circadian rhythm, or taking planned naps);
- specific activities (e.g. eating, exercising, social activities);
- light exposure (either natural light or controlled exposure to bright light);

- pharmacological treatment, including melatonin (and melatonin agonists),benzodiazapines, other tranquillisers/hypnotics, stimulants (primarily caffeine),biochemical precursors (e.g. tyrosine, glycine, l-tryptophan), antihistamines, antidepressants, antipsychotic drugs, and herbal treatments (e.g. valerian).

A particularly large body of research has been conducted on the efficacy of melatonin in overcoming jet lag (out of 180 abstracts that dealt with management of jet lag, 99mentioned melatonin). The issue of melatonin treatment might be judged to underlie the explosion of research on jet lag (see Figure 11.1). In the mid-1990s it was hailed as a wonder drug, not just for jet lag but as a treatment for cancer and to ameliorate the effects of ageing.

Figure 11.1 Growth of research on jet lag since 1965*

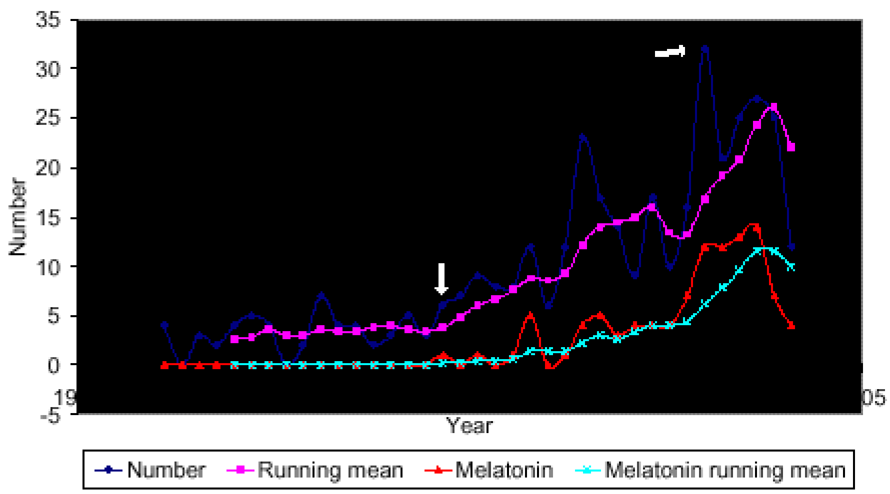

*Figure for 2001 is estimated. Running mean is the mean annual number for five years up to and including the index year.

The balance of current thinking seems to be that melatonin is not recommended except under medical supervision. While it is generally accepted that melatonin can alleviate jetlag, there is uncertainly over the mechanism of the effect, required formulation and dosage, long-term side effects and contra-indications (including possible interactions with other drugs).

Conclusions on the usefulness of the various approaches have varied widely between authors, from those who extol the virtues of a particular approach to those who conclude that it is ineffective or even dangerous. It is not the task of this review to recommend a cure for jet lag but some general observations are pertinent:

- there is not universal agreement as to the best treatment, hence a weak basis for making confident and consistent recommendations to travellers;

- there is a market for a cure, much as there is for the common cold, both conditions being widespread, accepted as almost inevitable yet widely resented as an inconvenience;

- no research has thoroughly addressed the range of management approaches under well-controlled conditions, to find the best combination for particular circumstances.

Gaps in knowledge

Much of the work on the effect of jet lag has focused on detailed physiological mechanisms and performance on tasks outside of a real world context. This research is far from comprehensive or definitive but, more importantly, there is a lack of understanding of important effects at the policy-relevant level: the health, safety and work performance of passengers and crew.

The factors that exacerbate, alleviate or interact with jet lag are poorly understood, undermining the authority of guidance.

The best means of direct management of jet lag is also debated, with a wide range of opinions. This is particularly of concern in light of anticipated ultra-long-haul operation patterns.

Research needs

The short-term and long-term health and safety implications of jet lag need to be established, for the population in general and for susceptible groups.

The short-term and long-term economic implications of jet lag need to be established, so that working people and their employers have a better basis for policy concerning air travel.

Depending on conclusions on the seriousness of the consequences of jet lag, there maybe a case for publicly funded work on management of jet lag. There is probably already sufficient justification of privately funded research for those who offer treatments for sale, but this must be handled in such a way as to avoid doubts over bias in the work.

12. Conclusion and recommendations

Introduction

In this chapter, we draw together the conclusions, first concerning the current state of knowledge and then on needs for further research. Population groups at particular risk are also identified, other than the obvious groups of crews and frequent fliers. Much of this section repeats what has gone earlier in the report, but restructured to focus on the different types of research. Consequently, it place greater emphasis on the inherently stronger types of research.

This review has investigated the current state of knowledge, and needs for further research, on each of the five issues identified in the client s specification. The field of aircraft cabin health is extremely topical and more than a little controversial and fuelled by press speculation. This review is considered to be the most comprehensive and balanced possible at this time, in what is a very highly charged and fast moving research area.

We conducted an extensive search of medical and engineering databases, the Internet, and current research activities, identifying some 2800 relevant abstracts. We then reviewed the relevant material that was identified in the search. Together with the advice of experts in the field of aviation medicine, this review has been used to prepare guidance for the Department as to those areas of aircraft cabin health that most require further research.

Each section follows the order of topics from the preceding chapters, i.e.:

- DVT
- CAQ: pressure and oxygen
- CAQ: temperature
- CAQ: relative humidity
- CAQ: pollutants
- transmission of infection
- cosmic radiation
- jet lag and work patterns.

It must be borne in mind that many of the causal factors that are relevant to these issues interact. This may be as significant as any of the individual risk factors and is therefore given due attention at the end of this chapter.

Deep vein thrombosis

Summary of evidence

Plausible mechanism

Working from first principles on DVT, there are plausible mechanisms whereby the aircraft cabin environment could increase the risk of DVT, some more definitely established than others. The three fundamental predisposing factors for DVT are slowing of blood flow, increased blood coagulability and damage to or abnormality of the blood vessel wall. These factors can, in turn, be related to characteristics of the cabin environment, as follows.

Maintaining an immobile seated posture will affect all three fundamental predisposing factors and there is evidence from other environments that it does in fact increase the risk of DVT. This, it itself, is no different from any other situation in which people sit for long periods.

Most authors assume that dehydration will occur on an aircraft, but the evidence is contradictory (see summary of Humidity, below) as to whether the rate of water loss would be sufficient to be of concern in relation to DVT. There are also uncertainties over the effects of a low-humidity environment on water distribution in the body, as distinct from overall water loss. Most authors assume that, if dehydration does occur, it will increase the risk of thrombosis. While this is logical (since it should affect the clotting tendency of the blood), the evidence is lacking and there is even some indirect evidence that dehydration may be protective against DVT.

The balance of evidence is that exercise of the foot or leg will, by increasing venous flow rates, reduce oedema formation in the leg. However, this has not been empirically associated with DVT risk. Also, the type or continuity of the exercise may be critical since there is evidence that, between exercises, the leg undergoes a continuous swelling process, which is only interrupted by the exercises. If this is the case, the relatively frequent exercise while seated might be more beneficial than occasional walks round the cabin.

Two types of hypoxia may be relevant global due to decreased partial pressure of oxygen in the cabin air and local in the leg due to decreased blood flow. Local hypoxiahas the potential to damage to venous valve linings and thus increase the risk of thrombosis, but this has been demonstrated only in dogs and rabbits. However, any local hypoxia due to venous stasis would be worsened by any degree of global hypoxia. Hypoxia also causes vasodilation and increased capillary permeability, which would tend to worsen oedema.

Reduced barometric pressure may increase blood coagulability and thus the risk of DVT but the evidence is weak at present, being based on uncontrolled experimentation or generalisation from high altitude flights and decompression following sea diving. The one controlled experiment found no effect on oedema formation at reduced barometric pressure.

Case reports and case series

Many cases have been reported - at least 312. These provide circumstantial evidence of an association between air travel and DVT and, without such evidence, any hypothesis of a causal link between air travel and DVT would be suspect. However, is impossible to quantify risk from these studies without knowing the likelihood of air travel in the rest of the population from which the cases are drawn. If long-distance/air travel is reasonably common in the population, there is a chance that anyone (including DVT/PTE patients) will have recently undertaken a journey within the last month or so.

The proportion of those with DVT who had recently travelled by air varies greatly in these studies from 1.6% to 50%. Part of the variation can be explained by different definitions of what constitutes long-distance travel and how recent it was. Another reason could be differences in the way medical records information is analysed.

While studies of this type can never provide strong evidence of a causal relationship, they do help to characterise the risk in a way that informs the design of other studies. Three important considerations are:

- the normal time course of DVT development is days, rather than hours to become symptomatic;
- hence, multiple air trips may have a cumulative effect, which may persist for days or weeks;
- the presence of a DVT may go undetected until a sudden movement causes anembolus to break off.

Case-control studies

Of three case-control studies, two found a positive association of all long-distance travel with DVT/PTE but have the possibility of recall and referral bias. The third study avoided referral bias but did not find an association. Taken together, we would concur with the conclusion of the HSE (2001): 'Overall the epidemiology is probably able to exclude the possibility that travel is an independent and extremely strong risk factor for clinically significant DVT, although unable to provide a more precise consideration of risk, if any.'

To put this another way, most of the risk arises from non-travel factors. While case-control studies permit estimation of relative risks, this is only one type of risk that is important. At population level, a low relative risk can be significant if a large number of people are exposed and/or the baseline risk is high. No doubt the individual passenger will be interested in his/her own absolute risk.

Longitudinal/intervention studies

This type of study offers the opportunity to obtain the strongest evidence but only one such study has been carried out to date. This prospective study found an apparent 10%risk of symptom less DVT in passengers not wearing compression stockings, compared with no risk for passengers wearing the stockings. This study has been criticised on a range of methodological grounds, and it is not a basis for firm conclusions at present. However, it does indicate an approach that could usefully be developed further.

Groups at risk

Individual risk factors for DVT are well documented and include age (over 40), obesity, chronic heart disease, cancer, chronic renal failure, smoking, pregnancy, hormonal medication, previous DVT and recent trauma or surgery.

Research needs

The driving force for work on DVT is a high level of risk, as perceived by the public and fuelled by press reports. While the best epidemiological evidence is of a low risk, the strength of evidence is insufficient to be a basis either for reassuring travellers or for requiring the air travel industry to take specific actions. Hence, the fundamental requirement is for improved case-control studies that are adequately powered and methodologically rigorous. Such work should follow agreement between key parties as to what would constitute an acceptable control group.

There should be further prospective studies. For ethical and practical reasons, it is likely that these studies would need to be based on unsymptomatic DVT. They should be rigorously designed and methodologically independent of any parties that might benefit financially from the demonstrations of risk reduction from particular interventions. Interventions other than stockings should be considered, and more needs to be understood about how the presumed precursors of DVT actually progress.

Further case reports and case series of consecutive patients diagnosed with DVT(looking for a history of recent travel) are unlikely to add much to the debate, except perhaps in clarifying the estimates of the incidence of recent travel in DVT patients, as this has varied widely in the case series to date. However, with modest extra effort, case reports can be generated from case-control studies.

There is also a place for further case reports of thromboses at other locations (e.g. cerebral and arterial thromboses) in association with air travel. These are much rarer than DVT/PTE and were out with the scope of this review. They provide circumstantial evidence of a generalised 'thrombotic tendency' in association with the aircraft environment rather than necessarily a connection to the seated posture, immobility etc.

Research as recommended above would serve to estimate risk, but would be of limited use in recommending approaches to risk management, should the risks indicate such action. Adequate biomedical research is particularly important when it comes to giving advice to passengers on DVT prevention. Any suggested measures should be backed up by experimental evidence rather than based purely on 'common sense'. This research will need to take into account possible conflicts in recommendations. For example, exercise may reduce the risk of DVT but could increase the degree of hypoxia.

Biomedical studies mimicking the aircraft cabin environment should have adequate controls to separate out the possible effects of decreased cabin pressure, low PO_2, the stress of being in an enclosed environment etc. There would be some merit, in such studies, of measuring markers of clotting activation as a surrogate for DVT formation.

Cabin air quality: hypoxia and cabin pressure

Summary of evidence

Plausible mechanism

The potential effects of low cabin pressure are well recognised, which is why virtually all commercial aircraft cabins are pressurised.

The issue is, therefore, whether there are risks up to the widely accepted minimum cabin pressure, equivalent to a maximum cabin altitude of 8000 feet (2440 m). Based on evidence from research on the ground, it is plausible that some people will experience mild hypoxia at lower altitudes, the symptoms of which include impaired mental performance, reduced exercise capacity, fatigue. Some individuals suffer mild hyperventilation, headache, insomnia or digestive dysfunction. The effects are not great, and would not necessarily be of significance in most cases, although accident risk could increase. The risk would also depend on the duration of the flight.

It can also be speculated that fatigue resulting from hypoxia would discourage exercise and, therefore, increase the risk of DVT. Conversely, exercising to avoid DVT might increase the risk or effects of hypoxia.

Mild levels hypoxia may be accentuated by travellers drinking alcohol or smoking cigarettes. This can lead to erratic behaviour and loss of impulse control. It may be speculated that the current phenomenon of air-rage is related to this effect.

The reduction of applied external pressure also leads to the air trapped in the body cavities to expand (by 38% at 8000 ft cabin altitude). The cavities of concern are the ears, sinuses, stomach, intestines and lungs (and, for some people, teeth and eyes).This gas expansion can cause discomfort for the occupant (for example, ears popping)but in some susceptible cases it can also present a health risk.

Not only is the absolute pressure important but also the rate of change of pressure, particularly for the ears, which can be damaged by rapid changes. In practice, the rate of change in passenger aircraft should not be a problem for most people. Susceptible individuals may experience discomfort on descent and need to clear their ears. There are some indications of a trend towards faster ascent/descent in newer aircraft, so that more time is spent a cruising altitude. The effects of any such trend should be monitored.

The body s response to hypoxia is to increase the rate and depth of breathing: this maybe hindered in aircraft passengers by drowsiness, immobility, cramped seating conditions and gastrointestinal distension due to the decreased cabin pressure.

Case reports and case series

A number of studies have shown moderately reduced levels of arterial oxygen saturation under normal flight conditions, with large inter-individual differences. While these studies would create an expectation that some people would experience mild hypoxia during flights, some authors have concluded that short term exposure to cabin altitudes is well tolerated by travellers, even by those with COPD.

There have been no case-control studies or longitudinal/intervention studies.

Groups at risk

The maximum cabin altitude standard has been developed from the tests of hypoxia on healthy young males. This is obviously not a representative sample of the current travelling population and risks are expected to be greater for:

- the elderly;
- those suffering COPD, cystic fibrosis or other cardiopulmonary conditions;
- people who are fasting or otherwise deprived of food;
- anyone who has recently spent time diving to depth under water.

The relative risks for these groups have not been quantified, although there is guidance on which groups should be provided with supplementary oxygen during flights.

An upper respiratory tract infection makes it more difficult for the sufferer to equalise pressures and is therefore increases the risk of discomfort or damage to the ears. Babies and young children are not always able to equalise ear pressure efficiently. Anyone close to cardiac failure could also be at greater risk from gas expansion.

Research needs

Current practice in relation to hypoxia is based on experimental studies of a single population group and a confidence that has developed in the industry on the basis that there have apparently been no serious consequences of current operating procedures(or none that cannot be handled by the availability of supplementary oxygen).

While this may be a sufficient indicator that the population risk is low, there is insufficient knowledge of the extent to which oxygen desaturation is likely to be a problem among all groups of the travelling public. The current trend in aircraft operation is to fly at higher cabin altitudes (lower cabin pressure) and it is therefore urgent that such information be obtained. This could be achieved by an investigation into the in-flight oxygen saturation of a wide range of crew members and passengers, including those with risk factors such as COPD and cystic fibrosis. Non-invasive oximetry techniques could be used for this, allowing for the measurement error on individual measurements.

As part of the same study, it would be informative to monitor pressures and rates of change on commercial flights, particularly on descent from cruise to approach. This information would normally be available routinely from the aircraft instruments.

Interaction with DVT and exercise should be considered in any research on hypoxia.

The changes of pressure in the cabin as the flight progresses can be a problem for individuals at risk (e.g. owing to upper respiratory tract infections). It should be possible to examine any risks due to gas expansion from in-flight medical reports.

Cabin air quality: temperature

Summary of evidence

Plausible mechanism

Based on the literature concerning other environments, the initial indication is that, since extremes of temperature are highly unusual in normal aircraft cabin conditions, temperature in aircraft is a comfort issue rather than a health issue. The limited evidence from in-flight monitoring is that temperatures tend to be a little higher than the norm in climate-controlled buildings, but that this is compensated by reduced humidity and expectations of lower levels of activity and clothing insulation. Given the large number of people in close proximity, each with different requirements and behaviour, it is inherently unlikely that all would be satisfied with the temperature.

However, the distinction between health and comfort is not always clear, and temperatures in the normal range can have an indirect effect on other health and air quality issues:

- temperature will affect the rate of dehydration of passengers and crew;
- in buildings, both high temperatures (within the comfort range) and low relative humidity have independently been associated with increased risk of sick building syndrome (SBS) - acute non-specific symptoms such as fatigue, headache and irritation of the skin and mucous membranes;
- effects on fatigue or alertness could also have implications for safety, on board or after disembarking;
- perceived air pollution is greater as the temperature increases (and also as humidity increases, the key factor possibly being enthalpy);
- temperature affects the generation of body odour and the rate of emission of VOCs from cabin materials, thereby affecting the pollutant concentration in the cabin air.

There are some issues of temperature that are more specific to the aircraft environment. One is the possible occurrence of steep temperature gradients throughout the cabin, and another is the sharp change in temperature that sometimes occurs between the aircraft cabin and the outside ambient air, when boarding or disembarking. There is also a suggestion that air velocities can occur in aircraft cabins than are greater than those normally encountered in buildings.

In principle, there could be other interactions involving temperature but these are poorly understood:

- the risk of DVT could be affected by cabin temperature, not so much because of its direct affect on the body but because people tend to be less active at higher temperatures;
- the combination of temperature and humidity could affect the viability of airborne pathogens and/or the ability of the body to resist infection;
- high temperature and jet lag could combine in causing some symptoms, such as fatigue and headache.

Case reports and case series

The very limited literature reveals complaints about the temperature, mainly that it is too high or too variable.

There have been no case-control studies or longitudinal/intervention studies.

Groups at risk

In general, the elderly and infants are most susceptible to temperature extremes but there is little evidence of this being a particular issue in aircraft.

Research needs

The available literature indicates a number of potential problems with temperatures on aircraft being too high and/or too variable. The evidence on actual problems is almost non-existent. Effects of temperature can easily be misattributed to other factors, especially air pollution. Thus, effort could be misdirected at other factors, missing out the relatively simple approach of reducing the temperature.

Temperature should be measured and/or controlled whenever possible in studies of other air quality parameters, acute non-specific symptoms, DVT, infection, jet lag and accident risk.

It is entirely plausible that such studies would support the desirability of operating aircraft at lower temperatures. It is therefore important to obtain a clearer understanding of the dynamics of thermal comfort on aircraft, and how it can be achieved by the majority of cabin occupants. This should involve questionnaire data in addition to in-flight measurement of air, radiant, surface and operative temperatures over time at different locations and heights, measurement of air velocities, and investigation of temperature non-uniformity. Prediction from buildings and climate chambers is not acceptable.

The effect of temperature on emission of VOCs from cabin materials is not the subject of much work, but as the principles are reasonably well established in buildings, there is no particular need for fundamental work to be repeated in aircraft. Specific products could be tested for their suitability for use in aircraft.

Cabin air quality: humidity

Summary of evidence

Plausible mechanism

Unlike temperature, the levels of relative humidity (RH) that occur on aircraft are not typical of other indoor environments in most countries. Although the cabin RH can be quite high while the aircraft is on ground, once at cruise altitude it is generally between5% and 15%: much lower than in most buildings, and much lower than recommended by most standards and guidelines (20-40%). However, guideline limits are set in buildings in the context that it is normally relatively straightforward to achieve 30% RH. Also, perceived humidity is dependent on temperature and air pollutants, and maintaining higher RH in buildings would possibly partly compensate for overheating and air pollution at ground level.

Low humidity can have direct effects on health and comfort (with secondary implications for safety), the range of effects depending on the humidity, the duration of exposure and other factors (e.g. temperature, water ingestion, wearing contact lenses, use of moisturiser). The main potential problems are:

- drying of the body surface (mucous membranes and skin);
- dehydration;
- perception of poor air quality at high RH;
- effects on thermal comfort (feeling cooler at lower RH, especially at higher temperatures).

In addition, humidity has many indirect effects, relating to several other factors that are addressed in this report:

- dehydration is a possible factor in DVT and jet lag;
- RH (in combination with temperature) affects the generation of body odour and emissions from materials;
- at altitude, humidification may cause condensation on surfaces, with associated risks of microbial growth;
- humidity affects the viability of some pathogens in the air, some being favoured by low RH and some by high RH;
- the effectiveness of the mucous membranes in defending against infection could also be compromised by low humidity.

Another potential problem in low RH environments is static electric shock.

Some of the factors affected by RH would be improved at higher RH, and others are improved at lower RH but the principal concern is low RH. While air humidification maybe a solution, consideration also needs to be given to the possible problems of microbial growth in air-conditioning units, condensation problems and corrosion. The relative merits of increasing the moisture content of the air and reducing the temperature also need to be considered.

Case reports and case series

Much of the literature concerning RH on aircraft focuses on ocular discomfort and dryness of airways. While findings generally go with the expectation of symptoms related to dryness, there is no true demonstration of causation or quantification of the risks, either of low humidity or of having humidifiers.

Most authors assume that dehydration will occur on an aircraft but the evidence is contradictory. The basic physiological evidence is that the rate of water loss would be too low to be of great concern. However, some studies show evidence of dehydration during flights. The degree of dehydration that occurs during air travel is therefore uncertain. This may be because of differences between real world and theoretical or laboratory settings. For example, passengers might experience a sensation of thirst or dry mouth because of superficial drying of the body surface. They might respond to this by drinking alcoholic or caffeine-containing drinks, which have a diuretic effect.

There have been no case-control studies or longitudinal/intervention studies.

Groups at risk

Other than groups at risk from secondary effects (as noted in other chapters), the principal risk groups are contact lens wearers and people with medical conditions leading to dry or irritated skin or mucous membranes.

Research needs

RH is an important cross-cutting issue, affecting many other aspects of health on aircraft. Without a proper understanding of the effects of low humidity, other areas of work will not be fully informed. Although there is a large literature on RH in buildings, the accumulated knowledge cannot be directly applied to aircraft.

While there are several potential health problems with low humidity in aircraft, there is little evidence on the actual situation. Neither is it clear to what extent passengers can self-manage their health, for example through water intake, use of moisturisers or taking out contact lenses.

There is a need for research to bridge the gap between the measured RH levels on aircraft, and the established knowledge of RH in buildings and other environments. The needs are to establish typical cabin conditions, investigate the effects of these conditions (singly and in combination), and investigate solutions and improvements. The following work is therefore recommended:

- in-depth analysis of literature on direct and indirect health effects of very low RH levels in indoor environments;
- study of the effect of altitude (and therefore reduced air pressure) on recommended levels of RH;
- work, with robust methodology, to measure RH on aircraft, and to investigate physical, chemical, biological and physiological effects of lower RH, in controlled /simulated cabin environment;
- study of air humidification at very low RH in aircraft.

Cabin air quality: air pollutants

Summary of evidence

Plausible mechanism

By definition, air pollutants can be harmful, but the risk is in the dose, which depends on the concentration in the air and the duration of exposure. Many pollutants are liable to be present in aircraft cabins, and have well-documented health effects at elevated concentrations.

Carbon dioxide (CO_2) is a useful indicator for ventilation rate in a space occupied by a constant number of people, and concentrations in aircraft cabins have been measured often. Most studies show that, although concentrations often exceed the 1000 ppm level recommended for comfort (odour control) in buildings, the levels were always within health recommendations, and would not be expected to have significant adverse effects on health (except possibly in combination with other cabin conditions). The highest concentrations of CO_2 generally occur while power to the ventilation system is reduced ,for example while the aircraft is on the ground, during take-off and during landing. Sublimation of dry ice (used for chilling food) can cause transient high levels.

There have been many studies of other air pollutants on aircraft, but many of them describe fairly ad-hoc measurements. There are relatively few significant studies with comprehensive and robust measurement methodologies. Where measurements of pollutants have been made, concentrations have been generally well within recommended guidelines on non-smoking flights. This applies to:

- carbon monoxide (CO), on non-smoking flights;
- ozone (O_3), where catalytic deozonisers are fitted;
- respirable particles, on non-smoking flights and especially where HEPA (high efficiency particulate air) filters are used;
- bacteria and fungi, especially where HEPA filters are used;
- organic compounds (although there is a need for further measurements of semi-volatile organic compounds).

While there are provisos to most of these statements, the norm is now for flights to be non-smoking (hence tobacco smoke is not included in this review), and for aircraft to befitted with ozone catalysts and HEPA filters. Clearly, maintaining good air quality will depend on the available equipment being maintained in good condition.

Within the cabin, the low humidity during flight would mitigate against colonisation by the fungi and mites that are common sources of allergens in buildings. However, allergens (especially cat allergen, Fel d1) have a tendency to adhere to clothing and would collect on aircraft seats if they are not adequately cleaned.

Two types of organic compound have attracted particular concern, and require special comment: insecticides and organophosphates.

Disinsection is used on some routes to minimise the risk of insects carrying diseases (such as malaria and dengue fever) being carried on the flight. Depending on the procedure used, disinsection is sometimes carried out with passengers on board, and sometimes with crew only on board. The pesticides generally used have not been shown to have adverse human effects, but the long-term health effects of repeated exposure to possibly fairly high levels of the pesticides needs to be evaluated.

Organophosphates (OPs) are present in minute quantities in some aviation jet fuels and hydraulic fluids. These are chemicals of high toxicity, capable of producing serious adverse neurological and other effects. In normal cabin conditions, exposure to these chemicals is minimal. However, there is some concern that low concentrations entering the cockpit and cabin due to oil or lubricant leaks could cause both short-term and long-term health risks. There is strong concern about this issue, but little substantial evidence to support the perceived risk.

Case reports and case series

There are occasional case reports, in medical records or the media, of specific incidents of problems caused by poor air quality. These are generally poorly documented and based on supposition rather than evidence.

There have been no case-control studies or longitudinal/intervention studies.

Groups at risk

While there is little evidence of any risk, it is difficult to define risk groups. However, the potential risk groups are asthmatics, people with allergic conditions and those who are hypersensitive to chemicals or have cardiopulmonary illness.

Research needs

The overriding research need is to benchmark the air quality in current aircraft. This should involve a comprehensive set of measurements, using agreed methodologies, made on a sufficiently large number of flights to be typical, if not fully representative. Such measurements are important because much can be deduced from information on dose, without the added difficulty of making health assessments in flight. These measurements would obviously need to include parameters other than air pollutants as well. This should be done alongside crew and passenger questionnaires, and even physiological tests.

The conclusion from the few measurements that have been made would be that there should not be problems health problems from pollutants on aircraft. However, passengers and crew still report adverse health effects that they attribute to air quality. Therefore, having characterised as far as possible the normal level of CAQ, the next research need is to investigate the physiological and subjective responses of people in simulated cabin conditions to combinations of environmental, chemical and physical parameters.

There is a lack of strong evidence behind two contentious issues exposure to OPs in cabin air, and the additivity or otherwise of effects of multiple chemical exposure. These areas should be investigated further, keeping in mind the need to consider interactions with other cabin conditions. Part of the problem is that investigations into suspected incidents are, by their nature, retrospective, which means there is little evidence about the composition of the air when the problem occurred. It would be advantageous to have a portable kit that the crew could use to sample the air when fuel or other odours are noticed.

Passengers often express a preference for adjustable air supply nozzles (gaspers).The pros and cons of these should be clarified, in relation to air supply to the individual passenger, drying of the body surface, air distribution in the cabin and movement of pathogens.

Most studies have been concerned with aircraft in flight but the greater problem might be with aircraft on the ground, hence there is a need for monitoring of pollutant concentrations during taxiing, take-off, climb and landing.

There is little information on the levels of insecticides in aircraft cabins following disinsection, the personal exposures of crew (especially) and passengers. Long-term and short-term health effects of repeated exposure to low levels of pesticides in dry environments, and repeated exposure to fairly high levels of pesticides during disinsection, should be considered.

Controlling the levels of many pollutants relies on correct installation and maintenance of HEPA filters, but there are some reports of poor maintenance. It is not clear how widespread a problem this is. It would be useful to look further at this, perhaps with a survey of airlines on their maintenance procedures and even spot checks on the condition of filters. The potential for using carbon filters to remove pollutants in the vapour phase (especially while aircraft are on the ground) could be investigated.

Transmission of Infection

Summary of evidence

Plausible mechanism

There is, prima facae, potential for a disease to be transmitted via aircraft from areas of the world where it is endemic to passengers on aircraft and to regions where the disease has a lower incidence. The transmission of disease in aircraft cabins can occur by a number of means:

- contaminated water or food (e.g. cholera, food poisoning);
- toilets (e.g. *Shigella* dysentery);
- direct contact or body fluids (AIDS, hepatitis);
- insect vectors (e.g. malaria, dengue);
- airborne person-to-person spread.

This review is concerned only with airborne transmission of infection between people while they are on board aircraft. The model for understanding such spread appears to be *tuberculosis* (TB), which is caused by airborne transmission of *Mycobacteriumtuberculosis* from an infected person to an uninfected person. While other diseases maybe spread in a similar way, from colds, influenza and Norwalk virus gastroenteritis to more serious illnesses, TB is more persistent once acquired, without being rapidly fatal. It is also a disease with which approximately one third of the world s population is infected, most being unsymptomatic at any one time. TB is also readily diagnosed with certainty and creates sufficient public concern to generate research funding. All these factors make it a good model.

In addition to TB there is a wide range of infectious diseases that may be transmitted as a consequence of the conditions on or surrounding aircraft and air travel. The various diseases have different mechanisms of transmission and this means different approaches to the investigations. Each of these warrants some concern and a possible outbreak of malaria caused by the carriage of mosquitoes is potentially serious, as are cholera infections transferred by unhygienic practices both on board and off the aircraft.

Case reports and case series

The limited evidence from case studies leads to the conclusions that:

- TB can be transmitted during air travel but none of the infected persons has developed active TB to date;
- there is no evidence that air recirculation facilitates transmission of M. tuberculosis aboard;
- in case of ground delays of more than 30 minutes, provisions must be made to supply adequate ventilation on board;
- risk of TB among cabin crew is similar to that of the general population;
- logically, there is a greater risk of onward transmission from cabin crew than from passengers or flight crew, but there is no evidence for or against this;
- the likelihood of transmission of TB is low and is limited to people in close proximity on an aircraft for an extended period of time.

From the perspective of future research needs, the report is quite clear that given the scale of infection world-wide, the routine use of BCG vaccination, and the numbers of people travelling that Further epidemiological studies on TB transmission in aircraft would be time and resource consuming. In case of exposure to *M. tuberculosis* infection during air travel, tracing and information of passengers and crew may be warranted.

There have been no case-control studies or longitudinal/intervention studies.

Groups at risk

Immunosuppressed or frail people.

Research needs

In general, the microbiological loading of aircraft cabins has not been widely researched. Only a small number of studies have been carried out and these have adopted a range of methods and procedures. A more clear understanding of the level of infectious agents within cabin air would be useful.

In the case of TB in particular the incidence of the bacterium in the air, furnishings and filters on flights from countries where TB is endemic would provide evidence on the likelihood of infection and of the ventilation system s capability to remove bacteria from the air. Particular attention should be given to conditions of reduced ventilation, when the aircraft is on the ground.

Where *M. tuberculosis* is identified on a flight, passengers on that flight could be followed up to determine whether the illness has spread.

As part of the understanding of the incidence of the bacterium in the aircraft, a study of cabin cleaning procedures and effectiveness would be valuable (such a study would also usefully include allergens).

The significance of the cabin environment in airborne transmission of infection is unclear. Temperature and humidity may have only a small effect on the viability of airborne pathogens, over the distances involved in person-to-person spread, but their effect on resistance to infection should be explored. The role of poor local ventilation effectiveness, which may increase the risk of transmission local to the infected passenger, should also be investigated.

The overall risks of acquiring TB on aircraft could be assessed by comparison of aircraft carrying larger or smaller numbers of infected passengers, although the follow-up would be difficult. Follow up of flights known (retrospectively) to have carried a highly infectious person is more realistic but less useful for estimating risk.

In addition to the studies relating solely to the transmission of TB, the effectiveness of disinsection practice, and the interaction between disinsection and air quality, needs to be considered in the context of removing other vectors for other diseases. Toilets and aircraft food should be reviewed separately as possible causes of disease.

Cosmic radiation

Summary of evidence

Plausible mechanism

The plausible mechanism is clear: cosmic radiation (CR) is ionising radiation, and it is known from the effects of other sources that ionising radiation is carcinogenic and teratogenic. The three main types of health concern associated with in-flight exposure to CR are radiation-induced cancers, genetic damage that might be passed on by parents to offspring, and direct radiation damage to the foetus.

Measurements in flight provide a basis for estimating risk, although the interpretation of measurements is debated. The CR exposure cumulative dose regarded as a risk (e.g. of developing cancer) is 6 mSv/year (0.3 of the occupational dose limit recommended by the International Commission on Radiological Protection). Concorde is perhaps the commercial aircraft that is most vulnerable to CR, because of the height and latitude at which it flies. Nevertheless, studies on suggest that less than 4% of Concorde cabin crew flying between London and Tokyo could reach or exceed the 6 mSv/year level.

The connection with carcinogenesis and teratogenesis is difficult to prove by current methods and epidemiological studies are subject to many confounding factors. It has been calculated that a crew member working 700 block hours / year for 30 years would incur a lifetime risk of developing CR induced fatal cancer of 1 in 190, while in the general population of USA 1 in 4 adults will eventually die of cancer. Thus, although the possibility of harm from exposure to CR while flying cannot be excluded, it would be impossible to establish that an abnormality or disease in a particular individual resulted from such exposures.

Airline pilots are exposed to magnetic fields by the aircraft s electrical system, and it has been suggested that this may increase the risk of CR-induced cancers. There is laboratory evidence of enhanced chromosomal aberrations in human lymphocytes when there is exposure to both ionising radiation and 60 Hz magnetic fields. In other studies there is found a potentiating effect of magnetic fields on ionising damage in cultured cells.

One of the most sensitive issues involving possible CR damage in flying is its effect on human reproduction in genetic damage to (possibly both) parents before conception, damage to the foetus during pregnancy, and to the infant who may be more susceptible to radiation effects. In European legislation, once pregnancy is declared, the requirement is that the CR exposure is kept as low as is achievable such that the dose to the foetus is unlikely to exceed 1 mSv during the remainder of the pregnancy. Hence, it is unlikely that evidence will be obtained of risks to the unborn child.

Case-control studies

Some case-control studies have concluded that air crews have an increased risk of some or all cancers but the findings are inconsistent, particularly in relation to which cancer types crew members are at risk of. The main review papers and studies from the UK conclude that there is no marked cancer risk attributable to CR, and that the highly elevated risk of skin cancer among pilots is probably associated with solar (UV)exposure.

There have been no useful case reports, case series or longitudinal/intervention studies.

Groups at risk

Unborn children, infants, children and the elderly.

Research needs

CR shielding is not an option in aircraft and neither air crew nor passengers can easily reduce flying hours or transfer to low altitude or low latitude flights. Neither can airlines or pilots easily co-ordinate flights with solar activity. Hence, any serious risk management strategy is likely to have a high cost. As a consequence, very strong epidemiological evidence on the magnitude of risk is likely to be needed before significant new action is likely to be taken.

Epidemiological studies on aircrew have suffered from a low statistical power with confounding factors of other noxious agents and lifestyle. The considerable funds often spent on epidemiological studies are sometimes regarded as questionable, but it may be that more money must be spent on a major project, so that definitive data can be generated. Improved dosimetry would be beneficial for such studies.

DNA damage is apparently greater with acute rather than chronic CR exposure and this requires further investigation with regard to use of biological markers and exploration of possible adaptive responses. Solar flares and related high levels of exposure would be of particular concern here.

More information is required on limits of exposure for passengers, especially pregnant women and frequent fliers, and private jet pilots and their passengers.

There is a need to discriminate the cause of cases of cancer that are suspected of arising from CR exposure. In particular, there needs to be good control of the possibility that skin cancers have been caused by UV exposure rather than CR.

Jet lag

Summary of evidence

Plausible mechanism

Unlike the other topics reviewed in this report, the issue with jet lag is not whether air travel causes it or how likely it is to occur. In the technical literature, as among travellers, it is taken as read that jet lag is a normal consequence of transmeridian flight. The primary consequences of jet lag include, by definition, desynchronisation of circadian rhythms from the local day/night hours and, consequently, difficulties in getting to sleep and/or remaining asleep or awake at times consistent with local norms.

The consequential risks for most groups do not appear to have been specifically researched. While the consequences to individuals are usually minor, they are not desirable, as evidenced by the body of work on management of jet lag. At population level, the consequences may be significant in terms of the costs of accidents (e.g. when driving or operating machinery), medical treatment, impaired performance at work (e.g. making important decisions while mentally below par) and days of work missed. The research has focussed more on management of jet lag.

A number of interactions have been identified, whereby jet lag may increase the risks from other causes, or other factors might exacerbate jet lag. In each case, the evidence comes from only one study but the following could be of interest when considering further research:

- transmeridian flight causes changes in lymphocytes and related cells (could affect susceptibility to infection but both positive and negative changes were observed);
- measures of risk for DVT were affected by circadian rhythm;
- interaction between jet lag and temperature/humidity (possibly confounded by the use of melatonin to manage jet lag, since another paper suggests that melatonin acts by suppressing core body temperature);
- interaction with exposure to elevated carbon dioxide concentration (paper in Russian, English abstract unclear about the nature of the effects);
- an interaction between circadian rhythms and radiation (again, a Russian paper with an unclear English abstract the radiation referred to could be visible light or cosmicradiation);
- shifting the circadian rhythm increased alcohol consumption by rats (while this is some way from a valid conclusion about humans, anything that increased the tendency to drink during or after flights would have the potential to interact with other risks).

Case reports and case series

From case studies, it appears that the flight characteristics that increase jet lag are:

- number of time zones crossed;
- eastbound travel, i.e. a shortening of the day (the human diurnal cycle tends to be longer than 24 hours in the absence of day/night cues).

Also, consumption of alcohol can exacerbate jet lag.

The time course of desynchronisation and resynchronisation has been reasonably well studied and modelled but is not entirely predictable. Resynchronisation can take up to 10days. Other direct effects have been listed as:

- fatigue;
- reduced alertness/concentration;
- impairment of mental performance, including memory;
- reduced motivation;
- irritability;
- nausea/digestive problems.

There have also been suggestions that jet lag directly causes stress/anxiety, largely based on cortisol measurements. The research to date does not seem adequate to exclude the possibility that stress is due to other flight-related factors, or to difficulties in functioning with impaired mental performance.

Case-control studies

Findings on mental performance have not been entirely consistent and it is not clear why results vary from study to study, for example whether it is related to the motivation of the subjects or to some other confounders in the study design.

Of those papers that focus on a particular group of people, the most common target is aircraft crews. In this context, it seems to be implicit that crews suffering from jet lag (or fatigue for any other reason) is a health and safety issue on the aircraft. However, overall there is not definitive evidence of the magnitude of the accident risk due to jet lag, either for air accidents, accidents on board or accidents after disembarking.

The only other professional group that appears to have been studied is sportsmen/women. The evidence is not convincing that sports performance is affected, so long as motivation is intact.

Longitudinal/intervention studies

The strongest research has been focussed on management of jet lag, rather than establishing its causes and effects. Strategies offered for reducing the impact of jet lag can be broadly classified as:

- schedule management (e.g. adapting activities to the time zone rather than the circadian rhythm, or taking planned naps);
- specific activities (e.g. eating, exercising, social activities);
- light exposure (either natural light or controlled exposure to bright light);
- pharmacological treatment, including melatonin (and melatonin agonists), benzodiazapines, other tranquillisers/hypnotics, stimulants (primarily caffeine),biochemical precursors (e.g. tyrosine, glycine, l-tryptophan), antihistamines, antidepressants, anti psychotic drugs, and herbal treatments (e.g. valerian).

The balance of current thinking seems to be that melatonin is not recommended except under medical supervision. While it is generally accepted that melatonin can alleviate jetlag, there is uncertainly over the mechanism of the effect, required formulation and dosage, long-term side effects and contra-indications (including possible interactions with other drugs).

Conclusions on the usefulness of the various approaches have varied widely between authors, from those who extol the virtues of a particular approach to those who conclude that it is ineffective or even dangerous. No research has thoroughly addressed the range of management approaches under well-controlled conditions. Since there is not universal agreement as to the best treatment, there is a weak basis for making confident and consistent recommendations to travellers.

Groups at risk

Groups identified as possibly at greater risk are:

- the elderly;

- people suffering from other conditions that involve disruption of melatonin metabolism and/or circadian rhythms (i.e. mania, anorexia/starvation, chronic fatigue syndrome, or depression, especially seasonal affective disorder);
- people suffering from psychiatric disorders generally;
- those suffering from other pre-existing illness;
- introverts (morning types).

Research needs

Although the effects of jet lag are widely thought of as minor and transitory, the number of people adversely affected is much greater than for the other issues dealt with in this report. Hence, at population level, its overall impact may be greater. The short-term and long-term health and safety implications of jet lag need to be established, for the population in general and for susceptible groups.

Much of the work on the effect of jet lag has focused on detailed physiological mechanisms and performance on tasks outside of a real world context. This research is far from comprehensive or definitive but, more importantly, there is a lack of understanding of important effects at the policy-relevant level: the health, safety and work performance of passengers and crew. The short-term and long-term economic implications of jet lag need to be established, so that working people and their employer shave a better basis for policy concerning air travel.

The factors that exacerbate, alleviate or interact with jet lag are poorly understood, undermining the authority of guidance. The best means of direct management of jet lag is also debated, with a wide range of opinions. This is particularly of concern in light of anticipated ultra-long-haul operation patterns. Depending on conclusions on the seriousness of the consequences of jet lag, there may be a case for publicly funded work on management of jet lag. There is probably already sufficient justification of privately funded research for those who offer treatments for sale, but this must be handled in such a way as to avoid doubts over bias in the work.

Summary of interactions

There are many possible interactions between health outcomes and risk factors. Risks from cosmic radiation are relatively independent but all the other issues are inter-related, both in determining cabin conditions (e.g. a high ventilation rate reduces pollutant and pathogen concentrations but decreases the humidity of the air) or in leading to particular health end-points (e.g. hypoxia, jet lag, alcohol, air pollutants and low RH may all be associated with mild neurological effects, and hence with consequences such as accident risk). Factors outside the remit of the review will also interact, for exampl emotion sickness can lead people to perceive that there is insufficient fresh air. While it is plausible that stress and anxiety will interact with the reviewed risks, no evidence of such interaction was found.

The situation is compounded by the potential for both interactions and direct effects to vary between the various population groups that are more susceptible to one hazard or another. This means that, for each issue, the wider implications need to be considered when planning research or risk management.

The overall situation is complex but can be represented by the following possible causal chains (refer to the text for the evidence on each link in the chains).

Low cabin pressure → Hypoxia → DVT

Low cabin pressure → DVT

Hypoxia, high temperature, jet lag, aircraft seating → Low mobility → DVT

Concern over DVT → Exercise, carbon dioxide → Hypoxia → DVT

High temperature, low RH, aircraft seating → Discomfort → Jet lag

High temperature, low RH → Alcohol, caffeine consumption → Dehydration → DVT

High temperature, low RH, close proximity of people, hypoxia → Infection risk

Low ventilation rate → Infection risk, odour, carbon dioxide exposure

High ventilation rate → low RH ← High temperature

Hypoxia, jet lag, alcohol, air pollutants, low RH → Neurological effects → Accident risk

Hypoxia, jet lag → Digestive disturbances

DVT ← Jet lag → Infection risk

Jet lag → Alcohol → Jet lag

High temperature, air pollutants, air movement, aircraft motion → Perceived air quality

High temperature, low RH, air pollutants, air movement, → Acute non-specific symptoms

The situation is compounded by the potential for both interactions and directs effects to vary between the population groups that are more susceptible to one hazard or another.

Towards improved risk management

Much of the recent publicity concerning health in aircraft has appeared to founded on the notion that there can be risk-free travel. The reality is more likely that most people only expect carriers to take reasonable measures to reduce risks, and to be clear in communicating the risks and how to avoid them. Nevertheless, such a view is easy to cultivate in a society in which air travel is becoming a normal activity for the majority. In such a culture, people might reasonably come to the view that no precautions or advice need be taken, any more than medical consultation would precede catching a bus.

Therefore, management of health and safety in aircraft should be reviewed in depth and clear official guidance produced for passengers, crew, employers and those who offer medical advice to travellers. This should be based on research into what kind of advice works.

Research priorities

Introduction

Current knowledge is deficient in each of the areas covered by this review, and the research needs are many. Therefore, a prioritisation of research needs is required, and is proposed in this section. For each of the topics, needs are identified as priority high, medium or low. Some other suggestions, of lower priority, are noted in the main text of the report.

The highest priority items relate to risk characterisation. Depending on the outcome of research of this type, priorities for research on risk management may change. This is not to say that there is no case for improved risk management at present: the management of health and safety in aircraft should be reviewed in depth and clear official guidance produced for passengers, crew, employers and those who offer medical advice to travellers. This should be based on research into what kind of advice works.

High Priority

DVT

- Improved case-control studies (with particular attention to the selection of controls).
- Prospective studies, probably based on measurements of very early stages of clot formation, prior to DVT symptoms becoming apparent. This work should involve more than one type of approach to reducing DVT risks.
- Interaction with hypoxia and exercise should be considered in any research on DVT.

Cabin air quality (CAQ)

- An investigation into norms for the key CAQ parameters in flight, with multiple parameters measured in one study. Relevant parameters include the oxygen saturation of a range of crew members and passengers, pressures and rates of change, temperature, air movement, humidity, ventilation rate and concentrations of common pollutants and organophosphates . The research should also relate these factors to self-reported health and comfort on the flights.

Jet lag

- Inclusion of jet lag as a confounding effect in studies of DVT, CAQ and infection risk (could be assessed using a few simple questions to passengers/crew).

Medium Priority

DVT

- Experimental biomedical research, to separate out the possible effects of decreased cabin pressure, low partial pressure of oxygen, the stress of being in an enclosed environment etc., and thus to underpin advice to passengers on DVT prevention.

Cabin air quality

- As for high priority recommendation, but for aircraft on the ground.
- Laboratory/simulation studies of the above parameters and barometric pressure, particularly the effects of interactions between parameters.
- Depending on the outcome of the above, intervention trials on the impact of altering parameters that correlate with health outcomes (e.g. humidification, gas phase air filters, reduced temperature).
- Measurement of exposure to insecticides and organophosphates on high risk flights.

Transmission of infection

- The incidence of infectious agents should be determined in the air, furnishings and filters on flights from countries where TB is endemic. This could be done in combination with the CAQ investigations that are suggested above, to assess the impact of cabin environment factors on pathogen movement and viability.

Cosmic radiation

- Exposure monitoring.
- Further development of biological markers for cancer risk.

Low Priority

DVT

- Co-ordinated case studies to clarify estimates of the incidence of recent travel in DVT patients (if possible, in association with case-control studies).

Cabin air quality

- A survey of air filter condition and maintenance (this would also be relevant to transmission of infection).

Transmission of infection

- The pros and cons of adjustable air supply nozzles (gaspers) should be clarified, in relation to air distribution in the cabin and movement of pathogens (this could be done as part of the medium priority study, and would also be relevant to CAQ).
- Where M. tuberculosis is identified on a flight, passengers on that flight could be followed up to determine whether the illness has spread.
- The overall risks of acquiring TB on aircraft could be assessed by comparison of aircraft carrying larger or smaller numbers of infected passengers, although the follow-up would be difficult.

Cosmic radiation

- A large epidemiological study on the magnitude of risk, including discrimination of skin cancers risks from CR and UV exposure.

Jet lag

- Desk study of the short-term and long-term health and safety implications of jet lag, and the economic implications.

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Disclaimer

The views expressed in this report are those of the authors and of BRE, and do not constitute either the opinion or policy of the DTLR.

Appendix 1. Search profiles

Terms used

The search terms were grouped as follows to cover all the different aspects of cabin air/cabin health as set out in the original terms of reference. The symbol $ indicates that any character string (or none) in that position will be accepted in the search.

1) ((Commercial or passenger)(aircraft or airline$ or aeroplane$)) or cabin $ or aviation or air travel)

AND

(DVT or thrombo$ or cardiovascular or blood circulat$ or blood pressur$ or heart or blood clot$ or pulmon$ or PTE or haemoglobin or hemoglobin or oxyhaemoglobin oroxyhemoglobin or oxy-haemoglobin or oxy-hemoglobin or oxygen saturat$ or (blood and oxygen) or hypoxia or hypoxemia or hypoxaemia or hyperoxia, or oedema, or edema, orc oagulation, or contraceptive$)

2) ((Commercial or passenger) (Aeroplane$ or aircraft or airline$))or cabin $ or aviation or air travel)

AND

(Air filt$ or airflow or air flow or air quality or ventil$ or (oxygen and partial pressure) orPO2 or atmosphere$ or environment$ or HEPA filt$ or high-efficiency particulate air or recirculated air or temperature or thermal degradation or humid$ or air change or air cleaning or air conditioning or air distribution or air movement or air velocity or IAQ assessment or microclimate or micro climate or IAQ assessment or indoor air quality)

3) ((Commercial or passenger) (Aeroplane$ or aircraft or airline$)) or cabin$ or aviation or air travel)

AND

(Hygien$ or toilet$ or WC$ or water closet$ or lavator$ or Pollutant$ or volatile organic compound$ or organo-phosphate or leakage or insecticide$ or antigen or benzene oratopy or biocontamina$ or contamina$ or dry$ or irrita$ or fragrance or odour or odor orspores or genotoxic$ or toxic$ or inflamm$ or flamm$ or micro-organism$ ormicro organism$ or MMMF or mineral man-made fibres or mould or mold or mutagenicityor nasal mucosa or nicotine or particle$ or particulat$ or pentachlorophenol or pesticide$or physiolog$ or polycyclic aromatic compound$ or rhinolog% or rhinostereometry orrhinitis or sensory irrit$ or smoke or source control or source$ or suspended particle$ orparticulate$ or aerosol or aldehydes or allerg$ or bioaerosol$ or biocide$ or (bio$contamin$) or carbon monoxide or carbon dioxide or chemical sensitiv$ or chemical$ orclimate or CNS symptoms or combustion product$ or decipol or disinfect$ or draught ordust or emission$ or endotoxin or ETS or fibre$ or formaldehyde$ or fung$ or immun$ or inorganic compound$ or ions or microbial or mycotoxin$ or neurotoxicity or nitrogendioxide or nitrogen oxide or oil residue or ozone or PM10 or PM 2.5 or smok$ or SVOCor TVOC or VOC or VVOC or volatile organic compound$, or TOCP or TCP orphosphate$)

4) ((Commercial or passenger) (Aeroplane$ or aircraft or airline$))or cabin$ or aviation orair travel)

AND

(Infect$ or vir$ or communic$ or measles or TB or tuberculosis or influenza or flu ordisease$ or illness$ or respir$ or bacteria or health or cancer or asthma or pneumonia or hyper-reactivity or hyperreactivity or hypersensitivity or symptom$)

5) ((Commercial or passenger) (aircraft or Aeroplane$ or airline$)) or cabin$ or aviation or air travel)

AND

(Cosmic radiation or ultra violet ray$ or UV rays)

6) ((Commercial or passenger) (Aeroplane$ or aircraft or airline$)) or cabin$ or aviation or air travel)

AND

(Jet lag)

7) ((Commercial or passenger) (Aeroplane$ or aircraft or airline$)) or cabin$ or aviation or air travel)

AND

(Seat$ or space or ergonom$ or overcrowd$ or noise or stress or comfort or sensory orimmob$ or confined space$)

8) Economy class syndrome

9) Airway react$ (Passenger or commercial) (aircraft or aeroplane$ or airline$)

AND

(Comfort or air quality or health or cabin$)

The following terms were used in NOT searches to refine the results of the searches:

(Military or astro$ or cosmo$ or air traffic control or fire or crash$ or fuse$ or impact$ oremergenc$ or accident$ or approach or display or flight simulat? or equipment orparachute$ or shield$ or engine$ or turbo$ or fighter or helicopter$ or space or radio orsignal$ or task$ or wing$ or nondestructive or venture$ or duty or volcano$ or airport$ ornavigation or combustion or air force or composite or lubric$ or additive$ or meteor$ or weather or oils or turbulence or soils or hydraulic$)

In addition, the following subject classification codes were used in the Aerospace and European Aerospace Database (EAD) files only: 03 Air transportation/ safety; 05 Aircraft design, testing, performance; 52 Aerospace medicine.

Web sites

Aerospace Medical Association

http://www.asma.org/

Aviation Health Institute

http://www.aviation-health.org/

This is a non-profit registered charity aimed at promoting the health and well-being of airline passengers. It provides background information, news and health advice. The advice encompasses all areas of concern, including CAQ, blood clots, long haul travel and pregnancy, suggesting remedies and giving a brief outline of the problem. The 'Medical center' is aimed at GPs and gives information on contraindications to air travel. The full text of a consultation paper entitled 'Consultation paper into the aircraft cabin environment' by the Director of the Aviation Health Institute is available in HTML format. The site is also searchable.

Aviation Medicine Home Page

http://www.ozemail.com.au/~dxw/avmed.html

This resource is maintained by Dr Dougal Watson of the Institute of Aviation Medicine in Edinburgh (Australia) and is sponsored by the Environmental Tectonics Corporation and the Aviation Medical Society of Australia and New Zealand. The site provides a collection of links to Web resources including full text papers, books, journals, magazines, mailing lists, courses, societies, associations, organisations and search engines about all aspects of aviation medicine.

British Airways: Health Services

http://www.british-airways.com/health

Civil Aeromedical Institute

http://www.cami.jccbi.gov/

Cranfield Institute of Technology (UK)

http://www.cranfield.ac.uk

Aerade portal to aerospace and defence resources - http://aerade.cranfield.ac.uk/

Cranfield University Human Factors Group

http://www.cranfield.ac.uk/coa/tech-hf/hf-1.htm

The Human Factors Group is part of Cranfield University's College of Aeronautics. This site describes the range of interests, expertise and facilities available to students undertaking an MSc in Human Factors at the University. These include studies of passenger psychology, cabin evacuation trials, personnel selection and organisational behaviour within a range of industries. MSc, PhD and MPhil programmes are described, and a list of current thesis titles is provided. Biographic and contact details are provided for staff teaching on Human Factors Programmes.

FAA Human Factors Division, AAR

http://www.hf.faa.gov/index.htm

This Web site gives information about human factors research and applications as part of the National Plan for Civil Aviation Human Factors. The aim of the site is to provide information on human factors programs, products, and activities within government, academia, and industry. Information on STARS (Standard Terminal Automation Replacement System), the National Plan for Civil Aviation Human Factors and Human Performance Integrity are amongst the resources available.

Aeromedical Research Program - http://www.hf.faa.gov/medical.htm

FAA Office of Aviation Medicine

http://www.faa.gov/avr/aamhome.htm

This is the home page of the FAA Office of Aviation Medicine. The site includes links to information about customer service standards, the full text of 14 CFR Part 67, and the Aviation Industry Anti drug and Alcohol Misuse Prevention Programs. The Aeromedical Reference Material link provides a listing of FAA Aviation Medicine Orders and Directives, an Index of International Publications in Aerospace Medicine which covers mainly books and the Federal Air Surgeon's Medical Bulletin.

FAA Office of Aviation Research

http://research.faa.gov/aar/

The Federal Aviation Administration supports research and development initiatives in areas such as communication, navigation, surveillance, air traffic management, human factors, weather and safety and security technologies. The site includes the following resources: forthcoming events; media and press releases; AAR newsletter, Technology R&D fact sheets; technical reports (abstracts and selected full-text) and a large number of links to other related sites.

ICAO(International Civil Aviation Organisation) Aviation Medicine Section

http://www.icao.int/cgi/goto.pl?icao/en/med/aviomed.htm

MEDLINE via PubMed (database of medical bibliographical information)

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi

NASA SP 7011 : Aerospace Medicine and Biology

http://www.sti.nasa.gov/Pubs/Aeromed/Aeromed.html

This site provides access to this cumulative bibliography compiled by the NASA STI(Scientific and Technical Information) division. The subject coverage of the bibliography is the biological, physiological, psychological and environmental impacts on humans during flight or simulated flight in both space and the Earth's atmosphere. Each entry comprises both bibliographic information and an abstract. It is available in PDF format back to September 1995.

NASA Technical Reports Server (NTRS)

http://techreports.larc.nasa.gov/cgi-bin/NTRS

NTIS catalogue 1990

http://www.ntis.gov/search.htm

National Transportation Library - Aviation - Human Factors

http://ntl.bts.gov/ntl/subjects/av-humfact.html

The National Transportation Library is provided by the US Bureau of Transportation Statistics, the Transportation Administrative Services Center, the operating administrations, and the Office of the Secretary of the U.S. Department of Transportation. The Library holds materials from public and private organisations and makes this available to search over the Internet. It is both searchable and browseable and is updated every day. The aviation section is divided into several subjects which can be browsed, the aviation human factors section links to a number of full text documents which can be downloaded free of charge.

Royal Aeronautical Society : Library Catalogue

http://library.raes.org.uk/scripts/runisa.dll?WebOpac:SCRIPTHOMEPAGE:976459

The Royal Aeronautical Society is a UK-based professional body for the aerospace community world wide. The Society's library is the oldest aerospace library in the world and provides access to aeronautical and astronautical publications. The library catalogue is available on the web and can be searched in a variety of ways including author, title and subject. There are simple search and advanced search options. It is also possible to search for journal articles using this facility.

Transportation Research Information Services (TRIS) Database

http://tris.amti.com/sundev/search.cfm

The Transportation Research Information Services (TRIS) Database is the worlds largest and most comprehensive bibliographic resource on transportation information. TRIS is produced and maintained by the Transportation Research Board (TRB) at the National Academies of Sciences. TRIS contains almost a half million records of published and ongoing research on all modes and disciplines in the field of transportation. Each year over 20,000 new records are added to TRIS. Other features to note about the resource include the following: selected links to full text or sources of full text; links to the IRRD database for further coverage of international transportation; and searching by author, title, and subject.

University of Texas Human Factors Research Project : Research in Aerospace, Medicine and Other Safety-Critical Work Environments

http://www.psy.utexas.edu/psy/helmreich/nasaut.htm

The site describes research funded by grants from NASA and the Federal Aviation Administration and is intended for use by researchers and operational personnel concerned with aviation and space human factors. It also contains an overview of the project with specific pages dedicated to various research projects. The full text of several papers published in the British Medical Journal (BMJ) theme issue on error in medicine and written by researchers within the department are available in PDF format.

Appendix 2. Case-control studies of travel-related DVT(after HSE, 2001)

Case controls studies that permit some quantification of the risk of DVT from travel

Study	Ferrari et al (1999)
No. cases	160
Case ascertainment	Subjects hospitalised with VTEs[1] at French hospital July 1992 to August 1995
No. controls	160
Control ascertainment	Consecutive cardiology patients at the same French hospital without limited mobility and not on anticoagulants or antiplatelet treatment
Travel assessment	Questionnaire All travel greater than or equal to 4 in preceding 4 weeks whatever the means of travel 39 cases (24.4%) 12 controls (7.5%) Mode of travel cases: 9 plane, 28 car, 2 train
Risk **(Odds Ratios ORs)**	Travel greater than or equal to 4h unadjusted OR = 3.98 (95%CI 1.9 8.4)

Study	Kraaijenhagen et al (2000)
No. cases	186
Case ascertainment	Clinically suspected DVTs (n=788) April 1997 to January 1999 presenting at a Dutch hospital[2] that late object[3] diagnosis confirmed
No. controls	602
Control ascertainment	Clinically suspected DVTs (n=788) April 1997 to January 1999 presenting at a Dutch hospital that later diagnosis shows not to be DVT
Travel assessment	Questionnaire Travel more than 3 hours in previous 4 weeks. Identification of duration of travel and mode of transport 9 cases (5%) 43 controls (7%)
Risk **(Odds Ratios ORs)**	Any travel OR=0.7 (95%CI 0.3, 1.4) Plane OR=1.0 (95%CI 0.3, 1.4) Car/bus OR=0.6 (95%CI 0.2, 1.6) Train (0 cases 2 controls) Multivariate adjustments for age, sex and other risk factors caused no change in these ORs

Study	Samama (2000)
No. cases	494
Case ascertainment	Objectively confirmed DVTs[3] identified through 624 General practices in France October 1990 to December 1991
No. controls	494
Control ascertainment	Selected at same practices by GP as patient following DVT with influenza or rhinopharyngeal syndrome matched on sex and age ± 10 years
Travel assessment	Long distance travel in previous 3 weeks recorded on reports forms by GPs 62 cases (12.8%) 31 controls (6.3%
Risk **(Odds Ratios ORs)**	Age/sex adjusted ORs for travel 2.35 (95%CI 1.45, 3.80)

1 Diagnosed by ultra sound echo-Doppler examination. Study outcome VTEs included diagnosed DVTs and PEs.

2 It is assumed this study was of a Dutch hospital but given the study was reported as a

3 Diagnosed by compression ultra sonography and venography with clinical follow-up. Repeat negative testing with uneventful clinical 3 month follow up indicated absence of DVT.

4 DVT diagnosed by at least one of, venography,

letter little information was available. An email has been sent to the author requesting this clarification.

duplex ultraconography, B-mode ultrasomnography, and/or impedance plethysmography.