



Flying and thromboembolism

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Summary

The risk of deep vein thrombosis and pulmonary embolism increases during, and for several weeks after, flights of four or more hours. Venous stasis due to prolonged immobility and obstruction to venous return from the legs is believed to accentuate any inherent predisposition of the traveller to venous thromboembolism. The incidence increases with flight duration, oestrogen ingestion, a prior episode of venous thromboembolism and coexisting medical or surgical conditions associated with increased risk. Clinically evident episodes occur at an incidence of about one per 4500 long-haul flights. The incidence increases in patients with other risk factors for thromboembolism, so prophylaxis with low molecular weight heparin can be considered. In people at low risk the adverse effects of prophylaxis outweigh the potential benefits.

Key words: economy class syndrome, heparin.

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Introduction

Deep vein thrombosis and pulmonary embolism related to air travel are a cause of concern. The risk of venous thromboembolism is influenced by the conditions prevailing during flight, and the passenger's inherent predisposition to develop venous thrombosis.

Factors implicated in increasing the risk of venous thromboembolism include the duration of the flight and the prothrombotic situation created by venous stasis in the lower limbs. This stasis has been attributed to prolonged immobilisation, obstruction of venous return by compression of lower limb veins and as part of a general reduction in blood flow due to in-flight dehydration. In view of the cramped conditions the problem has been called 'economy class syndrome', but this is probably a misnomer.

Features of the individual traveller associated with an increase in risk of venous thromboembolism include certain physical attributes, female gender, oral contraceptive use, inherited or acquired states that predispose to venous thromboembolism, and a previous history of venous thromboembolism.

Coexisting medical conditions which also increase the risk of venous thromboembolism include active cancer and congestive cardiac failure. These features help to determine a traveller's risk of developing venous thromboembolism.

What is the risk of venous thromboembolism in healthy travellers?

Surveys have sought to identify flight conditions and passenger characteristics that confer increased risk to healthy or 'low-risk' travellers. One relatively large study that obtained statistically significant values for certain risk factors has been helpful.¹ The increase in the risk of developing clinically significant venous thromboembolism is very low in flights of less than about four hours or 4000 km. After four hours the risk increases progressively with increasing flight duration. The average increase in incidence of venous thromboembolism relative to not undertaking a flight is about one event per 4500 passenger flights in excess of four hours. Thromboembolism is therefore a relatively uncommon event in healthy travellers on long-haul flights.¹

Most clinically significant events occur at the end of a long-haul flight or soon afterwards, with the incidence falling to baseline levels after about 2–4 weeks. People who have to take several long-haul flights increase their risk of thromboembolism.¹

Risk factors in healthy travellers

Several factors increase the relative risk of venous thromboembolism on long-haul flights (Table 1). The risk appears moderately higher in females, in keeping with the overall slightly greater on-ground risk in women. Taking a combined oral

Table 1

Factors that confer risk of venous thromboembolism on long-haul flights

Moderate risk	Relatively high risk
Oral contraceptive use	Previous venous thromboembolism
Excess body mass index	Recent surgery
Inherited thrombotic states	Congestive cardiac failure
Varicose veins	Active cancer
Short stature	Combination of moderate risk factors
	Very long-haul flights (more than 10 000 km)
	Prolonged immobility

contraceptive pill increases this risk by a similar degree to that in women who are not undertaking long-distance air travel. The risk does not increase as much in older healthy people as would be expected from the trend normally associated with increasing age.¹

Thromboembolism is more likely to occur in association with prolonged immobility, above normal body mass index, and short stature.¹⁻³ These physical characteristics have the potential to reduce venous return from the legs although venous stasis is yet to be confirmed under flight conditions. In another survey, obesity and window seating were associated with increased venous thromboembolism risk, in keeping with the likelihood of reduced mobility in those seats.³

There is evidence that healthy individuals seated for prolonged periods in aeroplane seats on the ground develop leg oedema in about four hours. There is a decrease in popliteal venous return of about 40%, with an even greater reduction if the feet do not reach the floor. It is reasonable to extrapolate that such adverse physiological consequences are equally relevant to long journeys in vehicles. While the relationship has not been scrutinised as much as in air travel, there is an association between long-distance ground travel and venous thromboembolism.

Oral contraceptives

Oral contraceptive use has been incriminated as a risk factor for venous thromboembolism during long-haul flights. This gives rise to questions about the type of oral contraceptive and whether stopping or changing to an alternative form of contraception will lower the risk of venous thromboembolism.

The increased risk of venous thromboembolism is mainly associated with the combination of oestrogen and progestogen. Later 'generation' formulations have not been associated with a lower risk. After stopping a combined oral contraceptive pill the risk of venous thromboembolism gradually returns to baseline, although this takes the equivalent of 2-3 menstrual cycles. Progestogen-only preparations have less risk of venous thromboembolism, but there is still a 2-3 month delay before the increased risk subsides if the woman switches to them from a combined pill.

Prophylaxis in low-risk travellers

While regular walks around the cabin during long-haul flights could be expected to avert the risk conferred by prolonged lower limb venous stasis, restrictions imposed by blockages in the aisle and by immobility during sleep make this impractical. It remains to be proved that performing the airlines' currently recommended leg exercises while seated will be beneficial during long-haul flights.³ However, a study under controlled conditions on the ground found that vigorous ankle flexion with feet against resistance causes prompt recovery of lower limb venous return after prolonged immobility.

Studies on small numbers of travellers have claimed to show a reduction in deep vein thrombosis from the use of lower leg compressive stockings. This benefit remains to be proven in the prevention of clinically significant venous thromboembolism in low-risk travellers.³

Antiplatelet drugs such as aspirin, or anticoagulants such as low molecular weight heparin or warfarin, have not been proven to be of benefit in reducing the incidence of venous thromboembolism in low-risk travellers. These drugs can induce bleeding so they are not recommended in this population. The known risk of adverse effects outweighs the chance of possible benefit.

Factors conferring moderate to high risk

Table 1 shows the factors associated with a moderate to high risk of venous thromboembolism during or soon after long-haul flights. While pulmonary embolism is associated with high-risk factors such as previous venous thromboembolism, active cancer and heart failure, many cases occur in patients who only have moderate risk factors.² These factors closely resemble those that confer an increased risk of venous thromboembolism under different circumstances, such as surgery or prolonged immobility in bed-bound patients. It is therefore reasonable to consider that the pathogenesis of flight-related venous thromboembolism is similar to venous thromboembolism in other situations. If the person is at high risk of thromboembolism on the ground, they will be at a greater risk during a long-haul flight. Under these circumstances the benefit of anticoagulant prophylaxis may outweigh the risk of adverse effects.

Assessing high-risk travellers

An example of an individual at high risk of venous thromboembolism would be someone with a previous history of venous thromboembolism, particularly if associated with laboratory evidence of inherited states, such as Factor V Leiden, or acquired states that predispose to venous thromboembolism (thrombophilia). While screening tests for thrombophilia have an important role in evaluating thrombotic events, they have limited value in predicting significantly increased risk during flight in healthy people. Their predictive value does however increase with a family history of venous thromboembolism or use of oral contraceptives.

Predictive value of tests

Screening tests for thrombophilia can reveal abnormalities that increase the risk of venous thromboembolism, however many other factors have a major impact on the degree of risk. The personal and family history of venous thromboembolism is particularly important information. Detection of an inherited abnormality in a healthy person with no personal or family

history of venous thromboembolism does not indicate a greater than average risk of venous thromboembolism in relation to an event such as a plane flight. Thrombophilia screening is therefore unhelpful in an intending traveller. Conversely, an unequivocal family history of venous thromboembolism indicates increased risk. Thrombophilia screening is then appropriate to evaluate whether heritable contributors to the increased risk can be identified and whether they have been transmitted to the intending traveller.

Prophylaxis in high-risk travellers

Travellers at high risk of venous thromboembolism are candidates for anticoagulant prophylaxis during the period of increased risk imposed by lengthy air travel. Those at particular risk include, for example, passengers with a history of venous thromboembolism, active cancer or recent surgery, especially orthopaedic surgery to the lower limbs. There is no evidence that aspirin protects against venous thromboembolism. Either subcutaneous low

molecular weight heparin or oral warfarin reduces the risk of venous thromboembolism. Low molecular weight heparin injected immediately before flight, in the recommended dose for prophylaxis in high-risk settings, is considerably more convenient than anticoagulation with warfarin.

References

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Flying and thromboembolism: a patient's perspective

Hannah Baird, a 38-year-old professional manager, developed a problem after the five-hour flight from Sydney to Perth.

HB: I had a deep vein thrombosis a few years ago so I wanted to reduce the risks of recurrence by drinking lots of water and moving around the cabin as much as possible. However, after standing for about 10 minutes I was asked by the flight attendant to return to my seat. The next day my left calf was a bit sore. There was no swelling so I thought it was just some muscle stiffness from sitting down for a long time. I went for a walk to try and loosen it up, but that made no difference. There was a low level ache in my calf that came and went. After two days my leg was more painful and swollen and the ache more continuous. As it was more difficult to walk, I went to an accident and emergency department.

AP: *What did the hospital say?*

HB: The doctors thought it was unlikely I had a deep vein thrombosis as my calf swelling was minimal. I had an ultrasound and was told that I had 'phlebitis'. The treatment was a daily dose of enoxaparin for six weeks. I was given one demonstration of how to inject myself and then I was discharged with no follow-up. I was told to find a general practitioner and get a referral for a nuclear medicine scan.

The hospital said that I should not fly for a month, however given the impracticalities of not returning home to Sydney

they agreed that flying after one week was possible. I could do little else but rest in my hotel, as it was difficult to walk.

AP: *How did you manage the treatment?*

HB: The injections stung a bit. I suffered bruising after my first injection, but I got better at injecting myself in the abdomen every morning. About two weeks into the six-week course my leg had improved.

At the end of the course I had a lot of syringes and needles. My local general practice would not take them because of the cost of disposal, nor could I find a pharmacy to take them. My local council has a needle disposal service, but it only operates between 9 am and 5 pm, Monday to Friday. That's not much good for people who work full-time.

AP: *Did you have further assessments?*

HB: I have no family history of thrombosis, I don't smoke and I was not taking oestrogens so my general practitioner referred me to a specialist for investigation. The specialists described my initial blood tests as 'strange', so just repeated them. These repeat tests did not show any clotting problems.

AP: *What advice were you given for future flights?*

HB: The specialist recommended that I wear stockings, drink water, no alcohol and inject a small dose of enoxaparin before and after flights, trains or car journeys of over two hours. Everybody tells you to wear support stockings, but