

Venous thromboembolism and travel: is there an association?

ABSTRACT—This paper reviews the literature on the association between venous thromboembolism and travel. There are plausible physiological reasons why sitting still for long periods (particularly in the cramped conditions of most aircraft) might predispose to venous thromboembolism. This may have been the explanation for the apparent excess of deaths from pulmonary embolism seen during the first months of the London blitz. No published controlled studies of thromboembolism and travel were identified, but eight case reports were analysed. They covered 25 people aged from 19 to 84 years with deep vein thrombosis or pulmonary embolism following travel. The reports suggest that long journeys are a particular risk and that there are often no symptoms until many hours after leaving the plane (so conventional methods of assessing the hazards of air travel may underestimate the problem). It is concluded that the literature tends to support the hypothesis that venous thromboembolism is associated with travel, but that carefully controlled studies are needed to test this properly.

Is there an association between venous thromboembolism and long air journeys? This question has been raised recently by a new book on the health hazards of air travel [1] and, more anecdotally, by the experiences (both clinical and personal) of local physicians.

An initial review of the literature on air travel and health allows three points to be made. First, venous thromboembolism has received relatively little attention, with most discussion focussing on the health of aircraft crews and on the prevention and management of in-flight emergencies affecting passengers [1–5]. The few writers who have discussed thromboembolism, however, appear very confident of its association with air travel.

Second, there are plausible physiological reasons why long journeys on modern passenger aircraft might predispose to venous thromboembolism. Sitting still for long periods produces venous stasis (Virchow first observed that venous stasis predisposes to deep vein thrombosis formation in 1856 [6]), haemoconcentration and reduced blood flow in the legs [7]. Sitting in cramped conditions also directly compresses the leg veins [8]. These physical triggers to thrombosis are

likely to be exacerbated by the dehydration caused by low humidity air in aircraft and by drinking alcohol [9], as well as possibly by the low atmospheric pressure in passenger aircraft (equivalent to a height of about 6000 feet [10]). Third, venous thromboembolism arising from sitting in cramped aircraft seats also seems likely by analogy with the experience during the London blitz. In 1940, Simpson reported an association between sitting overnight on deck chairs in air-raid shelters and death from pulmonary embolism [8]. While in September/October 1939 he had diagnosed four cases of pulmonary embolism at autopsy in his work in London, in September/October 1940 he diagnosed 24 cases, 21 of which had occurred in, or soon after leaving, air-raid shelters. He attributed these to 'obstruction, stasis, oedema and thrombosis' as a result of sitting for long periods, and observed: 'It is noteworthy that cases of fatal pulmonary embolism are already decreasing again, concurrently with the provision of bunks for sleeping'.

This paper reviews the clinical and epidemiological evidence on the risk of venous thromboembolism associated with travel. The review is not confined to air travel [11], both because many of the potential physiological hazards of sitting for long periods would apply with other forms of travel and because the earliest discussion of the association, published in 1954, included two patients who had suffered a deep vein thrombosis after long car journeys [12]. On the other hand, arterial thrombosis is excluded, even though cases associated with air travel have also been reported [13], because its aetiology differs from that of venous thromboembolism.

Methods

The English language literature was searched for case reports or controlled studies of the association of travel with venous thromboembolism, using a variety of sources: Medline on CD-Rom (going back to 1981); personal reference lists; follow-up of references quoted in other papers. The specialist aviation literature was not specifically searched. The reports and studies were collated, as far as possible, in a systematic way.

Results

Details of cases of venous thromboembolism associated with travel were found in eight papers [6,12,14–19], published between 1954 and 1988 (Table 1). All reports were descriptions of cases or of case-series;

RUAIRIDH MILNE, MB, MFPHM, Senior Registrar in Public Health Medicine, Radcliffe Infirmary, Oxford

Table 1. Case reports of venous thromboembolism and travel.

Year of publication	Number of cases described	Methods of transport	Number using method
1954 [12]	4	Plane	2
		Car	2
1968 [14]	1	Plane	1
1977 [6]	8	Plane	3
		Car	3
		Train	1
		Train/ship	1
1981 [15]	1	Plane	1
1983 [16]	3	Plane	3
1985 [17]	1	Plane	1
1985 [18]	1	Plane	1
1988 [19]	6	Plane	6

none had controls. In all, 25 cases were described, ranging in age from 19 to 84 years (Table 2), with a median of 51 years.

The earliest paper [12] described patients with deep venous thrombosis but made no reference to pulmonary embolism. All the later papers describe patients with embolism (one paradoxical [14], the rest pulmonary [6,15-19]), some of the patients having no clinically detectable deep vein thrombosis.

Information on the duration of the journey was given for 17 patients and could be estimated for four more. The journeys ranged from 3 to 30 hours (Table 3), with a median of 14 hours.

Table 4 shows the time between leaving the vehicle and the onset of the first thromboembolic symptoms. Cases fell into two groups: those with onset of symptoms during travel or immediately on leaving the vehicle; and those with onset after leaving the vehicle, between 90 minutes and 2 weeks later. The median interval for the latter group was 48 hours.

Seven of the papers gave no denominator, ie the number of cases of thromboembolism seen by the authors from which those associated with travel were drawn. However, Symington *et al* [6] drew their cases who 'developed acute symptoms after a journey' out of a group with pulmonary embolism diagnosed over a 3-year period.

A different approach was taken by Sarvesvaran [20], who reviewed 104 sudden natural deaths over 3 years at Heathrow airport, occurring either at the airport or during flights terminating there. The deaths were divided into three groups: spectators/staff (15 deaths), 'would-be' passengers (28 deaths) and passengers (61 deaths). All 11 deaths from pulmonary embolism occurred in the passenger group. Unlike the case reports (Table 2), this paper found more pulmonary embolism deaths in women. Nine of the 12 deaths (43%) in women were due to pulmonary embolism, but only two of the 40 deaths (5%) in men—a difference of 38% (95% confidence limits for the difference, 18% to 58%).

Table 2. Age and sex distribution of cases.

Age group	Men	Women	Total
19-29 years	0	1	1
30-39	2	1	3
40-49	5	3	8
50-59	4	1	5
60-69	3	3	6
70-79	1	0	1
80-84	0	1	1
All ages	15	10	25

Discussion

These case reports serve to highlight an important question: Is travel associated with venous thromboembolism?—but they do not answer it. They include all the reports I could discover but are, nonetheless, a selected sample; interestingly, at least three of the cases were doctors [12,19]. They lack controls and so cannot compare the levels of exposure to travel in those with thromboembolism to the levels in those without. Since most of the reports give no details on the number of thromboembolic episodes from which those associated with travel are drawn, it is impossible

Table 3. Duration of travel by different methods.

Duration	Plane	Car	Train ± ship	Total
No data	2	2	0	4
3-5 hours	2	1	1	4
6-11 hours	3	1	0	4
12-17 hours	6	1	0	7
18-23 hours	0	0	0	0
24-30 hours	5	0	1	6
Total	18	5	2	25

Table 4. Time till symptoms for different methods of travel.

Time till symptoms	Plane	Car	Train ± ship	Total
No data	1	1	0	2
During flight	1	0	0	1
Leaving plane	6	1	0	7
1.5-23 hours	3	0	1	4
24-47 hours	2	2	1	5
48-71 hours	1	0	0	1
72-95 hours	2	1	0	3
96 hrs or more	2	0	0	2*
Total	18	5	2	25

*These two cases developed symptoms 10 and 14 days after disembarkation.

to know how important the association might be in public health terms. The cases described by Symington *et al* [6] represented only 8 out of their 182 (4.4%) cases of pulmonary embolism over 3 years, suggesting that travel is not a major cause. This is supported by the findings of a current population-based case-control study of cardiovascular disease in young women in the Oxford Region. So far, 110 women with DVT/PE have been identified, of whom 18 answered 'yes' to a question about a period of not moving their legs before coming into hospital. Travel was given as the reason for the immobility by only 5 women (4.5%) (Vessey, Bale and Law, personal communication).

Despite these caveats, the reports give pointers for future enquiry. First, the findings of Sarvesvaran [20] suggest that women may be at greater risk than men, although this is not supported by the similar proportions of men and women found in the (admittedly uncontrolled) case reports. Second, the length of the journeys (Table 3) is of interest, with none reported as less than 3 hours. It is entirely plausible that an association of travel with thromboembolism would be stronger for longer journeys. This would also agree with the finding of Sarvesvaran that 10 of the 11 passengers who died from pulmonary embolism at, or on the way to, Heathrow airport over 3 years had had flights of more than 12 hours; none had had a flight of less than 6 hours [20]. Third, most of the cases are described in association with air travel, rather than other forms of travel. Whether this is because of a genuinely greater risk (perhaps because passengers cannot take breaks or readily walk around during air journeys) or merely because clinicians are more attuned to a travel link in patients who have been on plane journeys is, of course, unknown. Fourth, while 8 of the cases reported an onset of symptoms during the journey or immediately it was over, 15 developed symptoms later. This supports the common-sense view that reports of in-flight emergencies or deaths [2] or of deaths in airports [20] will underestimate the importance of venous thromboembolism as a hazard of air travel.

The central questions remain. There is no epidemiological evidence about whether travel is associated with venous thromboembolism at all and, if so, what the risks are for particular modes of travel and for particular groups of people. These questions can only be answered with a controlled study that pays careful

attention both to case definition and to the assessment of exposure. This should not be too difficult to achieve but, until then, the question will remain open.

Acknowledgements

I gratefully acknowledge the encouragement and help of Martin Vessey at every stage of the production of this paper.

References

- 1 Kahn FS. *The curse of Icarus: the health factor in air travel*. London: Routledge, 1990.
- 2 Anonymous. Illness in the clouds. *Br Med J* 1975;**1**:295.
- 3 Mills FJ, Harding RM. Medical emergencies in the air. I. Incidence and legal aspects. *Br Med J* 1983;**286**:1131-2.
- 4 Mills FJ, Harding RM. Medical emergencies in the air. II. Equipment and prevention. *Br Med J* 1983;**286**:1204-6.
- 5 Anonymous. Emergencies in the air. *Lancet* 1985;**i**:28-9.
- 6 Symington IS, Stack BHR. Pulmonary thromboembolism after travel. *Br J Dis Chest* 1977;**71**:138-40.
- 7 Moyses C. Economy class syndrome. *Lancet* 1988;**ii**:1077.
- 8 Simpson K. Shelter deaths from pulmonary embolism. *Lancet* 1940;**ii**:744.
- 9 Carruthers M, Arguelles AE, Mosovich A. Man in transit: biochemical and physiological changes during intercontinental flights. *Lancet* 1976;**ii**:977-80.
- 10 Mills FJ, Harding RM. Fitness to travel by air. I. Physiological considerations. *Br Med J* 1983;**286**:1269-71.
- 11 Voorhoeve R, Bruyninckx CMA. Economy class syndrome. *Lancet* 1988;**ii**:1077.
- 12 Homans J. Thrombosis of the deep leg veins due to prolonged sitting. *N Engl J Med* 1954;**250**:148-9.
- 13 Collins REC, Field S, Castleden WM. Thrombosis of leg arteries after prolonged travel. *Br Med J* 1979;**4**:1478.
- 14 Beighton PH, Richards PR. Cardiovascular disease in air travellers. *Br Heart J* 1968;**30**:367-72.
- 15 Thomas JEP, Abson CP, Cairns NJW. Pulmonary embolism: a hazard of air travel. *Cent Afr J Med* 1981;**27**:85-7.
- 16 Lederman JA, Keshavarzian A. Acute pulmonary embolism following air travel. *Postgrad Med J* 1983;**59**:104-5.
- 17 Hart Y, Holdstock DJ, Lynn WA. Medical emergencies in the air. *Lancet* 1985;**i**:353-4.
- 18 Holliday J. Atypical presentation of multiple pulmonary emboli in a young air traveller. *J R Coll Gen Pract* 1985;**35**:497.
- 19 Cruickshank JM, Gorlin R, Jennett B. Air travel and thrombotic episodes: the economy class syndrome. *Lancet* 1988;**ii**:497-8.
- 20 Sarvesvaran R. Sudden natural deaths associated with commercial air travel. *Med Sci Law* 1986;**26**:35-8.

Address for correspondence: Dr R. Milne, Department of Public Health and Primary Care, Gibson Buildings, Radcliffe Infirmary, Oxford OX2 6HE.