Thrombosis prophylaxis when travelling

Scientific information for healthcare professionals
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Effective thrombosis prophylaxis

Increase safety while travelling.

Traveller’s thrombosis is always caused by the interplay of exogenous and endogenous risk factors. Prolonged sitting in a cramped position, with the knees tightly flexed and mechanical pressure on the popliteal vein probably play a central role – in addition, individual risk factors are involved.

The frequency of travel, and longer distances is increasing. It is astonishing, therefore, that no uniform and reliable figures exist on the incidence of traveller’s thrombosis. Two things are certain:

• Certain groups of people are at considerably higher risk of developing traveller’s thrombosis.
• The type, duration and frequency of travel have a very decisive effect on the individual risk.

In this brochure, we would like to inform you about new study results on traveller’s thrombosis. The studies concern the pathogenesis, incidence and risk of traveller’s thrombosis. Emphasis is also placed on recommendations for simple preventive measures, such as the wearing of graduated compression stockings. This is because graduated thrombosis prophylaxis stockings have already been proven in the clinical setting – new studies now show that travel stockings, such as medi travel, are also suitable for preventing traveller’s thrombosis and can markedly reduce the individual risk of its development.

"With travel becoming a more important part of lives, our exposure to thromboembolic problems will increase.

medi have provided a comprehensive scientific review outlining the risks and efficacy of prophylaxis. There is no down side to the use of compression socks and with more studies demonstrating the benefit, it is difficult to see why compression socks are not recommended for all travellers.

The number of studies continues to increase and the overwhelming conclusions are clearly expressed but we still have problems in communicating this message.

This publication goes a long way to putting the problem in perspective, addressing the issues and providing sensible advice based on scientific research.”

John Scurr
vascular surgeon, London (UK)
**Background: Pathology of traveller’s thrombosis**

Long-distance journeys – whether by aeroplane, train or car - have one thing in common: The travellers spend several hours in a sitting position and their freedom of movement is severely limited. This leads to an increased risk of venous stasis, with the possible development of deep vein thrombosis of the leg. Various endogenous and exogenous factors can also increase the likelihood.

**Introduction**

Traveller’s thrombosis can occur on any long journey – not just in an aeroplane. Whenever travellers are in a sitting position for a prolonged period, this puts a strain on the lower limbs and can lead to oedema and/or thromboembolic events of the arterial and particularly the venous system.

The professional phlebology and angiology societies of Germany, Austria and Switzerland define traveller’s thrombosis as follows:

“The occurrence of a thrombosis of the deep venous system of the lower limb (with or without complications associated with pulmonary embolism) in association with a journey of many hours’ duration, mainly undertaken in a sitting position by persons who showed no indication of acute venous thromboembolism at the start of the journey.”

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**Pathology of traveller’s thrombosis**

But what exactly causes traveller’s thrombosis? It is probably a multifactorial process, in which exogenous effects interact with individual endogenous risk factors. Sitting for a long period in a constricted and cramped position in an aeroplane, bus, car or train is certainly the most important exogenous trigger of traveller’s thrombosis. The sitting position reduces the venous flow in the lower limbs by at least half.

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*Development of venous thrombi*
Lack of movement, particularly inactivity of the calf-muscle pump, and the mechanical stress on the popliteal vein through the pressure of the edge of the seat or crossing the legs further increase the venous stasis.\(^4\)

If the knee joint is tightly flexed for a long period, the venous stasis in the lower leg is particularly marked due to circulation changes in the popliteal vein. Age-dependent endothelial thickening of the venous wall can enhance this effect.\(^3\) In addition, as the venous stasis continues, biochemical changes occur: endothelial lesions with platelet and fibrin aggregation are found;\(^4\) haematocrit and the plasma protein concentration can increase markedly.\(^5\) If fluid intake is too low during the journey, the resultant dehydration increases the blood viscosity.

Air travel appears to be linked to an additional risk of thrombosis. At a cabin pressure of approximately 75 kPa, there is a fall in oxygen partial pressure and oxygen saturation. The resultant mild hypoxia can have a coagulant effect – findings include markers of activated coagulation.\(^6,7\)

In summary, the local stasis and changes in the blood composition and the vascular wall form the main exogenous triggers of traveller’s thrombosis (Virchow’s triad). The resultant specific risk of illness may initially be slight. It is considerably increased, however, by additional endogenous factors.

**Virchow’s triad describes three causes that can lead to thrombosis:**

1. Impaired blood flow: slowed flow rate, local stasis
2. Changed blood composition (viscosity, tendency to coagulation)
3. Changes in the vascular wall and endothelial reaction

**Prophylaxis with compression socks**

One possible preventive measure is the use of special compression socks for the journey:

Graduated compression stockings increase the venous blood flow\(^9\) and restore the valvular function of the veins.\(^10\) Furthermore, they reduce the venous diameter, counteract venous hypertension\(^11\) and limit the development of oedema.\(^12\) Therefore they have a favourable effect on the principal thrombosis triggers of Virchow’s triad.\(^13\)
Introduction
To date, as a result of methodological differences, prospective studies have not yet determined a uniform incidence of traveller’s thrombosis. The values vary between 0% and 10% (median of the studies listed in Table 1: 3.65%). In a large case-control study, the risk of traveller’s thrombosis was therefore investigated, paying particular attention to individual risk factors. One focus was on the effect of body weight and height, an inherited tendency to thrombosis and hormonal contraception.

Methods
Study design: 1,906 patients with a first occurrence of venous thrombosis or pulmonary embolism were questioned about their medical history and the period immediately preceding the thrombotic event. In addition, blood and DNA samples were obtained. The patients’ partners were enrolled in the study as the control group (Table 2).

Results
Out of a total of 1,906 patients, 233 patients (12%) had undertaken a journey of more than four hours’ duration during the eight weeks prior to the thrombotic event (control group: 9.5%). Of these 233 thrombotic events, 68 (29%) were diagnosed within one week of the end of the journey. Thereafter, the incidence decreased incrementally.

The following factors were associated with an increased risk (Figure 1):

- No risk factors
- Factor V Leiden mutation
- BMI > 30 kg/m²
- Height (> 1.90 m)
- Oral contraceptives

Figure 1: Increase in the thrombosis risk in travellers compared with non-travellers. (Risk sometimes even higher in association with air travel).

Table 1. The incidence of traveller’s thrombosis determined in prospective studies varies due to methodological differences.

<table>
<thead>
<tr>
<th>Year/Source</th>
<th>2001³</th>
<th>2001⁴ (LONFLIT1)</th>
<th>2001⁴ (LONFLIT2)</th>
<th>2002³</th>
<th>2003³</th>
<th>2003⁴</th>
<th>2003⁵</th>
<th>2003⁶</th>
<th>2003⁷</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Passengers</td>
<td>116</td>
<td>744</td>
<td>422</td>
<td>82</td>
<td>102</td>
<td>964</td>
<td>899</td>
<td>878</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>62</td>
<td>46</td>
<td>44.8</td>
<td>47</td>
<td>42.1</td>
<td>52</td>
<td>45</td>
<td>53.4</td>
<td></td>
</tr>
<tr>
<td>Incidence</td>
<td>10%</td>
<td>1.4%</td>
<td>4.5%</td>
<td>4.8%</td>
<td>5.8%</td>
<td>2.8%</td>
<td>0%</td>
<td>1%</td>
<td></td>
</tr>
</tbody>
</table>

*Alter = median; †The diagnosis ‘deep vein thrombosis of the leg’ was determined after ultrasonographical examination and sometimes with an additional D-dimer assay. Pre-existing deep vein thrombosis of the leg was excluded prior to the start of the journey.

Table 2. Characteristics of 1,906 patients with venous thrombosis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patient number (percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>18–69 (median 50.4) 1,906</td>
</tr>
<tr>
<td>Gender</td>
<td>Women 938 (49)</td>
</tr>
<tr>
<td></td>
<td>Men 965 (51)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>DVT(L) 1,082 (57)</td>
</tr>
<tr>
<td></td>
<td>PE 611 (32)</td>
</tr>
<tr>
<td></td>
<td>DVT(L) + PE 213 (11)</td>
</tr>
</tbody>
</table>

DVT(L): deep vein thrombosis of the leg; PE: pulmonary embolism.

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2 Chee, Y.L. et al. (2005): Air travel and thrombosis, in Br J Haematol; 130, p. 671–680
No risk factors: In travellers with no additional risk factors, the thrombosis risk was increased 2-fold compared with non-travellers. There was no significant difference between the types of journey undertaken. In travellers who did present with certain risk factors, however, air travel in particular was associated with a marked increased thrombosis risk.

Factor V Leiden: In travellers who carried a factor V Leiden, the thrombosis risk was increased 8-fold compared with travellers without factor V Leiden. In association with air travel, the probability was increased 13.6-fold in this group.

BMI > 30 kg/m²: There was a 10-fold increase in the thrombosis risk in travellers with a BMI > 30 kg/m².

Height: In very tall people (≥ 1.90 m), the risk of thrombosis was increased 4.7-fold compared with non-travellers of average height (1.60–1.90 m). In association with air travel, the risk was increased 6.8-fold in this group. In travellers of smaller stature (< 1.60 m), a flight also increased the likelihood of thrombosis.

Oral contraceptives: In women, intake of oral contraceptives additionally increased the probability of developing traveller’s thrombosis by a factor of 2.4 for car, bus or train journeys and by a factor of 4.9 for air travel.

Conclusions
For travellers without any additional risk factors, there is a 2-fold increase in the possibility of thrombosis — irrespective of the type of journey.

Endogenous factors increase the individual risk (factor V Leiden, BMI > 30 kg/m², height [≥ 1.85 m; < 1.65 m], oral contraceptives).

In travellers with such indicators, air travel affects the individual thrombosis risk to a greater extent than other types of travel (up to 13.6-fold in travellers with factor V Leiden).

The thrombosis risk therefore appears to derive mainly from the long period of immobility. The mildly hypoxic conditions during a flight can additionally promote the development of a thrombosis in certain groups of people.

Information on individual risk factors
(recommended by Bartholomew and colleagues):

The review by Bartholomew et al. (2011) summarises current findings with regard to the thrombosis risk associated with air travel:

Age
- Advanced age (the risk increases from 40 years of age)

Weight
- Body mass index > 30 kg/m²

Medicines
- Oral contraceptives
- Hormone replacement therapy

Medical risk factors
- A history of venous thromboembolism (deep vein thrombosis, pulmonary embolism)
- Varicose veins
- Serious diseases (congestive heart failure, chronic obstructive pulmonary disease, stroke with paralysis or paresis, pneumonia)
- Pregnancy (up to six weeks postpartum)
- Cancer and chemotherapy
- Central venous catheter
- Thrombophilia (e.g. factor V Leiden, prothrombin G20210A mutation, protein C and protein S deficiency, antithrombin deficiency, antiphospholipid syndrome, factor VIII increase)
- Recent confinement to bed lasting longer than three days
- Recent fixation / immobilisation (e.g. of a lower limb)
- Recent surgery with general or local anaesthesia (within the 12 weeks prior to a flight)
- Recent trauma with venous compression (haematoma, fracture)

Height
- < 1.65 m
- > 1.85 m

Flight duration
- Single long-haul flight, longer than eight to ten hours
- Several long-haul flights, each longer than four hours

Introduction
In view of the large number of long-haul flights, the aim of this meta-analysis was to determine any possible association between journey duration and the travel-associated thrombosis risk.

Methods
Included in the analysis were observational studies and clinical studies that investigated the frequency of venous thromboembolism (VTE) in travellers. Diagnoses were made using ultrasonography or venography. Studies published up to March 2008 were included in the analysis. A total of 14 studies with 4,055 VTE cases were included in the evaluation. The following were assessed:

1. How the VTE risk differs between travellers and non-travellers and
2. What part the journey duration plays.

Results
Taking the studies as a whole, the increase in the travel-associated VTE risk was between 2.0-fold and 2.8-fold. Four studies investigated the association between dose and effect. They showed that every 2-hour prolongation of travel time increases the VTE risk by 18%.3-6 If the focus was purely on air travel, the VTE risk increased by as much as 26% for every additional 2 hours of flying time.

Conclusion
Travel is associated with an up to 3-fold rise in the VTE risk, which, however, increases significantly with the journey duration. Air travel leads to a greater increase than other types of journey (Figure 1).

Air travel, in particular, can promote the development of traveller’s thrombosis.7

Introduction
Air travel is suspected of increasing the risk of pulmonary embolism (PE). In one study, Lapostolle et al. investigated this association and compared the risk of short-, medium- and long-haul flights.

Methods
This study was based on data from passengers who were admitted to hospital with suspected PE between November 1993 and December 2000 following their arrival at Paris Charles de Gaulle airport (France). Of these passengers, those in whom a diagnosis of PE was confirmed on the basis of ventilation/perfusion scan, pulmonary angiography or computed tomography were enrolled in the study. Data on the length and duration of the flight and individual risk factors were collected from these passengers.

Results
During the course of the study, 170 air passengers with suspected PE were admitted to a local hospital; the diagnosis of PE was confirmed in 56 of these passengers. The mean age of the patients was 57 ± 12 years. In four of these 56 patients, a high endogenous thrombosis risk was determined on the basis of individual factors. In the majority (87.5%), however, this risk was moderate (average thrombosis risk). Three-quarters of the patients stated that they had not left their seat during the flight. Analysis of the travel data showed a significant association between the flight distance and the PE incidence. The incidence increased from 0.11 for flight distances of less than 5,000 km to 4.77 for flight distances of more than 10,000 km (Figure 2).

Figure 1: The travel-associated VTE risk increases with the journey duration
Conclusion
The flight duration represents a significant risk factor for PE. Therefore, recommendations for avoiding thrombotic events should particularly be heeded on long-haul journeys. These include regular movement, sufficient fluid intake, avoidance of alcohol and the wearing of compression stockings.

Introduction
In 2010, over 2.5 billion passengers worldwide undertook a flight and travelled 4.685 billion kilometres – corresponding to an increase of 8% compared with the previous year. And the numbers are increasing all the time: for 2016, the International Air Transport Association predicts an increase to 3.6 billion passengers. Despite the growing rate of air travel, the airlines appear to have only minimal awareness of the problem of traveller’s thrombosis, at least according to the study by Scurr et al.: it investigated to what extent airlines address the issue of in-flight thrombosis on their websites.

Methods
Three independent investigators analysed the official websites of 107 airlines that fly to Heathrow airport (UK) and John F. Kennedy airport (USA) (2007). All the airlines included offer long-haul flights. The assessment considered whether
(1) airlines point out the risk of traveller’s thrombosis and whether they
(2) make recommendations with regard to its prevention.

Results
Only approximately 25% of the airlines (27/107) mentioned the possibility of traveller’s thrombosis on their websites. On 10% of the websites, this risk was merely stated, without any explanation of risk factors or preventive measures (Figure 1).

Conclusion
Despite the increase in travel, most airlines provide their passengers with only inadequate information on the issue of traveller’s thrombosis. Passengers should be given more information about their individual risk and about simple preventive measures.

Relevance: Behaviour while travelling and risk awareness

Travellers are rarely informed about thrombosis prophylaxis by the airlines themselves - there is potential for the airlines to improve the amount of information available for the benefit of travellers.

15% of the websites named explicit risk factors, such as medical history and familial clustering of venous thrombosis, thrombophilia, age, cancer, obesity, pregnancy, oral contraceptives, hormone replacement and recent surgery. Approximately one-third of the websites advised doing regular exercises and taking in sufficient fluid during the flight. Less than 15% of websites mentioned graduated compression stockings for thrombosis prophylaxis while travelling.

Figure 1: 25% of airlines indicate the risk of traveller’s thrombosis on their websites. Only 15% name individual risk factors (last revised: 2007).

References
1 Scurr, J.R. et al. (2010): Traveller’s thrombosis: airlines still not giving passengers the WRIGHT advice!, in: Phlebology; 25, p. 257–260
Prophylaxis of traveller’s thrombosis with graduated compression stockings

Compression stockings are a long-established measure in the treatment of venous disorders and are considered basic therapy. Their use in thrombosis prophylaxis while travelling is therefore a logical consequence.1

Introduction
The efficacy of graduated compression stockings in thrombosis prophylaxis has been clearly documented in the clinical setting.2 The aim of this study was to investigate whether graduated compression stockings are also suitable for the prevention of traveller’s thrombosis.

Methods
This systematic review examined studies that had investigated the effect of graduated compression stockings on the frequency of deep vein thrombosis of the leg after air travel. Only those studies in which air passengers were randomly allocated to treatment and control groups were considered.

Table 1: Graduated compression stockings for the prevention of traveller’s thrombosis

<table>
<thead>
<tr>
<th>Study</th>
<th>Flight duration (h)</th>
<th>Risk group</th>
<th>Compression mm Hg</th>
<th>Treatment group</th>
<th>Control group</th>
<th>Difference (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[1]*</td>
<td>n.s.</td>
<td>n.s.</td>
<td>18–21</td>
<td>0/100 (0)</td>
<td>12/100 (12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>[2]*</td>
<td>10–15</td>
<td>3</td>
<td>25</td>
<td>1/411 (0.2)</td>
<td>19/422 (4.5)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>[3]*</td>
<td>7–8</td>
<td>1,2</td>
<td>14–17</td>
<td>0/179 (0)</td>
<td>4/179 (2.2)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>[4]*</td>
<td>11–12</td>
<td>1,2</td>
<td>14–17</td>
<td>0/136 (0)</td>
<td>3/135 (2.2)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>[5]*</td>
<td>7–8</td>
<td>1,2</td>
<td>14–17</td>
<td>0/97 (0)</td>
<td>0/98 (0)</td>
<td></td>
</tr>
<tr>
<td>[6]*</td>
<td>11–12</td>
<td>1,2</td>
<td>14–17</td>
<td>0/75 (0)</td>
<td>0/71 (0)</td>
<td></td>
</tr>
<tr>
<td>[7]*</td>
<td>7–8</td>
<td>1,2</td>
<td>20–30</td>
<td>0/72 (0)</td>
<td>0/72 (0)</td>
<td></td>
</tr>
<tr>
<td>[8]*</td>
<td>11–12</td>
<td>1,2</td>
<td>20–30</td>
<td>0/64 (0)</td>
<td>2/66 (3.0)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>[9]*</td>
<td>11–12</td>
<td>3</td>
<td>14–17</td>
<td>1/103 (1.0)</td>
<td>6/102 (5.9)</td>
<td>&lt;0.025</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td>2 of 1237 (0.16%)</td>
<td>46 of 1245 (3.69%)</td>
<td></td>
</tr>
</tbody>
</table>

In all studies, deep vein thrombosis of the leg was diagnosed using ultrasonography; *Measured at the ankle (data refers to the treatment group); #Thrombosis prophylaxis with graduated compression stockings; n.s. = not specified; Risk group: 1− low risk (no additional risk factors); 2− moderate risk (pregnancy, age, clinically relevant disease, thrombophilia, tendency to thrombosis, venous insufficiency, oral contraceptives, hormone replacement therapy, obesity, dehydration); 3− high risk (history of venous thromboembolism, malignant or other severe disease, immobilisation [e.g. plaster cast], previous surgery).
In the treatment groups, various graduated compression stockings were used. The primary endpoint was deep vein thrombosis.

Results
Nine randomised controlled studies with a sample size of more than 2,000 passengers were analysed. Of these passengers, 55% had a low or moderate thrombosis risk and 45% had a high thrombosis risk.

All nine studies investigated the effect of air travel of at least seven hours’ duration.

In the treatment group (n= 1,237), two cases of deep vein thrombosis of the leg occurred; in the control group without prophylaxis through compression (n=1,245), the corresponding figure was 46 (Table 1).

Thus, the incidence of deep vein thrombosis of the leg was 0.16% when graduated compression stockings were worn. In the untreated control group, the corresponding figure was 3.69% (Figure 1).

Conclusion
Graduated compression stockings are appropriate for significantly reducing the risk of a flight-associated deep vein thrombosis of the leg in passengers with a moderate or high risk of thrombosis.


medi travel — compression socks for people with a healthy venous system.

- medi travel women: semi-transparent below-knee sock
- medi travel men: opaque knit fine-rib below-knee sock
  - quick and easy donning
  - soft material that is pleasant next to the skin

medi travel compression socks are available without prescription from specialist medical retailers.

mediven plus — the medical compression stocking available on prescription for travellers with an indication

- All-round stocking, also suitable when travelling
- Particularly advisable for sensitive or very wide thighs
- For moderate to severe venous disease, for varicose veins or after thrombosis
- Opaque knit that conceals e.g. varicose veins
- Soft but hardwearing, opaque material — also available in thigh-length and as a pantyhose
Recommendations and summary

Risk groups and recommendations

Recommendations for passengers at low risk of thrombosis (Group 1)
Travellers with no additional risk factors: In this case, the individual risk mainly derives from the duration of the journey. Moreover, even in persons with a low potential for thrombosis, preventive measures can be appropriate on very long journeys.

- Moving the lower limbs (calf-muscle pump) by regularly standing up and doing exercises while sitting down; regular breaks
- Fluid intake of > 0.25 L every two hours (water, juice)
- Avoid tranquilisers and sleeping tablets
- Avoid coffee and alcoholic drinks, due to their diuretic effect
- Wear loose and non-restrictive clothing
- Freedom of movement for the legs (no luggage in the footwell)

Recommendations for passengers at moderate risk of thrombosis (Group 2)
Passengers in Risk Group 2 have the following indicators (please note that two or more risk factors can increase the risk:
- Pregnancy, postpartum phase
- Age > 60 years
- Confirmed thrombophilia, tendency to venous thromboembolism
- Large varicose veins, chronic venous insufficiency
- Oral contraceptives, hormone replacement therapy
- Obesity (BMI > 30 kg/m²)
- Height (> 1.85 m and < 1.65 m)
- General measures as in Group 1
- Compression stockings with at least 10–20 mm Hg pressure area (but 20–40 mm Hg in chronic venous insufficiency)
- In individual cases – drug prophylaxis

Recommendations for passengers at high risk of thrombosis (Group 3)
Passengers in Risk Group 3 have the following indicators (please also note the points on the individual risk factors for airline passengers on page 11):
- Known thromboembolism
- Malignant or other severe disease
- Immobilisation (e.g. plaster cast)
- Recent surgical procedure
- General measures (Group 1)
- Compression stockings (Group 2)
- Drug prevention

Summary

We all enjoy travelling often, but cramped sitting conditions, lack of movement and insufficient fluid intake increase the risk of developing traveller’s thrombosis. Certain groups are at particularly high risk, such as those who are elderly, overweight or pregnant or patients with a familial clustering of varicose veins.

But even travellers without risk factors should consider thrombosis prophylaxis, as the risk of its development increases with the length of the journey.

Study data confirm: Travel stockings with a graduated compression, such as medi travel, can reduce the risk of traveller’s thrombosis. They increase the reflux of blood in the veins, the venous valvular function and ensure that venous hypertension and oedema formation are limited. In this way, deep vein thrombosis of the leg can be avoided.


medi Tipp
Pass on these tips during your patient consultations (e.g., in the form of an information sheet to take away), as many people fail to consider thrombosis prophylaxis when planning their holiday.