Traveller's Thrombosis: A Review of Deep Vein Thrombosis Associated with Travel

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There is an increasing suspicion among the travelling public and the international media of an association between the occurrence of deep venous thrombosis (DVT) and air travel. It was noted by the UK House of Lords Select Committee on Science and Technology that up to 20% of the total population may have some degree of increased clotting tendency. It follows that some air travellers are at risk of developing DVT when, or soon after, travelling. There have been no epidemiological studies published which show a statistically significant increase in cases of DVT when travelling in the absence of pre-existing risk factors. The literature was reviewed. Current evidence indicates that any association between symptomatic DVT and travel by air is weak, and the incidence is less than the impression given by recent media publicity.

Keywords: deep vein thrombosis, venous thromboembolism, traveller's thrombosis, economy class syndrome.

DEEP VEIN (or venous) thrombosis is a condition in which a small blood clot (thrombus) or clots (thrombi) develop(s) in the deep veins, usually of the leg. The condition itself is not dangerous, but the complication of pulmonary embolism (venous thromboembolism – VTE) can, of course, be life threatening.

There is increasing suspicion among the travelling public and the international media of an association between the occurrence of deep vein thrombosis (DVT) and air travel, but so far there is only circumstantial, rather than epidemiological evidence in support of this (8). It has been reported (Morrison. Personal communication; 2001) that a number of international airlines are receiving writs from lawyers representing passengers who have suffered DVT in flight.

This paper by the Air Transport Medicine Committee of the Aerospace Medical Association provides an overview of current scientific evidence.

Traveller's Thrombosis

The term 'economy class syndrome' was first used by Symington and Stack in 1977 (27), and again by Cruickshank et al. in 1988 (4). This description implies that DVT does not occur in business or first class air travellers, or in travellers using other forms of long-distance travel, or indeed in non-travellers. The Air Transport Medicine Committee of the Aerospace Medical Association agrees with the recommendation of the UK House of Lords Select Committee on Science and Technology that the term 'economy-class syndrome' is seriously misleading and the term 'traveller's thrombosis' is more appropriate (13).

Incidence

Kesteven and Robinson state that at least 200 cases of traveller's thrombosis have been reported in the last decade (17). The annual incidence of VTE in the northern European general population has been estimated at between 1.6 and 1.8 per 1000 (10, 22), while others have approximated this to 1 in 1000 per annum (2). There is an increasing incidence with increasing age.

The UK House of Lords Select Committee on Science and Technology notes that up to 20% of the total population may have some degree of increased clotting tendency (13).

The travelling public is drawn from the general population and because of pre-existing risk factors, it follows that some air travellers are at risk of developing DVT when, or soon after, travelling. However, there have been no epidemiological studies published which show a statistically significant increase in cases of DVT when travelling in the absence of pre-existing risk factors.

Homans suggested in 1954 that travel may precipitate VTE (12). He reported two cases after a car trip, two after a prolonged flight and one after a visit to the theatre. Thrombosis of leg arteries after prolonged travel was reported by Collins et al. in 1979 (3). A series published in 1986 of 104 natural deaths occurring during or immediately after flight showed that 12 were due to VTE (24). Eschwege and Robert reported an increased incidence of DVT in commuters caught up in the 1995 Paris bus strike (6). A study from Nice in 1999

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TABLE I. PUBLISHED SERIES OF TRAVELLER'S THROMBOSIS (17).

	Mercer (20)	Ferrari (7)	Rege (23)	Kesteven (18)	Milne (21)	Eklof (5)	Eklof (b) (5)
No. of subjects	32	39	20	24	25	44	36
Mean age (yr)		65.3		61		63	50
Median age	48		40		51		
Age range	19–80		22–66	42–84	19–84	32–86	23–83
Male:Female	27:5		5:15	11:13		24:20	
Total with at least one risk factor	74%		75%	87.5%		84%	
Previous VTE	18%			20%	33%		34%
Malignancy	18%			5%	4%		14%
Recent surgery	3%				4%		9%
Hormone treatment	3%			35%	12.5%		16%
Family history					21%		
Thrombophilia				30%			

reported that of 160 cases of VTE, 39 had recently travelled. However, only 9 were related to flying while 28 followed a trip by car and 2 by train (7).

Dimberg et al., in a personal communication to Kesteven (2000), reported a possible travel associated incidence of DVT among frequent travellers at the World Bank of between 0 and 4 per 10,000 travellers. However, the study showed the risk among travellers to be about equal to that of non-travellers, when adjusted for age and sex.

It has long been understood that DVT can be associated with the following:

- reduction in blood flow;
- changes in blood viscosity; and
- damage or abnormality in the vessel wall.

This is described as Virchow's triad (28).

Much of the current knowledge is based on studies of post-surgical patients and little is known to what extent air travel *per se* directly influences these factors. Indeed, it has been suggested that traveller's thrombosis may have a different natural history (17).

In the absence of any good prospective published study, the evidence linking DVT or VTE with flying is circumstantial. However, there is sufficient evidence accumulating to suggest that there may be an association, although not necessarily a causation. Whether DVTs and VTEs that occur in association with airline travel simply result from prolonged immobility in an individual with predisposing risk factors, or whether there is a causal or contributory relationship with the aircraft cabin environment is not known.

Kesteven and Robinson examined clinical data from a large cohort of patients with traveller's thrombosis (18). Of 86 patients who developed VTE within 28 days of flying, 72% had at least one risk factor for VTE prior to flight. They note that 87% of cases of VTE occurred following either a return trip or after an outward journey involving very long trips. An identifiable risk factor or earlier journey was absent in only 2 cases, and 92% of cases with VTE developed symptoms within 96 hours of their flight.

Table I was provided by Kesteven and summarizes findings from a number of these recently published series. None of the authors of these series noted clinical differences between traveller's thrombosis and the remaining VTE cases. However, Kesteven suggests three subtle distinctions:

- There appears to be a relatively young group in each series.
- The frequency of symptomatic pulmonary embolism may be higher than expected.
- The proportion of cases with pre-existing risk factors is higher (although this may be due to methodology).

Most research workers agree (5, 7, 9, 10, 13, 17, 18, 21, 23) that risk factors for the development of DVT include the following:

- Blood disorders affecting clotting tendency;
- Impairment of blood clotting mechanism, such as clotting factor abnormality;
- Cardiovascular disease;
- Current or history of malignancy;
- Recent major surgery;
- Recent trauma to lower limbs or abdomen;
- Personal or family history of DVT;
- Pregnancy;
- Oestrogen hormone therapy, including oral contraception;
- Increasing age above 40 yr;
- Prolonged immobilization;
- Depletion of body fluids causing increased blood viscosity (Note that this is not dehydration as a result of dry aircraft cabin air).

Some also suggest (17, 18) that, in addition, there may be a risk from tobacco smoking, obesity and varicose veins.

Many theories have been proposed for additional risk factors associating DVT with flying. These include dehydration, excessive alcohol, poor air quality, circadian dysrhythmia, seasonal shifts and hypoxia. It has also been suggested that immobility resulting from the use of hypnotics to promote in-flight sleep is a risk factor. However, there is little experimental evidence to support these theories, with one exception.

In 1999, Bendz et al. reported a study for the purposes of training competitive skiers (1). Twelve healthy male subjects lived in a hypobaric chamber for a week and blood samples were collected at intervals. The first pres-

sure change from sea level to 2000 m was made over 5-10 min, and was associated with subtle, but statistically significant, activation of the tissue factor pathway. The altitude was then increased to 4500 m, where it remained for the week. The tissue factor activation markers returned to normal while the 2000 m altitude was maintained, and did not reappear in the climb to 4500 m. The study did not include a control group, so it is difficult to know if the changes were due to the hypobaric or hypoxic changes, as concluded by the authors, or to the stress of spending a week in a hypobaric chamber.

As Kesteven has commented (17), it is unlikely that hypoxia or hypobaric changes are themselves etiological factors for VTE, as there is no reported increased incidence of VTE in populations living at high altitudes nor in patients with hypoxic lung disease. There is no evidence of any increased incidence of DVT among commercial airline pilots who spend their working lives sitting in a hypobaric environment (Johnson. Personal communication; 2001).

The clinical and biochemical changes in 12 healthy volunteers during 4 simulated 12-h flights were investigated by Landgraft et al. (19). No dehydration was shown, but there was retention of an average of 1150 ml of fluid which corresponded to the simultaneous swelling of the lower legs. This swelling was not pathological. The study took no account of potential confounding factors such as reduced ambient pressure, hypoxia or low humidity.

In 1980, Janvrin et al. showed that blood will clot faster when diluted with saline (15, 16). A prospective trial of patients undergoing laparotomy showed that the use of intravenous fluids may have contributed to an increased prevalence of venous thromboembolism. This suggests that dehydration is not a risk factor for the development of VTE, and may indeed be protective.

Using cadavers, Schmitt and Mihatsch demonstrated that when in the seated position, the popliteal vein develops transverse rippling (25). They concluded that this may be sufficiently damaging to the endothelium, or cause sufficient alteration to flow, as to trigger the initial thrombus formation (in accordance with Virchow's triad).

Scurr et al. have published the results of a prospective randomised controlled trial attempting to assess the effects of long-haul air travel and the risk of symptomless DVT (26). The study found that of 200 passengers taking a long-haul flight, those who wore special compression stockings throughout the flight had no evidence of symptomless DVT assessed by ultrasonography within 48 hours of flying. In the group not given stockings, 10% were found to have symptomless DVT in their calf veins.

In an accompanying commentary (11), Hirsh and O'Donnell conclude that the study of Scurr et al. study does not resolve the issue of air travel and the risk of DVT. The reported incidence of symptomless DVT among controls was at least 40-fold higher than previous estimates, and this might be attributable to inadvertent biased ultrasonographic assessment (11). Hirsh and O'Donnell comment that the diagnosis of calf-vein thrombosis was associated with a negative D-dimer (a very sensitive test for venous thrombosis), suggesting that the thrombi were either very small or were false-positive findings. There was no follow-up for confirmation by venography.

Seated immobility is recognized as a risk factor for the development of DVT, and being cramped is likely to aggravate the immobility. Currently, there is no evidence to suggest that other factors can be identified which are specific to air travel.

The UK House of Lords Select Committee on Science and Technology has recommended (13) that the UK Department of Health should commission an epidemiological research program of the case-control type as soon as possible, to gather data on DVT and flying. The Air Transport Medicine (ATM) Committee of the Aerospace Medical Association supports this recommendation.

The ATM Committee also supports the Australian multicenter case-control study to examine the association between extended duration travel and venous thromboembolism proposed by the Australasian Society of Thrombosis and Haemostasis and the School of Aviation Medicine, Griffith University, Brisbane.

The ATM Committee notes that a meeting of scientists and the airline industry was organised by the World Health Organization (WHO) in Geneva in March 2001. The planned WHO study on the issue of traveller's thrombosis is a valuable initiative.

Recommendations for Prevention of DVT

In the absence of prospective studies conclusively showing a causal relationship between deep vein thrombosis and flying, there is no scientific basis for giving recommendations for the prevention of DVT when travelling. However, the following recommendations are reasonably based on studies in other environments.

For passengers with no identifiable risk factors, it is recommended that they carry out frequent and regular stretching exercises, particularly of the lower limbs, during flight. They should also take every opportunity to change position and to walk about the cabin. (The seating arrangements in some aircraft cabins are not conducive to moving in and out of seats, particularly for large individuals. The UK CAA has commissioned a study of aircraft seating arrangements, including minimum dimensions.) However, the relative risk of injury from being unrestrained during unexpected air turbulence has not been compared with the risk of developing DVT as a result of immobility.

For passengers with one or more identifiable risk factors, the recommendations contained in **Table II** should be followed. Note that advice for travellers at moderate or high risk should be given by the individual's own medical practitioner.

Conclusions

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 (9).

TABLE II. SUGGESTED PROPHYLAXIS—ADAPTED FROM KESTEVEN (18).

	Risk Categories	Prophylaxis
Low Risk	Age over 40; obesity; active inflammation; recent minor surgery (within last 3 d)	Advice about mobilisation and hydration, ± support tights/non-elasticated long socks
Moderate Risk	Varicose veins; heart failure (uncontrolled); recent myocardial infarction (within 6 wk); hormone therapy (including oral contraception); polycythemia; pregnancy/postnatal; lower limb paralysis; recent lower limb trauma (within 6 wk)	Passenger advised to consult own medical practitioner who may recommend the above + aspirin (if no contra-indication) ± graduated compression stockings
High Risk	Previous VTE; known thrombophilia; recent major surgery (within 6 wk); previous CVA; malignancy; family history of VTE	As above, but passenger's medical practitioner may recommend low molecular weight heparin instead of aspirin

The Committee supports the recommendation by the UK House of Lords Select Committee on Science and Technology that the UK Department of Health should commission an epidemiological research program of the case-control type as soon as possible to gather data on DVT and flying.

The Committee also supports the proposed Australasian multicenter case-control study to examine the association between extended duration travel and VTE.

The initiative of the World Health Organization to begin a study on the issue of traveller's thrombosis is welcomed by the Committee.

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