



EDUCATIONAL OBJECTIVE: Readers will take steps to minimize the risk of venous thromboembolism in their patients who are contemplating long-distance air travel

JOHN R. BARTHOLOMEW, MD

Professor of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH; Head, Section of Vascular Medicine, Departments of Cardiovascular Medicine and Hematology/Oncology, Heart and Vascular Institute, Cleveland Clinic

JONATHAN L. SCHAFER, MD, MBA

Managing Director, eClevelandClinic, Information Technology Division, Cleveland Clinic

GEORGES F. McCORMICK, MD

Office of Medical Services, US Department of State, Washington, DC

Air travel and venous thromboembolism: Minimizing the risk

ABSTRACT

For those traveling on long flights, the risk of deep vein thrombosis or pulmonary embolism, generally referred to as venous thromboembolism (VTE), is real and dangerous if left unrecognized or untreated. The goal of this publication is to provide an overview of how best to prevent VTE during travel, and how to diagnose and treat it.

KEY POINTS

The risk of VTE is about three times higher in passengers on long-distance flights than in the general population, although the absolute risk is still low.

All long-distance air passengers should perform stretching exercises once an hour while in flight to prevent VTE. They should also stay hydrated.

For patients at higher risk due to hypercoagulable conditions, physicians can consider prescribing compression stockings or an anticoagulant drug (a low-molecular-weight heparin or a factor Xa inhibitor) to be taken before the flight, or both.

The evaluation of a patient with suspected VTE should include an estimation of the pretest probability of disease. If symptoms dictate, duplex ultrasonography of the upper or lower extremity to detect deep vein thrombosis or spiral computed tomography, ventilation-perfusion lung scan, or pulmonary angiography (where available) to diagnose an acute pulmonary embolism should be ordered.

Editor's Note: The views expressed in this article are solely those of the authors and do not reflect the official policy or position of the Department of State or the United States Government. This version of the article was peer-reviewed.

VENOUS THROMBOEMBOLISM (VTE) associated with travel has emerged as an important public health concern over the past decade. Numerous epidemiologic and case control studies have reported air travel as a risk factor for the development of VTE and have attempted to determine who is at risk and which precautions need to be taken to prevent this potentially fatal event.¹⁻⁷ Often referred to as “traveler’s thrombosis” or “flight-related deep vein thrombosis,” VTE can also develop after long trips by automobile, bus, or train.^{8,9} Although the absolute risk is very low, this threat appears to be about three times higher in travelers and increases with longer trips.³

See related patient information material, page 121

This article focuses on defining VTE and recognizing its clinical features, as well as providing recommendations and guidelines to prevent, diagnose, and treat this complication in people who travel.

WHAT IS VENOUS THROMBOEMBOLISM?

Deep vein thrombosis and pulmonary embolism represent different manifestations of the same clinical entity, ie, VTE. VTE is a common, lethal disease that affects hospitalized and nonhospitalized patients, frequently re-

curs, is often overlooked, may be asymptomatic, and may result in long-term complications that include pulmonary hypertension and the postthrombotic syndrome.

The leg veins are the most common site of deep vein thrombosis, accounting for nearly 90% of all cases; other locations include the arm and pelvic veins (FIGURE 1). Deep vein thrombosis in a proximal lower extremity (ie, involving the popliteal, femoral, common femoral, or external iliac vein) has an estimated 50% risk of migrating and leading to an acute pulmonary embolism if not treated, while approximately 25% of deep vein thromboses in the calf veins will, if not treated, propagate to involve the aforementioned veins.

Deep vein thrombosis of the upper extremities is generally related to an indwelling venous catheter or a central line being used for long-term administration of antibiotics, chemotherapy, or nutrition. A condition known as Paget-Schroetter syndrome or “effort thrombosis” may be seen in younger or athletic people who have a history of strenuous or unusual arm exercise.

■ RISK FACTORS FOR VTE

Most patients who develop VTE have one or more risk factors for it (TABLE 1), the presence of which is often referred to as a hypercoagulable state or thrombophilia. These risk factors are generally classified as either genetic (inherited) or acquired (environmental). Most VTE events are in fact associated with a combination of genetic and acquired risk factors.

Common inherited risk factors include:

- Factor V Leiden mutation
- Prothrombin gene mutation G20210A
- Hyperhomocysteinemia
- Deficiency of the natural anticoagulant proteins C, S, or antithrombin
- Elevated levels of factor VIII (may be inherited or acquired).

Acquired risk factors include:

- Older age
- Immobilization or stasis (such as sitting for long periods of time while traveling)
- Surgery (most notably orthopedic procedures including hip and knee replacement and repair of a hip fracture)
- Trauma

- Stroke
- Acute medical illness (including congestive heart failure, chronic obstructive pulmonary disease, pneumonia)
- The antiphospholipid syndrome (consisting of a lupus anticoagulant, anticardiolipin antibodies, or both)
- Pregnancy and the postpartum state
- Use of oral contraceptives or hormone replacement therapy
- Cancer (including the myeloproliferative disorders) and certain chemotherapeutic agents
- Obesity (a body mass index $> 30 \text{ kg/m}^2$, see www.nhlbisupport.com/bmi/)
- Inflammatory bowel disease
- Previous VTE
- A central venous catheter or pacemaker
- Nephrotic syndrome.

In addition, emerging risk factors more recently recognized include male sex, persistence of elevated factor VIII levels, and the continued presence of an elevated D-dimer level or deep vein thrombosis on duplex ultrasonography once anticoagulation treatment is completed. There is also evidence of an association between VTE and risk factors for atherosclerotic arterial disease such as smoking, hypertension, hyperlipidemia, and diabetes.

■ CLINICAL MANIFESTATIONS OF VTE

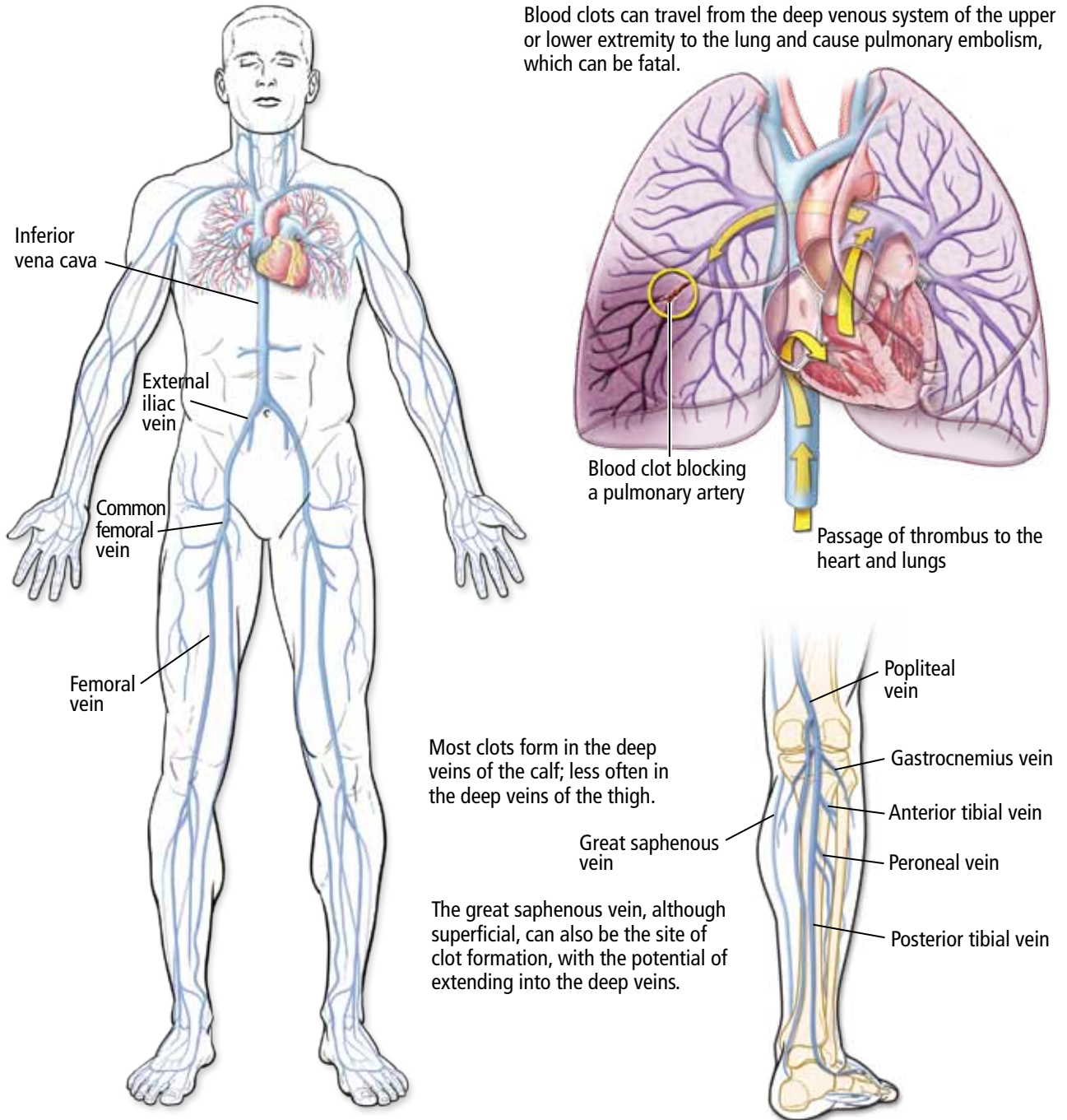
Patients with deep vein thrombosis may complain of pain, swelling, or both in the leg or arm. Physical examination may reveal increased warmth, tenderness, erythema, edema, or dilated (collateral) veins, most notable on the upper thigh or calf (for deep vein thrombosis in the lower extremity) or the chest wall (for upper-extremity deep vein thrombosis). The examiner may also observe a tender, palpable cord, which represents a superficial vein thrombosis involving the great and small saphenous veins (FIGURE 1). In extreme situations, the limb may be cyanotic or gangrenous.

A recommended clinical decision algorithm that can help assess a patient's risk for an acute deep vein thrombosis prior to testing is depicted in TABLE 2.¹⁰ Patients with acute pulmonary embolism are likely to complain of the sudden onset of shortness of breath, pleuritic chest pain (especially with breathing),

When VTE occurs, it is a life-altering and life-threatening event

Deep venous thrombosis and pulmonary embolism

Sitting for long periods during long flights can lead to venous stasis and deep venous thrombosis. Although the absolute risk is low, it is higher in those with preexisting risk factors for thrombosis, who may need preventive treatment (TABLE 6). All travelers should periodically stretch and move their legs (see patient education page).



CCF
Medical Illustrator: Bill Garriott ©2011

FIGURE 1

TABLE 1

Risk factors for venous thromboembolism

Age

Older age, with increasing risk after age 40

Weight

Body mass index > 30 kg/m²
(can be calculated as [mass in pounds × 703] / [height in inches²]; see www.nhlbisupport.com/bmi/)

Medications

Women taking oral contraceptives or hormone replacement

Medical or surgical issues

Previous venous thromboembolism, either deep venous thrombosis or pulmonary embolism

Varicose veins

Medical illness (congestive heart failure, chronic obstructive pulmonary disease, stroke with paralysis or paresis, pneumonia)

Pregnancy and up to 6 weeks postpartum

Active cancer or cancer chemotherapy

Central venous catheter placement

Thrombophilia disorders, including factor V Leiden mutation, prothrombin G20210A gene mutation, protein C and S deficiencies, antithrombin deficiency, antiphospholipid syndrome, elevated levels of factor VIII

Recently bedridden more than 3 days

Recent cast immobilization or major surgery (within 12 weeks before flying that required general or regional anesthesia)

Recent trauma within 3 months (or anything that compresses the veins such as a hematoma or fracture)

Additional risk factors specific to air travelers

Height

People who are under 165 cm (65 inches or 5 feet 5 inches) in height⁴

People who are over 185 cm (73 inches or 6 feet 1 inch) in height⁴

Flight duration

Single long-haul flights of more than 8 to 10 hours

Multiple long-haul flights of at least 4 hours (risk may persist up to 8 weeks after the flight)⁴

More frequent flights of any duration within a short time frame (ie, days or 3 weeks)

syncope, cough, or hemoptysis. A clinical decision algorithm that can help assess the risk of acute pulmonary embolism prior to testing is depicted in **TABLE 3**.¹¹

■ DIAGNOSIS OF VTE

Clinical examination alone is generally insufficient to confirm a diagnosis of deep vein thrombosis or pulmonary embolism. Venous

duplex ultrasonography is the most dependable investigation for deep vein thrombosis, but other tests include D-dimer and imaging studies such as computed tomographic venography or magnetic resonance venography of the lower extremities. A more invasive approach is venography; formerly considered the gold standard, it is now generally used only when the diagnosis is in doubt after noninvasive testing. The diagnosis of acute pulmonary embolism is best made by spiral computed tomography.

Other studies that may prove helpful include a ventilation-perfusion lung scan for patients who cannot undergo computed tomography due to a contrast allergy or renal insufficiency. Pulmonary angiography, while the gold standard, is less commonly used today, given the specificity and sensitivity of computed tomography.

Echocardiography at the bedside may be useful for patients too sick to move, although the study may not be diagnostic unless thrombi are seen in the heart or pulmonary arteries.

■ TREATMENT OF VTE

Treatments for VTE are summarized in **TABLE 4**. The length of treatment for acute VTE is generally 3 to 6 months. Patients with a known precipitating cause such as recent surgery or oral contraceptive use normally require 3 months of therapy, while those who had an unprovoked (idiopathic) event require longer therapy, sometimes continuing indefinitely.

For acute deep venous thrombosis

Acute deep vein thrombosis is now treated on an outpatient basis under most circumstances.

Unfractionated heparin is given intravenously for patients who need to be hospitalized, or subcutaneously in full dose for inpatient or outpatient treatment.

Low-molecular-weight heparins are available in subcutaneous preparations and can be given on an outpatient basis.

Fondaparinux (Arixtra), a factor Xa inhibitor, can also be given subcutaneously on an outpatient basis. Equivalent products are available outside the United States.

Warfarin (Coumadin), an oral vitamin K inhibitor, is the agent of choice for long-term

TABLE 2

Clinical decision rule to help estimate the pretest probability of deep vein thrombosis

CLINICAL FEATURES	POINTS
Active cancer (treatment ongoing or within the previous 6 months or palliative treatment)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden for more than 3 days or major surgery within 12 weeks requiring general or regional anesthesia	1
Local tenderness along the distribution of the deep venous system	1
Entire leg swelling	1
Calf swelling (more than 3 cm greater than the asymptomatic side) measured 10 cm below the tibial tuberosity	1
Pitting edema in the symptomatic leg	1
Collateral superficial veins	1
Previous deep vein thrombosis	1
Alternative diagnosis at least as likely	-2

The clinical probability of deep vein thrombosis is high if the total score is 3 or more, intermediate if the score is 1 or 2, and low if the score is 0.

USED WITH PERMISSION AND ADAPTED FROM WELLS PS, OWENS C, DOUCETTE S ET AL. DOES THIS PATIENT HAVE DEEP VEIN THROMBOSIS? JAMA 2006; 295:199-207.

management of deep vein thrombosis.

Other oral agents are available outside the United States.

For pulmonary embolism

Outpatient treatment of pulmonary embolism is not yet advised: an initial hospitalization is necessary. The same anticoagulants used for deep vein thrombosis are also used for acute pulmonary embolism.

Empiric treatment in underdeveloped countries

VTE may be an even greater concern on an outbound trip to a remote area, where medical care capabilities may be less than ideal and diagnostic and treatment options may be limited.

If there is a high pretest probability of acute VTE (TABLE 2, TABLE 3) and no diagnostic methods are available, empiric treatment with any of the parenteral anticoagulant agents listed in TABLE 4 is an option until the diagnosis can be confirmed. Caveats:

- Care must be taken to be certain there is not a strong contraindication to the use of anticoagulation, such as bleeding or a drug allergy.

- Neither unfractionated heparin nor any of the low-molecular-weight heparins should be given to a patient who has a history of heparin-induced thrombocytopenia.
- In patients who have chronic kidney disease (creatinine clearance less than 30 mL/minute), the dosage of low-molecular-weight heparins must be adjusted and factor Xa inhibitors avoided. Both of these types of anticoagulants should be avoided in patients on hemodialysis.

More aggressive therapy

Under select circumstances a more aggressive approach to the treatment of VTE may be necessary. These options are usually indicated for a patient with a massive deep vein thrombosis of a lower extremity and for certain patients with an upper extremity deep vein thrombosis. Treatments include catheter-directed thrombolytic therapy and endovenous or surgical thrombectomy.

Thrombolytic therapy is recommended for a patient with an acute pulmonary embolism who is clinically unstable (systolic blood pressure lower than 90 mm Hg), if there is no contraindication to its use (bleeding risk or recent stroke or surgery). Thrombolytic therapy

Clinical examination alone is generally insufficient to confirm a diagnosis of deep vein thrombosis or pulmonary embolism

TABLE 3

Clinical decision rule to estimate the pretest probability of pulmonary embolism

CLINICAL FEATURES	SCORE
Clinical signs and symptoms of deep venous thrombosis	3
Pulmonary embolism is as likely as or more likely than an alternative diagnosis	3
Heart rate > 100 beats/minute	1.5
Immobilization or surgery in the previous 4 weeks	1.5
Previous pulmonary embolism or deep vein thrombosis	1.5
Hemoptysis	1
Cancer (receiving treatment or treated in the last 6 months or palliative care)	1

Pulmonary embolism is likely if the total score is more than 4, unlikely if the score is 4 or less.

USED WITH PERMISSION AND ADAPTED FROM ARNASON T, WELLS PS, FORESTER AJ. APPROPRIATENESS OF DIAGNOSTIC STRATEGIES FOR EVALUATING SUSPECTED VENOUS THROMBOEMBOLISM. *THROMB HAEMOST* 2007; 97:195-201.

The length of treatment for acute VTE is generally 3 to 6 months

is also an option for those at low risk of bleeding with an acute pulmonary embolism who have signs and symptoms of right heart failure proven by echocardiography.

Surgical pulmonary embolectomy for acute massive pulmonary embolism and **mechanical thrombectomy** for extensive deep vein thrombosis are generally available only at highly sophisticated tertiary care centers.

An inferior vena cava filter is advised in patients with acute deep vein thrombosis or pulmonary embolism who cannot be fully anticoagulated, to prevent the clot from migrating from the lower extremities to the lungs. These filters are available as either permanent or temporary implants. Some temporary versions can remain in place for up to 150 days after insertion.

PREVENTION OF VTE

Prevention is the standard of care for all patients admitted to the hospital and in select individuals as outpatients who are at high risk of VTE.

A number of anticoagulant drugs are available in the United States for prophylaxis, including unfractionated heparin, low-molecular-weight heparin preparations, and fondaparinux (all of these given subcutaneously) and warfarin. In Europe and Canada, additional low-molecular-weight heparin preparations, factor Xa inhibitors, and direct thrombin inhibitors

are available that have proven to be equally effective (**TABLE 5**).

Mechanical compression (graduated compression stockings, intermittent pneumatic compression devices) has proven effective in reducing the incidence of deep vein thrombosis and pulmonary embolism postoperatively in patients who cannot take anticoagulants. One study has demonstrated that compression stockings may also be effective in preventing VTE during travel.¹²

ABSOLUTE RISK IS LOW

Over the past decade, special attention has been paid to travel as a risk factor for developing VTE.¹³ Traveler’s thrombosis has become an important public health concern. Numerous publications and epidemiologic studies have targeted air travel in an attempt to determine who is at risk and what precautions are necessary to prevent this complication.^{1-7,9}

The incidence of VTE following air travel is reported to be 3.2 per 1,000 person-years.⁴ While this incidence is relatively low, it is still 3.2 times higher than in the healthy population that is not flying.

The more serious complication of VTE, ie, acute pulmonary embolism, occurs less often. In three studies, the reported incidence ranged from 1.65 per million patients in flights lon-

TABLE 4

Treatments for venous thromboembolism**PHARMACOLOGIC METHODS****Heparin in full doses^a**

Intravenous: 80 units/kg bolus followed by 18 units/kg/hour

OR

Subcutaneous: 5,000 units intravenous bolus followed by 17,500 units subcutaneously every 12 hours

OR

333 units/kg subcutaneous bolus followed by 250 units/kg subcutaneously every 12 hours

Low-molecular-weight heparins^{a,b}

Enoxaparin (Lovenox) 1 mg/kg subcutaneously every 12 hours, assuming renal function is normal

Dalteparin (Fragmin) 200 units/kg subcutaneously every 24 hours

Tinzaparin (Innohep) 175 units/kg subcutaneously every 24 hours

All low-molecular-weight heparin preparations must be dose-adjusted if there is renal insufficiency (creatinine clearance < 30 mL/min) and are contraindicated in patients on hemodialysis

Fondaparinux (Arixtra)^{a,b}

Weight-dependent dosing:

5 mg subcutaneously every 24 hours for patients weighing < 50 kg

7.5 mg subcutaneously every 24 hours for patients weighing 50 to 100 kg

10 mg subcutaneously every 24 hours for patients weighing over 100 kg

All factor Xa inhibitors are contraindicated if there is renal insufficiency (creatinine clearance < 30 mL/min) or patients on hemodialysis

Warfarin (Coumadin)^b

Available in tablets of 1, 2, 2.5, 3, 4, 5, 6, 7.5, and 10 mg

Tissue plasminogen activator (Activase)^a

100 mg intravenously over 2 hours for acute pulmonary embolism in life-threatening conditions (hemodynamic instability) or at the physician's discretion if signs of right heart failure are present

Contraindicated if bleeding risk exists or recent stroke or surgery

MECHANICAL METHODS**Inferior vena cava filters (temporary or permanent)****Mechanical thrombectomy for deep vein thrombosis, pulmonary embolectomy for pulmonary embolism**

These procedures are generally performed only at tertiary medical centers

Graduated compression stockings

30 to 40 mm Hg to prevent the postthrombotic condition. Should be given to *all* patients with lower-extremity deep vein thrombosis. If they are unable to comply with that much compression, a lower-compression stocking may be substituted (ie, 20 to 30 mm Hg).

^a See package insert for additional instructions and specific contraindications

^b Other agents of this class are available outside the United States

TABLE 5

Methods to prevent venous thromboembolism during air travel

PHARMACOLOGIC METHODS

Low-molecular-weight heparins

Enoxaparin (Lovenox) 40 mg subcutaneously prior to departure (just once a day)

Dalteparin (Fragmin) 5,000 IU subcutaneously prior to departure (just once a day)

All low-molecular-weight heparin preparations must be dose-adjusted if there is renal insufficiency (creatinine clearance < 30 mL/min) and are contraindicated in patients on hemodialysis. There are additional equivalent low-molecular-weight heparins available in other countries.

Factor Xa inhibitors

Fondaparinux (Arixtra) 2.5 mg subcutaneously prior to departure (just once a day)

Rivaroxaban (Xarelto) (approved in Europe and Canada; not approved in the United States for prophylaxis)

All factor Xa inhibitors are contraindicated in patients with renal insufficiency (creatinine clearance < 30 mL/min) or on hemodialysis

Direct thrombin inhibitor

Dabigatran (Pradaxa in Europe and United States, Pradax in Canada); not approved in the United States for prophylaxis

MECHANICAL METHODS

Exercises while traveling (see patient education page)
 Graduated compression stockings (15–30 mm Hg)

ger than 8 hours to a high of 4.8 per million patients in flights longer than 12 hours or distances exceeding 10,000 km (6,200 miles).^{5,14,15} For the 400 passengers on the average long-haul flight of 12 hours, there is at most a 0.2% chance that somebody on the plane will have a symptomatic VTE).

RISK FACTORS IN LONG-DISTANCE TRAVELERS

The risk of traveler’s thrombosis has recently attracted the attention of passengers and the airline industry. Airlines are now openly dis-

cussing the risk and providing reminders such as exercises that should be undertaken in-flight (see the patient information page that accompanies this article). Some airlines are recommending that all patients consult their doctor to assess their personal risk of deep vein thrombosis before flying.

The most common risk factors for VTE in travelers are well established and are additive (TABLE 1). The extent of the additive risk, however, is not entirely clear.

What is clear is that when VTE occurs it is a life-altering and life-threatening event. If it occurs on an outbound trip, the local resources and capabilities available at the destination may not be adequate for optimal treatment. If a traveler experiences a VTE event on an outbound trip, an emergency return trip to the continental United States or a regional center of expertise may be required. There is an additive risk with this subsequent travel event if the patient is not given immediate treatment first (TABLE 4). Hence, treatment prior to evacuation should be strongly considered.

The traveler must also be aware that VTE can be recognized up to 2 months after a long-haul flight, though it is especially a concern within the first 2 weeks after travel.^{2,4,16,17}

RECOMMENDATIONS FOR LONG-DISTANCE AIR TRAVELERS

Each person should be evaluated on a case-by-case basis for his or her need for VTE prophylaxis. Medical guidelines for airline passengers have been published by the Aerospace Medical Association and the American College of Chest Physicians (ACCP).^{18,19} In general, travelers should:

- Exercise the legs by flexing and extending the ankles at regular intervals while seated (see the patient information material that accompanies this article) and frequently contracting the calf muscles.
- Walk about the cabin periodically, 5 minutes for every hour on longer-duration flights (over 4 hours) and when flight conditions permit.
- Drink adequate amounts of water and fruit juices to maintain good hydration.¹⁷
- Avoid alcohol and caffeinated beverages, which are dehydrating.
- Be careful about eating too much during

TABLE 6

Estimation of venous thromboembolism risk for travelers

The absolute risk of venous thromboembolism (VTE) is low. This tool has been devised in an effort to help guide the clinician in making a decision about when to use low-molecular-weight heparin or an anti-Xa inhibitor for VTE prophylaxis for individuals traveling on long-haul flights (more than 8 to 10 hours). This has not been tested in any study, but rather it is based upon an estimation of the increased risk for VTE that the following conditions cause.

As for all travelers, standard thromboprophylaxis precautions (exercises and compression stockings) should be strongly recommended for travelers who have the following risk factors for VTE:

- Pregnancy or recent delivery within 6 weeks
- Use of contraceptives or hormone replacement therapy or tamoxifen
- Autoimmune disorders
- Congestive heart failure, pneumonia, chronic obstructive lung disease
- Leg varicosities
- Obesity (body mass index > 30 kg/m²)
- Tall stature (> 185 cm or 73 inches)
- Short stature (< 165 cm or 65 inches)
- Age > 70 years
- Family history of VTE or thrombophilia (hypercoagulable states)

When a patient who will have air travel lasting more than 8 to 10 hours has several of the above risk factors, the clinician should consider adding low-molecular-weight heparin or a factor Xa inhibitor. Pharmacologic thromboprophylaxis should be strongly considered when the patient's risk of thrombosis exceeds the potential for an adverse reaction from the use of these anticoagulants.

Any one of the following conditions should prompt the clinician to recommend low-molecular-weight heparin or a factor Xa inhibitor (unless currently on full-dose anticoagulation or bleeding risk is prohibitive), which should be given prior to departure:

- Prior provoked VTE with ongoing risks
- Recurrent VTE or unprovoked VTE at any time
- Known thrombophilia (hypercoagulable states including factor V Leiden mutation, prothrombin gene mutation G20210A, elevated factor VIII, deficiency of proteins S, C, or antithrombin), or the antiphospholipid syndrome
- Myeloproliferative disorders (especially essential thrombocythosis or polycythemia vera with a hematocrit > 55%)
- Malignancy and ongoing chemotherapy treatment
- Flaccid leg paralysis, inability to ambulate, or a nonremovable long leg cast or brace
- Major surgery within the prior 4 to 12 weeks, most notably total hip and knee replacements, or hip fracture, or recently bedridden for more than 3 consecutive days
- Recent major trauma

the flight.

- Request an aisle seat if you are at risk
- Do not place baggage underneath the seat in front of you, because that reduces the ability to move the legs.
- Do not sleep in a cramped position, and avoid the use of any type of sleep aid.
- Avoid wearing constrictive clothing around the lower extremities or waist.

If a patient has risk factors in addition to more than 8 to 10 hours of flying (TABLE 1, TABLE 6), the physician should consider additional preventive measures including compression stockings or an anticoagulant drug as mentioned above, or both.

We recommend that all airplane pas-

sengers take the steps listed above to reduce venous stasis and avoid dehydration, even though these measures have not been proven effective in clinical trials.¹⁹

The ACCP further advises that decisions about pharmacologic prophylaxis of VTE for airplane passengers at high risk should be made on an individual basis, considering that there are potential adverse effects of prophylaxis and that these may outweigh the benefits. For long-distance travelers with additional risk factors for VTE, we suggest the following:

- Use of properly fitted, below-the-knee graduated compression stockings providing 15 to 30 mm Hg of pressure at the ankle (particularly when large varicosities or leg edema is present)

- For people at very high risk, a single prophylactic dose of a low-molecular-weight heparin or a factor Xa inhibitor injected just before departure (TABLE 5)
- Aspirin is not recommended as it is not effective for the prevention of VTE.²⁰

SUMMARY FOR THE AIR TRAVELER

All travelers on long flights should perform standard VTE prophylaxis exercises (see the patient information pages accompanying this article). Although VTE is uncommon, people with additional risk factors who travel frequently either on multiple flights in a short period of time or on very long flights should be evaluated on a case-by-case basis for a more aggressive approach to prevention (compression support hose or prophylactic administration of a low-molecular-weight heparin or a factor Xa inhibitor).

Should a VTE event occur during travel, the patient should seek medical care immediately. The standard evaluation of a patient with a suspected VTE should include an estimation of the pretest probability of disease (TABLE 2, TABLE 3), followed by duplex ultrasonography of the upper or lower extremity to detect a deep vein thrombosis. If symptoms

dictate, then spiral computed tomography, ventilation-perfusion lung scan, or pulmonary angiography (where available) should be ordered to diagnose acute pulmonary embolism. A positive D-dimer blood test alone is not diagnostic and may not be available in more remote locations. A negative D-dimer test result is most helpful to exclude VTE.

Standard therapy for VTE is immediate treatment with one of the anticoagulants listed in TABLE 4, unless the patient has a contraindication to treatment, such as bleeding or allergy. Immediate evacuation is recommended if the patient has a life-threatening pulmonary embolism, defined as hemodynamic instability (hypotension with a blood pressure under 90 mm Hg systolic or signs of right heart failure) that cannot be treated at a local facility. An air ambulance should be used to transport these patients. If the patient has an iliofemoral deep vein thrombosis, it is also advisable that he or she be considered for evacuation if severe symptoms are present, such as pain, swelling, or cyanosis. Unless contraindicated, all patients should be given either full-dose intravenous or full-dose subcutaneous heparin or subcutaneous injection of a readily available low-molecular-weight heparin preparations or factor Xa inhibitor at once.²¹

REFERENCES

1. **Brenner B.** Interventions to prevent venous thrombosis after air travel, are they necessary? Yes. *J Thromb Haemost* 2006; 4:2302–2305.
2. **Cannegieter SC, Doggen CJM, van Houwelingen HC, et al.** Travel-related venous thrombosis: results from a large population-based case control study (MEGA Study). *PLoS Med* 2006; 3:1258–1265.
3. **Chandra D, Parisini E, Mozaffarian D.** Meta-analysis: travel and risk for venous thromboembolism. *Ann Intern Med* 2009; 151:180–190.
4. **Kuipers S, Cannegieter SC, Middeldorp S, et al.** The absolute risk of venous thrombosis after air travel: a cohort study of 8,755 employees of international organizations. *PLoS Med* 2007; 4:1508–1514.
5. **Kuipers S, Schreijer AJM, Cannegieter SC, et al.** Travel and venous thrombosis: a systematic review. *J Intern Med* 2007; 262:615–634.
6. **Lehmann R, Suess C, Leus M, et al.** Incidence, clinical characteristics, and long-term prognosis of travel-associated pulmonary embolism. *Eur Heart J* 2009; 30:233–241.
7. **Philbrick JT, Shumate R, Siadaty MS, et al.** Air travel and venous thromboembolism: a systematic review. *J Gen Intern Med* 2007; 22:107–114.
8. **Cruickshank JM, Gorlin R, Jennett B.** Air travel and thrombotic episodes: the economy class syndrome. *Lancet* 1988; 2:497–498.
9. **Bagshaw M.** Traveler's thrombosis: a review of deep vein thrombosis associated with travel. Air Transport Medicine Committee, Aerospace Medical Association. *Aviat Space Environ Med* 2001; 72:848–851.
10. **Wells PS, Owens C, Doucette S, et al.** Does this patient have deep vein thrombosis? *JAMA* 2006; 295:199–207.
11. **Arnason T, Wells PS, Forester AJ.** Appropriateness of diagnostic strategies for evaluating suspected venous thromboembolism. *Thromb Haemost* 2007; 97:195–201.
12. **Clarke M, Hopewell S, Juszczak E, Eisinger A, Kjeldstrøm M.** Compression stockings in preventing deep vein thrombosis in airline passengers. *Cochrane Database of Syst Rev* 2006; Apr 19(2):CD004002. DOI: 10.1002/14651858.
13. **Kuipers S, Cannegieter SC, Middeldorp S, et al.** Use of preventive measures for travel-related venous thrombosis in professionals who attend medical conferences. *J Thromb Haemost* 2006; 4:2373–2376.
14. **Perez-Rodriguez E, Jimenez D, Diaz G, et al.** Incidence of air travel-related pulmonary embolism in the Madrid-Barajas Airport. *Arch Intern Med* 2003; 163:2766–2770.
15. **Lapostolle F, Surget V, Borron SW, et al.** Severe pulmonary embolism associated with air travel. *N Engl J Med* 2001; 345:779–783.
16. **Kelman CW, Kortt MA, Becker NG, et al.** Deep vein thrombosis and air travel: record linkage study. *BMJ* 2003; 327:1072–1076.
17. **Eklof B, Kistner RL, Masuda EM, et al.** Venous thromboembolism in association with prolonged air travel. *Dermatol Surg* 1996; 22:637–641.
18. **Moyle J.** Medical guidelines for airline travel. *Aviat Space Environ Med* 2003; 74:1009.
19. **Geerts WH, Bergqvist B, Pineo GF, et al.** Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2008; 133:381S–453S.
20. **Rosendaal FR.** Interventions to prevent venous thrombosis after air travel: are they necessary? No. *J Thromb Haemost* 2006; 4:2306–2307.
21. **Kearon C, Ginsberg JS, Julian JA, et al.** Fixed-Dose Heparin (FIDO) Investigators. Comparison of fixed-dose weight-adjusted unfractionated heparin and low-molecular-weight heparin for acute treatment of venous thromboembolism. *JAMA* 2006; 296:935–942.

ADDRESS: John R. Bartholomew, MD, Heart and Vascular Institute, J3-5, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail barthoj@ccf.org.