The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism

2008

U.S. Department of Health and Human Services

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Message from the Secretary
U.S. Department of Health and Human Services

Over the last several decades we have seen dramatic drops in the mortality rates from cardiovascular disease, the leading cause of death in this country. Yet challenges remain, and certain areas of medicine have not seen improvements. One of the biggest challenges relates to blood clots in the legs (a disease know as deep vein thrombosis or DVT), which can not only cause pain, swelling, and other discomfort, but also frequently travel to the lungs, causing a potentially fatal pulmonary embolism (PE).

The best estimates indicate that 350,000 to 600,000 Americans each year suffer from DVT and PE, and that at least 100,000 deaths may be directly or indirectly related to these diseases. This is far too many, since many of these deaths can be avoided. Because the disease disproportionately affects older Americans, we can expect more suffering and more deaths in the future as our population ages–unless we do something about it.

The Institute of Medicine has classified the failure to provide appropriate screening and preventive treatment to hospitalized, at-risk patients as a medical error, and the Agency for Healthcare Research and Quality has ranked the provision of such preventive treatment as one of the most important things that can be done to improve patient safety. Proven, effective measures are available to prevent and treat DVT and PE in high-risk individuals. Yet today the majority of individuals who could benefit from such proven services do not receive them. Too few Americans know what DVT or PE is, how to recognize the symptoms, or how to talk with their clinicians about prevention, diagnosis, and treatment. Too few health care professionals are aware of the evidence-based practices for identifying high-risk patients and providing preventive, diagnostic, or therapeutic services.

Additionally, as in any area of medicine, gaps still remain in our knowledge about how best to care for certain patient subpopulations, and further research is needed.

This Surgeon General's *Call to Action* represents an opportunity for multiple stakeholders to come together in a coordinated effort to reverse the projected trends and to dramatically reduce the pain and suffering caused by DVT and PE in this nation through specific steps in communication, action, research and evaluation. With the involvement of individuals, families, communities, all aspects of research and health care systems, organizations, governments, and the media, we can bring better health to this country. I urge everyone with an interest in improving health to work with the Surgeon General to achieve this *Call to Action's* ambitious and essential vision.

Michael O. Leavitt
Secretary of Health & Human Services
United States Public Health Service

Foreword from the Acting Surgeon General U.S. Department of Health and Human Services

As the acting Surgeon General, my primary role is to provide the American people with the information they need to improve their health and reduce the risk of injury and illness. This first "Call to Action to Prevent Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)," provides vital information on critical health problems that cause enormous health consequences and numerous deaths in our country. Estimates suggest that at least 350,000, and as many as 600,000, Americans each year contract DVT/PE, and at least 100,000 deaths are thought to be related to these diseases each year. Many of those who survive have complications that have a serious and negative impact on the quality of their lives. Without the joint efforts of all stakeholders, including clinicians and families, the problem will only worsen as the population ages.

This Call to Action came out of a Surgeon General's Workshop on DVT/PE held in May 2006. The message from that workshop was clear—there is great hope and optimism about prevention, diagnosis and treatment of these diseases. The presentations and discussion that took place during those two days demonstrated that we have made progress in our knowledge of how to prevent, diagnose and treat DVT/PE. It is also clear that we are not applying that knowledge on a systematic basis. The workshop highlighted the tremendous gap in understanding and knowledge that exists about these diseases. In order to address that gap, we must disseminate information more widely about the availability of effective interventions to prevent and treat DVT/PE. We must also continue to invest in basic scientific, clinical and epidemiological research related to DVT/PE. In addition, our investment in translational research is essential in order to ensure that the public and the medical community can put the latest evidence into practice quickly and easily. To make this vision a reality, the Surgeon General's Call to Action is intended to serve as a stimulus for the development of a coordinated plan to reverse the current trend and dramatically reduce the morbidity and mortality caused by DVT/PE. The kinds of activities that are part of this plan are outlined in this document. The critical step for all stakeholders is to come together and address this important health problem. We seek to engage all levels of government as well as individuals and private sector institutions and organizations in a coordinated, multifaceted effort to prevent and reduce the incidence of deep vein thrombosis and pulmonary embolism.

I am encouraged by the participation of so many people and organizations in the May 2006 workshop and the development of this Call to Action. I would like to thank them for their willingness to assist us in gathering the best scientific evidence as a catalyst for improvement. Efforts to reduce the incidence of DVT/PE will demand the full attention and committed efforts of all stakeholders. I am confident that working together we can take real steps to reduce the burden of these diseases. The reward for this effort will be to prove the forecasters wrong. Instead of ever-increasing numbers of individuals developing and suffering from DVT/PE, we will see dramatic reductions in the incidence and prevalence of these conditions.

Steven K. Galson, M.D., M.P.H.
RADM, U.S. Public Health Service
Acting Surgeon General

Message from the Director of the National, Heart, Lung, and Blood Institute, National Institutes of Health

Thousands of Americans suffer from deep vein thrombosis (DVT) in the United States today, and many will die from its complication, pulmonary embolism (PE). The tragedy of these diseases is that their diagnosis is easy to overlook because the signs and symptoms are often diffuse and difficult to recognize. In many cases, there are no clinically apparent signs at all. Perhaps as many as 50 percent of the cases of DVT are "silent." Very often the first symptom of DVT is a fatal PE.

There are few public health problems as serious as DVT/PE, yet these diseases receive so little attention. Some estimates suggest that these conditions cause more deaths each year than breast cancer, AIDS, or motor vehicle incidents—illnesses or injuries that are well understood by most Americans. Up until now, levels of public awareness and knowledge about the risks of these diseases have been extremely low. The "Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism" finds the status quo unacceptable.

The National Heart, Lung, and Blood Institute (NHLBI) is the primary agency within the National Institutes of Health that is responsible for promoting research leading to improved diagnosis and treatment of DVT/PE. The NHLBI has a long and distinguished record of supporting and guiding seminal advances in thrombosis research that have yielded unprecedented improvements in the nation's health. It has supported basic research in venous biology for the development of improved treatment for venous diseases and their complications; indeed, much of the science contained in this Call to Action is a result of NHLBI-funded research. Despite these accomplishments, there are many factors that impede progress in research and treatment, including a limited understanding of venous biology and coagulation proteins, and the lack of a critical mass of investigators and providers devoted to this research. Without technological innovation, training opportunities, and committed investigators, progress will continue to be slow.

It is NHLBI's hope that this Call to Action will stimulate innovative research by investigators who are committed to finding new ways to prevent and treat these conditions. As the Surgeon General stated at his workshop on DVT in May of 2006, there are many differences in how health professionals deal with the issue, and there is no consensus nationally by practitioners and hospitals on the best way to approach this problem. There is also an urgent need to develop a consensus on science-based standards of care, especially for high-risk groups. It is critical that we identify new areas of research related to venous biology, DVT/ PE, their complications, and clinical interventions. This kind of basic and clinical science is needed to provide a foundation for the development of evidence-based guidelines.

This Call to Action concludes that in order to impact the incidence and burden of DVT/PE, stakeholders need to come together to increase public awareness, support the development of evidence-based practices, and carry out the scientific research that can address the gaps in knowledge. I urge all of us to work together to achieve this ambitious and essential vision. This is a vision that the NHLBI wholeheartedly supports.

Elizabeth G. Nabel, M.D.
Director, National Heart, Lung,
and Blood Institute
National Institutes of Health

Definitions of Deep Vein Thrombosis and Pulmonary Embolism

Deep vein thrombosis (DVT) refers to the formation of one or more blood clots (a blood clot is also known as a "thrombus," while multiple clots are called "thrombi") in one of the body's large veins, most commonly in the lower limbs (e.g., lower leg or calf) [1]. The clot(s) can cause partial or complete blocking of circulation in the vein, which in some patients leads to pain, swelling, tenderness, discoloration, or redness of the affected area, and skin that is warm to the touch. However, approximately half of all DVT episodes produce few, if any, symptoms [2]. For some patients, DVT is an "acute" episode (that is, the symptoms go away once the disease is successfully treated), but roughly 30 percent of patients suffer additional symptoms, including leg pain and swelling, recurrent skin breakdown, and painful ulcers [3-5]. In addition, individuals experiencing their first DVT remain at increased risk of subsequent episodes throughout the remainder of their lives [4, 6].

The most serious complication that can arise from DVT is a pulmonary embolism (PE) which occurs in over one-third of DVT patients [7]. A PE occurs when a portion of the blood clot breaks loose and travels in the bloodstream, first to the heart and then to the lungs, where it can partially or completely block a pulmonary artery or one of its branches. A PE is a serious, life-threatening complication with signs and symptoms that include: shortness of breath, rapid heartbeat, sweating, and/or sharp chest pain (especially during deep breathing). Some patients may cough up blood, while others may develop dangerously low blood pressure and pass out. Pulmonary embolism frequently causes sudden death [6], particularly when one or more of the vessels that supply the lungs with blood are completely blocked by the clot. Those who survive generally do not have any lasting effects because the body's natural mechanisms tend to resorb (or "lyse") blood clots. However, in some instances, the blood clot in the lung fails to completely dissolve, leading to a chronic serious complication that can cause chronic shortness of breath and heart failure. DVT and PE are commonly grouped together and sometimes referred to as "venous thromboembolism" (VTE).

SECTION I

Deep Vein Thrombosis and Pulmonary Embolism as Major Public Health Problems

Deep Vein Thrombosis and Pulmonary Embolism (DVT/PE) represent a major public health problem, exacting a significant human and economic toll on the Nation. These common conditions affect hundreds of thousands of Americans each year. A 25-year population-based study published in 1998 found that the overall age- and sex-adjusted annual incidence of VTE was 1.17 per 1,000 (.48 per 1,000 for DVT and .69 per 1,000 for PE) [8]. Applying these figures to today's population of approximately 300 million Americans suggests that more than 350,000 individuals are affected by DVT/PE each year [9]. A 1991 study that extrapolated findings from 16 short-stay hospitals in Worcester, Massachusetts is fairly consistent with these estimates. This study found that approximately 270,000 individuals were hospitalized for DVT/PE in 1991, including 170,000 new cases and 99,000 recurrent ones [10].

But there is reason to believe that the true incidence rate (and total number of cases) could be significantly higher, as several studies suggest that these diseases are often undiagnosed. The Worcester study cited above also concluded that more than half of the cases that actually occur are never diagnosed, and therefore as many as 600,000 cases may occur each year [10]. Another study found that the diagnosis of PE is often missed; this study of nursing home patients found that the condition was correctly diagnosed before death in only 39 to 50 percent of patients where it was confirmed in an autopsy [11, 12]. While the precise incidence and prevalence remain "elusive" [10] and a matter of some debate, one thing is undeniably clear—DVT/ PE are major national health problems that have a dramatic, negative impact on the lives of hundreds of thousands of Americans each year.

There is reason to believe that the magnitude of the problem will increase. Several studies have found that the incidence has remained relatively stable over time [8, 13], although one study found an increased incidence of DVT in hospitalized patients between 1979 and 1999 [14]. Assuming that the overall incidence remains the same, one would expect the total number of DVT/PE cases to grow at the same rate as overall population growth. However, the incidence of DVT/PE increases markedly with age. Thus, as the United States population increases in average age, it is quite possible that, in the absence of other influences such as better prevention, the growth in the total number of DVT/PE cases will outpace population growth. Given that DVT/PE are already common and devastating conditions, it is imperative that all stakeholders come together to halt, and hopefully reverse, the growth in the number of cases.

What Are the Consequences of DVT and PE?

Mortality

DVT and PE together may be responsible for more than 100,000 deaths each year. DVT alone does not frequently result in death; the National Center for Health Statistics reports that it is an underlying or contributing cause of death in over 10,000 cases per year [15]. PE is responsible for many more deaths, although estimates of the exact toll are also elusive [10] and vary widely, ranging from just below 30,000 to over 80,000. The most conservative estimates come from studies that review death certificate data. A 20-year review of data from 1979-1998 found that the age-adjusted death rate for PE was 94 per 1,000,000 individuals [16]. Extrapolating to today's population suggests that an estimated 28,200 people die each year

from this disease. But as noted previously, PE is often undiagnosed, and thus the true death rate is almost certainly substantially higher. In fact, community-based epidemiological studies suggest that roughly one in five individuals die almost immediately from PE, while 40 percent die within 3 months [17, 18]. Applying this 40 percent figure to the 207,000 recognized annual PE cases cited earlier suggests an annual death rate of 82,800.

Another way to estimate the death toll is to look at statistics related to both diseases. An estimated 30 percent of patients die within 3 months [6]. Applying this 30 percent figure to the previously cited estimates of between 350,000 and 600,000 cases each year suggests that at least 100,000, and perhaps as many as 180,000, individuals die directly or indirectly as a result of DVT/PE each year.

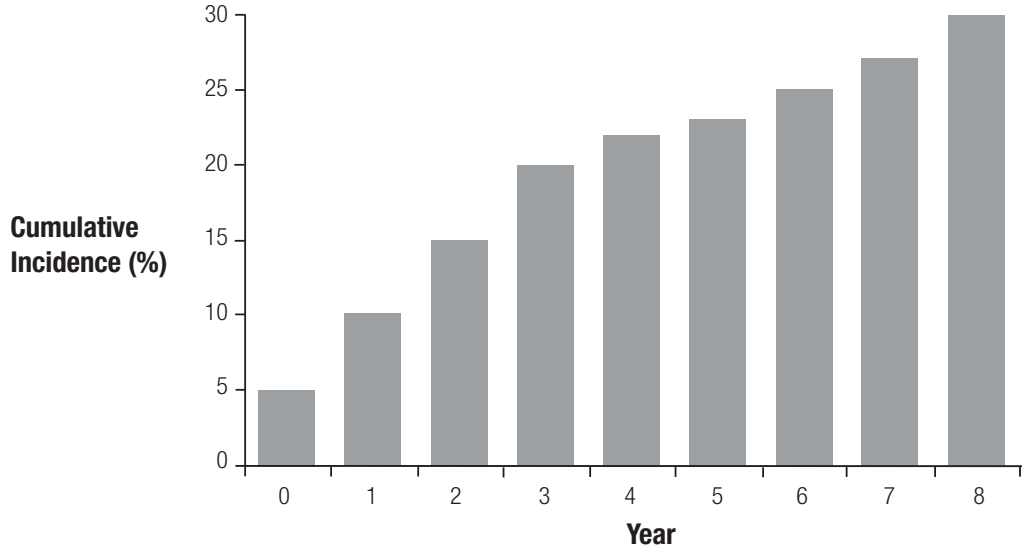
Morbidity

Many of those who survive will be affected for the rest of their lives. At a minimum, those who have had DVT or PE will remain at increased risk for another episode. (See figure 1). Roughly 30 percent of those who have a DVT in a given year will suffer from a recurrent episode sometime in the next 10 years, with the risk being greatest in the first two years [5, 6, 19, 20]. Recurrence is also more likely if the initial episode was "spontaneous"—that is, not provoked by transient (often one-time) events such as trauma, surgery, or hormonal changes due to pregnancy, oral contraceptives, or hormone replacement [4, 5]. Patients with symptomatic PE tend to have a higher risk of recurrent VTE than those presenting with DVT symptoms alone. The recurrence in those who initially presented with PE is more likely to be another embolism (as opposed to DVT alone) [21]. For reasons that remain unclear, the risk of recurrent VTE is higher among men than women. (See figure 2). [22]. To minimize the risk of recurrence, anyone who has had either disease must remain vigilant about avoiding and/or managing the potential impact of other risk factors such as prolonged air travel, surgery, or trauma.

Along with the potential for recurrence, individuals who suffer an initial episode may also experience chronic venous insufficiency (CVI), which is also referred to as postthrombotic syndrome or PTS, with 30 percent suffering from CVI either immediately or within 10-20 years of the initial episode [3, 19, 23]. In one cohort of VTE patients followed for 10 years, more than half showed signs of CVI, while six percent developed severe disease [20]. CVI occurs when the blood clot injures or destroys one or more of the venous valves that are located in the deep veins of the leg. When functioning properly, these valves work against gravity to help pump blood back to the heart when an individual is sitting or standing. When these valves are either damaged or destroyed, individuals may feel leg pain and experience swelling when standing. They may also develop other unpleasant symptoms, including mild or extensive varicose veins (which are cosmetically unappealing and can cause additional chronic pain and burning), skin breakdown, ulcers, and brownish skin pigmentation changes, which tend to be permanent and irreversible. The most severely affected patients may find that the skin inside their ankles becomes thickened, darkened, and prone to recurrent skin breakdown and painful ulcers (known as venous stasis ulcers) that often do not easily heal. CVI has been found to cause a significant reduction in the quality of life, similar to the impact caused by chronic heart, lung, or arthritic disease [24, 25].

Figure 1:

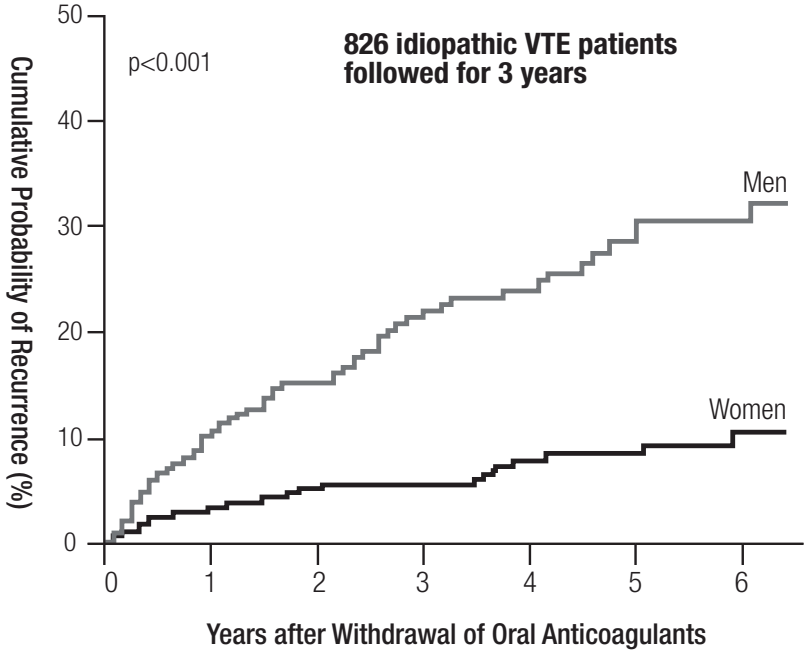
The Cumulative Incidence of Recurrent Venous Thromboembolism in Patients with a First Episode of Symptomatic Deep Venous Thrombosis.



Prandoni et al, Ann Intern Med 1996;125:1–7

Figure 2:

Kaplan-Meier Estimates of the Likelihood of Recurrent Venous Thromboembolism According to Sex.[22]



No. at Risk							
Men	373	263	183	133	95	65	42
Women	453	342	248	193	142	103	72

What Factors Raise the Risk for DVT and PE?

There are differential effects by gender, race, and age on individuals with DVT/PE. These diseases also disproportionately effect certain groups of individuals, such as those who:

- have experienced recent trauma
- have undergone major surgery
- are obese
- have cancer
- are pregnant
- use hormone therapy
- smoke

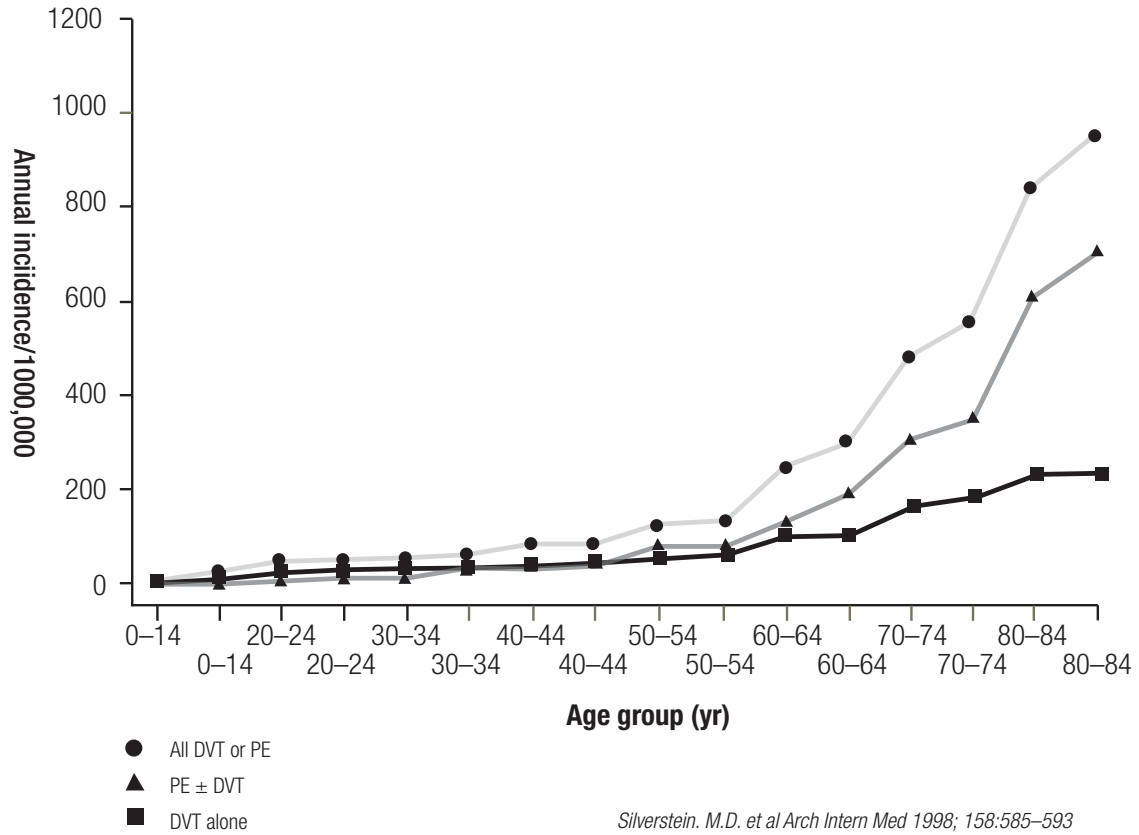
Age, Gender, and Race-Specific Incidence

Like many diseases, DVT/ PE disproportionately affect the elderly. (See figure 3). The incidence among children (under the age of 14) is quite low, at less than 1 per 100,000 measured in person-years. Incidence rates rise relatively slowly until the age of 50, then accelerate dramatically, reaching 1,000 per 100,000 person-years by the age of 85 [8].

Women have a higher incidence of DVT during their child-bearing years although this risk is still relatively low compared to risk levels for older men and women. However, after the age of 50 [8], men are at greater risk than women.

Figure 3:

Annual Incidence of all Venous Thromboembolism, Deep Vein Thrombosis (DVT) Alone, and Pulmonary Embolism (PE) With or Without Deep Vein Thrombosis (PE+-DVT) Among Residents of Olmstead County Minnesota from 1966 to 1990 by Age



Silverstein. M.D. et al Arch Intern Med 1998; 158:585–593

For reasons that are not completely understood, African Americans and Caucasians tend to have a greater risk for these conditions than those whose ethnic background is either Asian or Native American. African Americans have a 30 percent higher risk than do Caucasians, while Asian and Native Americans have a 70 percent lower risk [26, 27].

Genetic Factors That Raise Risk

Thrombophilia is an inherited blood clotting disorder caused by one or more genetic risk factors or mutations that make a person susceptible to DVT/ PE. These factors include deficiencies in the anticoagulation factors protein C, protein S, and antithrombin, and mutations in the factor V and prothrombin genes which result in Factor V Leiden and prothrombin G20210A [28] respectively. Over one-third (35 percent) of DVT patients have at least one of these five factors [29, 30]. An individual with such a genetic mutation will not necessarily develop these conditions, and fewer than 10 percent of those who carry the most common mutations will develop a detectable blood clot each year [31]. But the risks are much greater for those individuals with thrombophilia compared to the population at large, particularly for those who also have another risk, such as surgery, hospitalization, or a prolonged bed stay.

In almost all cases, the presence of an inherited blood clotting disorder in an individual indicates that at least one of the parents also has the disorder, and there is a 50 percent chance that any sibling or child of that individual will have it as well. Other blood relatives, including aunts, uncles, and cousins, may also have the mutation.

Following is a brief description of the most common genetic mutations:

- *Factor V Leiden:* Factor V Leiden is a relatively common mutation in the gene for clotting factor V that leads to an increased risk of DVT/PE. An estimated 15 to 20 percent of DVT/PE patients have this abnormality [29, 30]. This defect is most commonly found among Caucasians (with roughly five percent carrying it) [32], with Asians and Africans rarely carrying the mutation.
- *Prothrombin 20210:* Roughly two to three percent of Caucasians have a mutation in the gene that produces prothrombin, which is called clotting factor II [33]. Approximately six percent of all DVT/PE patients have this mutation, which leads to a threefold increase in the risk of thrombosis [(34)]
- *Antithrombin, Protein C,* and *Protein S Deficiency:* Mutations in the genes that produce protein C and its cofactor protein S are found in less than one percent of the population, while deficiencies in the gene that produces antithrombin are found in roughly 1 in 5,000 individuals [35, 36]. Deficiencies in the natural anticoagulants protein C, protein S, and antithrombin lead to a tenfold increase in risk of thrombosis in an individual who inherits the gene mutation from one parent, with the highest risk in those with antithrombin deficiency [37].

Acquired Factors That Raise Risk

Exposure to steroid hormones—especially estrogen—can raise the risk of developing a blood clot. Thus, women using oral contraceptives in their child-bearing years and postmenopausal women who use hormone therapy (HT) are at increased risk. Oral contraceptives that contain both estrogen and progestin increase the risk of a blood clot by two- to eight-fold [38-43]. (The risk may even be greater with patches that

contain transdermal contraceptives, since the amount of estrogen absorbed can be 60 percent higher [44]). An alternative to consider may be contraceptives that use only progestin as these do not appear to increase the risk of DVT or PE [45-47]. However, it is important to keep in mind that the absolute risk for women of fertile age who use oral contraceptives is fairly low—2 to 8 per 10,000 person-years, which is still substantially less than the risk faced by older women and men [48, 49].

Pregnancy increases the risk of DVT fivefold compared to nonpregnancy, with the risk being even greater postpartum [50]. DVT can be life-threatening in pregnancy, as pulmonary embolism is the most common cause of maternal death in developed countries [51]. Comorbiditites such as obesity and diabetes magnify the existing risk.

Post-menopausal women undergoing HT also have a higher risk of DVT/PE, with recent large studies suggesting a two- to four-fold increase in risk, with even larger increases in risk for those on high doses of estrogen (greater than 1.25 mg/day) [52-55]. Women with thrombophilia who also are exposed to oral contraceptives, pregnancy, or HT will face a significantly greater risk than the above statistics suggest [28].

Individuals who develop tumors have a greater tendency to develop blood clots, thus creating increased risk. About 10 percent of patients who present with DVT/PE will have an occult cancer diagnosed within two years of the thrombotic episode [56].

Although all patients with active cancer have an increased risk of DVT/PE, the risk appears to be higher for those with pancreatic cancer, lymphoma, malignant brain tumors, cancer of the liver, leukemia, and colorectal and other digestive cancers. The risk is especially high for patients whose cancer has spread to other parts of the body [57-60]. Cancer patients receiving chemotherapy are at even higher risk [57, 61-65]. Cancer patients with VTE face much worse outcomes than those with cancer alone. The probability of death within 183 days of initial hospital admission is over 94 percent for those with VTE and malignant disease, compared to

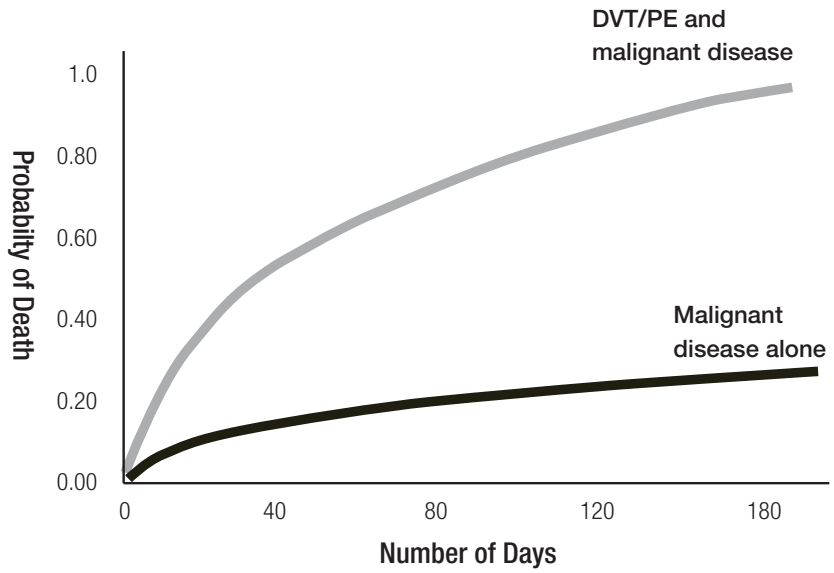
A Case Study

This is the story of a college-age girl with a genetic susceptibility to blood clots who experienced an unusual manifestation of venous thrombosis that ultimately claimed her life. Like many young women, she was very self-conscious about her complexion. Her gynecologist explained that one of the beneficial side effects of hormone-based contraceptives is to help clear one's complexion. So she began taking oral contraceptives and later switched to a patch. While the patch cleared her complexion, she and her parents did not know that she was one of 7,000,000 women in the U.S. with Factor V Leiden, a genetic abnormality that made her much more likely to develop DVT/PE [28]. The combination of a genetic predisposition and the use of oral contraceptives proved to be a deadly one, as she developed blood clots in the portal and hepatic veins of her abdomen. (The presence of clots in these locations is not technically classified as DVT, but it is considered a form of venous thrombosis, thus highlighting the fact that VTE can occur anywhere in the body.) After months of suffering from fatigue, nausea, and, ultimately, a markedly swollen abdomen, she died in May 2003 at the age of 21.

Figure 4:

Concurrent VTE and Cancer Increases the Risk of Death

Probability of Death within 183 days of intial hospital admission



adapted from Levitan et al Medicine 1999

less than 40 percent for those with cancer alone. (See figure 4) [66].

The incidence of DVT/PE is substantially higher for cancer patients than for non-cancer patients across all types of major surgery, including neurosurgery, head and neck, vascular, urologic, gastrointestinal, and orthopedic surgeries [67]. In the absence of preventive treatment, an estimated 40 to 80 percent of surgical cancer patients will develop DVT in the calf vein while 10 to 20 percent will develop DVT in a proximal vein. Between four and 10 percent of cancer patients undergoing major surgery will develop PE, and one to five percent are fatal [68]. Once a cancer patient develops a first episode of VTE, he or she has three times the risk of developing a subsequent episode (compared to noncancer patients) [56].

For reasons that are not entirely clear, people who are obese are at greater risk of DVT/PE. Individuals with a body mass index (BMI)* greater than 30 have a two- to threefold increase in the risk of developing a blood clot, with the risk being even higher for those with a BMI above 40 [69-71]. The combination of obesity and other risk factors increases the risk even further. For example, obese women on oral contraceptives face a tenfold increase in risk (compared to two- to threefold for nonobese women on oral contraceptives) [71].

The Role of Triggering Events

The majority of DVT/PE events are related to specific, identifiable triggering events such as hospitalization, major surgery, trauma, and prolonged periods of immobility (as can

* *BMI is the statistical measure of the weight of a person scaled according to height. In the U.S., BMI is calculated as follows: 703 x (an individual's body weight in pounds/the square of his or her height in inches).*

occur in a nursing home or during long flights). It is often the combination of an individual with genetic and/or acquired risk factors who also experience one of these triggering events that leads to the development of a DVT or PE.

Hospitalization for Acute Medical Illness

Hospitalization may be considered the single most important risk factor for developing a DVT/PE. Hospitalization has been shown to raise an individual's risk of an event as compared to living in the community [61]. Much of the increased risk is related to patients who must undergo major surgery (which is discussed separately in the next section). Those who are hospitalized for acute medical illness have more than a tenfold increased risk for VTE [61].

Most hospitalized patients have at least one risk factor, including immobility, cancer, infection, and/or surgery. In fact, in the absence of appropriate preventive treatment, 10 to 40 percent of medical and general surgery patients and 40 to 60 percent of patients requiring major orthopedic surgery develop thrombosis [68]. Many of these events are not clinically apparent, but they can potentially lead to later problems, such as PE. In fact, roughly one out of 10 hospital deaths are related to PE, and many times this disease was not suspected before death [72].

Recent research suggests that certain identifiable subsets of acute medical inpatients are at especially high risk of DVT/PE, including those over the age of 75; those who are obese; and those with any of the following:

- prior history of these conditions
- active cancer
- acute infection
- neurological disease combined with lower extremity weakness

A Case Study

July 17, 2005 started out as a normal Sunday for Heidi Blongastainer. She was 36 weeks pregnant and felt tired. She and her husband Brian were heading to her in-laws' summer cottage in Cape Cod for a barbecue. On their way home, a car driven by a drunk driver who was drag racing crossed the median strip of the highway and hit their car head on while traveling 90 miles per hour. Heidi felt her water break upon impact. She was trapped in the car for approximately 45 minutes, with the dashboard on top of her legs. (Brian suffered only minor injuries and was able to get out of the car and call for help.) After being pried out of the car, Heidi was brought to a small hospital near Cape Cod where they confirmed that her daughter, just a few weeks from being born, did not have a heartbeat. She was then brought to Brigham and Women's Hospital where she required emergency surgery and remained hospitalized for a week.

After returning home, Heidi had a walker and could walk only very short distances. Her feet and right hip were extremely swollen and bruised, making it difficult for her to move. During the next few days, her feet seemed to get worse, and she started to develop shooting pains in her back whenever she breathed. Thinking that the symptoms were due to cracked ribs, she downplayed them when talking to her doctors.

Her mother warned her about blood clots, but Heidi discounted her advice, not believing that an otherwise healthy 28-year-old woman could develop blood clots due to an automobile accident. Heidi

continued to downplay her symptoms at her followup visit with the surgeon. Later in the same week she started to experience shortness of breath and additional pain, soreness, redness, and swelling in her calf and feet. Sitting in bed, she could not catch her breath. That Saturday, 6 days after getting out of the hospital, she developed a fever. She paged her surgeon to tell him about her symptoms, focusing primarily on the pain and swelling in her feet. The surgeon told her to go to the Brigham and Women's Hospital Department of Emergency Medicine, where she was diagnosed with cellulitis of the leg. But doctors also questioned her about her other symptoms. After hearing her answers, she was immediately taken for a CAT scan to check for blood clots. When the doctor came back, Heidi was informed that she had multiple, large blood clots in her lungs. She was immediately put on anticoagulation therapy, which continued for 6 months. She also participated in a PE support group that met every 3 weeks.

When Heidi presented her story at the Surgeon General's Workshop—only 8 months after her accident—she still had pain in her calf and remained anxious about the possibility of developing a new clot (especially since discontinuing anticoagulation medication). But unlike before, she now knows what symptoms to look for and what to do if they develop.

- long-bone fracture
- chronic renal disease
- a prior superficial vein thrombosis
- prolonged immobilization [73, 74]

Trauma and Major Surgery

Any injury to body tissues, whether due to surgery or trauma, increases the risk of a blood clot, because the injury stimulates the body's clotting processes. Blood clots due to trauma and surgery occur relatively quickly, with most developing within two weeks of the event, and some happening much more quickly (within a few hours or even during surgery). DVT/PE also can occur up to several months after surgery or major trauma.

Individuals undergoing certain types of surgery or who experience certain types of trauma are especially prone to blood clots, including those having

- pelvic (gynecological and urological) surgery
- orthopedic surgery (including hip replacement or fracture repair)
- spinal cord paralysis
- multiple limb fractures
- pelvis/hip socket injury.

Nursing Home Residency

Nursing home residents are an often overlooked risk group for DVT/PE, even though they are more than twice as likely as nonresidents of nursing homes to develop these conditions, and they account for over 13 percent of all such events that occur outside the hospital [75].

Travel

Any sort of travel has the potential to increase the risk of DVT/PE. Prolonged air, car, and rail trips where the traveler is immobile for long periods of time appear to bring about the greatest risk. In fact, travel by air, car, train, or bus for four or more hours increases the risk about twofold for several weeks after the trip [76]. The risk is even greater for travelers with other risk factors.

The Economic Costs of DVT/PE

There are very few data available on the economic costs of VTE, and more research is needed on both the direct and indirect costs to individuals and society at large. As noted earlier, conservative estimates suggest that over 350,000 people are affected by DVT/PE each year, and the vast majority of these individuals will require expensive inpatient treatment. Those who survive the disease may live with a long-term, chronic disorder that is often characterized by repeated episodes that result in additional hospitalizations and treatments. Many individuals with these disorders may also be unable to remain productive members of the workforce (i.e., they may not be able to work at all, may miss work periodically, or may be able to work but at diminished productivity levels), thus creating an economic hardship for their family and diminishing the overall productivity and economic output of the Nation.

SECTION II

Reducing the Risk for DVT/ PE

Much is known today about how to prevent DVT/PE, and how to minimize the impact for those patients who suffer from these conditions. If this knowledge were applied consistently, the burden could be reduced substantially. Unlike other chronic diseases, there is at present little evidence on the impact of lifestyle changes on the risk for DVT/PE. While being overweight and smoking are known risk factors, it is not yet known whether smoking cessation, weight loss, increased physical activity, or other lifestyle changes significantly reduce risk. A recent study did find that a diet that includes more fruits, vegetables, and fish, and less red and processed meat is associated with a lower incidence of DVT/PE [77]. But further studies on the impact of diet and other lifestyle changes are warranted.

As noted earlier, about half of those who develop DVT/PE have two things in common. First, they have one or more identifiable risk factors for the disease. Second, they experience some sort of triggering event, such as hospitalization, trauma, surgery, or a prolonged period of immobilization (e.g., due to nursing home confinement or a long trip by air, car, or train) that leads to the formation of one or more blood clots. The other half of those who get the disease have "unprovoked DVT/PE"—that is, the reasons for the events are unknown. There is much that can be done, however, to prevent high-risk individuals from developing these conditions. Providing preventive treatment (or primary prophylaxis) to these individuals can dramatically reduce the likelihood of a blood clot or PE.

Several drugs have been found to be effective in reducing the likelihood of a blood clot in high-risk individuals. These drugs are known as anticoagulants or blood thinners because they slow down the coagulation processes, and thus reduce the likelihood that a blood clot will form. Numerous studies over a long period of time confirm the benefits of using blood-thinning medications as a preventive measure in high-risk individuals.

Addtionally, several mechanical devices exist to help prevent DVT and/or PE. These devices are often used for individuals who are at risk but are not able to tolerate anticoagulants. Mechanical devices deliver variable gradations of external pressure around the circumference of the leg to improve venous circulation.

Another preventive therapy option is the use of a permanent or retrievable implantable filter in the vena cava. These filters act like miniature umbrellas with holes that can trap blood clots—and thus prevent PE—without stopping the flow of blood. They have been used with success in a variety of patients, including those whose anticoagulation therapy must be stopped due to the need for urgent surgery, patients undergoing bariatric surgery, and patients who suffer multiple injuries from a motor vehicle accident. It is important to note, however, that these filters do not prevent DVT. Rather, they are designed to help prevent PE in those who are at high risk of DVT.

Existing Evidence-Based Guidelines, Standards, and Measures for DVT/PE

A search was conducted of the National Guidelines Clearinghouse™ (NGC), a comprehensive database of evidence-based clinical practice guidelines and related documents created by the Agency for Healthcare Research and Quality

(AHRQ) in partnership with the American Medical Association and American Association of Health Plans. The search was conducted at **www.guideline.gov** on June 27, 2006, and more than 100 guidelines related to PE and DVT were found. The initial search on the term "pulmonary embolism" produced 111 guidelines. While searching on the term "deep vein thrombosis" 88 guidelines were produced and the vast majority duplicated the initial search. These guidelines cover a wide variety of topics related to preventing, diagnosing, and treating DVT/ PE in general and specific populations. Multiple guidelines exist related to certain common issues, such as when and how to provide preventive treatment or prophylaxis. While all guidelines included in the NGC are based on scientific evidence, the strength of the evidence behind these guidelines varies. The NGC includes a summary of the strength of the evidence that underlies each guideline that is included in the clearinghouse.

The clearest consensus in the guidelines exists on the need to screen hospitalized patients for risk of DVT/PE and to provide appropriate prophylaxis to those at risk. The Institute of Medicine 1999 landmark report on medical errors noted that failure to provide prophylactic therapy when indicated is a hospital error [78]. AHRQ has evaluated and ranked the effectiveness of 79 safety practices based on strength of evidence, and found prevention to be the highest-ranked of all the practices evaluated [79]. Based on this finding, the National Quality Forum (NQF) now recommends that all hospitalized patients be evaluated upon admission and regularly thereafter, and that those found to be at risk be given prophylaxis for VTE [80].

Guidelines from the American College of Chest Physicians provide recommendations on what prophylaxis regimen to give to hospitalized patients with varying levels of risk factors. Regimens may range from early, aggressive ambulation to a combination of anticoagulation therapy, intermittent pneumatic compression, and/or graduated compression stockings.

Consensus Standards for Prevention and Care of DVT/PE

In May 2006, the National Quality Forum NQF endorsed a set of 20 national voluntary consensus standards around model policies, practices, and performance measures related to the prevention and care of VTE. This set of 20 standards, which had been developed under the leadership of the Joint Commission (formerly known as the Joint Commission on the Accreditation of Healthcare Organizations), includes a policy statement recommending that every healthcare facility have a written, evidence-based policy to drive quality improvement related to risk assessment, prevention, diagnosis, and treatment. It also contains 17 key characteristics of preferred practices including general recommendations and practices related to risk assessment/stratification, prevention, diagnosis, and treatment/monitoring. In addition there are two performance measures that can be used for public reporting [81]. The two measures relate to ordering and providing preventive treatment to hospitalized surgical patients. The specific measures are as follows:

- Surgery patients with recommended prophylaxis ordered
- Surgery patients who receive appropriate prophylaxis within 24 hours prior to surgery to 24 hours after surgery

The Joint Commission is still in the process of developing additional measures, and their work

is expected to be completed shortly. NQF will then consider endorsing these additional measures.

As noted, guidelines have been produced by a variety of organizations, often representing different medical specialties. Many researchers and clinicians who spoke at the Surgeon General's Workshop on DVT noted that some of the guidelines may conflict with each other or are confusing. The result is that clinicians may find it difficult to use the guidelines in everyday practice. It is critical, therefore, that stakeholders involved in guideline development come together to produce—to the extent possible based on today's best evidence—a more unified, synthesized, and clear set of guidelines related to the prevention, diagnosis, and treatment of DVT/PE in specific patient populations.

SECTION III

Gaps in Application and Awareness of Evidence-based Interventions

As discussed in the previous section, much is already known about how to prevent and treat DVT/PE. Yet the human and economic toll on both individuals and society as a whole remains high. Left unchecked, the aging of the population will increase this burden over time. Why do DVT and PE remain such serious problems, particularly given the availability of effective strategies for preventing and minimizing them? The answer lies primarily in the failure to consistently use evidence-based interventions in those high-risk individuals who need them. This failure may be due to clinicians' lack of awareness, and consistent adherence to evidence-based practices. An additional factor is a health care system that may not consistently provide coverage for the provision of high-quality preventive and therapeutic treatment.

Application of Guidelines

A substantial body of evidence suggests that evidence-based DVT/PE guidelines are not being routinely followed. Most of this evidence relates to prophylaxis, although some data on treatment exist as well. High-risk patients and those with identifiable symptoms are not routinely receiving prophylaxis that could help to prevent the development of DVT and/or PE. A large epidemiological study of 5,451 patients with ultrasound-confirmed DVT (seen at 183 different clinical sites) found that the majority had been given no prophylaxis prior to their diagnosis despite being at high risk. Men were 21 percent more likely than women to have received prophylaxis [82]. In other words, high-risk patients (especially women) are not being identified in a timely manner and provided with appropriate therapy designed to prevent the development of DVT/PE.

This finding is consistent across all age groups, in both academic and community hospitals, and throughout all regions of the United States. The gender difference persists even after adjusting for cancer, surgery, prior DVT, trauma, and age [83].

Other studies also confirm the failure to routinely provide preventive treatment to high-risk patients. A study of 2,017 patients in 16 short-stay Massachusetts hospitals found that only 32 percent of high-risk patients received appropriate prophylaxis, with rates across the hospitals ranging from 9 percent to 56 percent [84].
A recent small study of 44 medical and surgical patients found that 38.6 percent of those who were classified as having potentially preventable VTE did not receive adequate prophylaxis [85].

The failure to provide preventive therapy is not limited to the United States. A study of 446 medical patients at two teaching hospitals in Hamilton, Ontario found very similar results, with only one-third of high-risk patients receiving some form of prophylaxis [86]. While high-risk surgical patients appear to be more likely to receive prophylaxis than high-risk medical patients, preventive therapy remains underused in this population as well. A study of 1,907 high-risk surgical patients at 10 teaching and community-based hospitals found that 93.7 percent of high-risk orthopedic surgery patients and 75.2 percent of high-risk abdominal surgery patients received appropriate prophylaxis [87]. Another study found that 14.4 percent of high-risk orthopedic surgery patients received inadequate preventive therapy or none at all. The same study found that orthopedic surgery patients who do get anticoagulation therapy typically receive it for only three to five days.

This is in stark contrast to current recommendations, which suggests a minimum of seven to 10 days and perhaps as long as 30 days for these patients [88].

Lack of adherence to guidelines extends beyond preventive therapy to treatment of the disease as well. A 2005 study of 3,778 patients at 38 academic/teaching, community, and Veterans Administration hospitals concluded that in just under one-half of patients with DVT, PE, or both, anticoagulation therapy was discontinued too early. In addition, patients with DVT or PE were rarely discharged from the hospital with appropriate bridge therapy (an injectable anticoagulation agent plus warfarin) [89].
The reasons for poor adherence to established guidelines and standards are not entirely clear, although a variety of factors may be at play, including clinical concerns and other issues.

As noted earlier, one of the major themes of "The Surgeon General's Workshop on DVT" was the issue surrounding potential inconsistencies, conflicts, and ambiguities within and across the many different guidelines that exist today. Some clinicians may not be aware of existing guidelines, or may not believe that the evidence supporting them is adequate. Some time-pressed clinicians may inadvertently overlook existing guidelines, while those in some specialties may feel uncomfortable using anticoagulant therapy due to the potential risk of bleeding.

Whatever the reasons for poor adherence, the good news is that effective strategies appear to be available to support clinicians in their efforts to practice evidence-based care. A recent meta-analysis of 30 U.S. and international studies evaluating various strategies for increasing the use of prophylaxis came to the following conclusions [90]:

- Passive strategies (such as guideline dissemination by means of international or local publication) resulted in poor adherence to guidelines, with no more than half of patients receiving appropriate prophylaxis.
- More proactive strategies resulted in significantly higher adherence rates. These included computer-based clinical decision support systems, audit and feedback, documentation aids, and active monitoring of DVT/PE prophylaxis policies. Computer-based decision support resulted in nearly 100 percent compliance with guidelines, while the other strategies resulted in roughly 80 percent compliance. (See box below for a case example of a computerized reminder system that boosted use of prophylaxis and significantly reduced the incidence of both DVT and PE.)
- The use of multiple strategies consistently resulted in improved adherence to guidelines. Based on these findings, the authors of this study recommend a multipronged approach to increasing use of prophylaxis, including the following elements: continuing education to improve clinician knowledge of DVT/PE risk assessment and appropriate prophylaxis; documentation and/or computer-based systems to remind clinicians to assess risk and assist in prescribing appropriate prophylaxis; and ongoing assessment of the effectiveness of existing policies and interventions, with refinements as necessary [91].

Public Awareness about DVT

The American Public Health Association (APHA) commissioned a telephone survey of over 1,000 American adults to determine current levels of awareness of DVT among the public. The study found that DVT was the least known of the mentioned diseases and condi-

Computerized Reminders to Boost Adherence

While a variety of strategies are available to encourage physicians to adhere to evidence-based guidelines, one of the most effective appears to be electronic reminders that alert physicians to the potential need for a particular course of action based on the evidence. Brigham and Women's Hospital (BWH) used this approach with physicians whose high-risk patients were not receiving DVT prophylaxis. BWH conducted a randomized controlled trial of 2,506 patients, with 1,255 in the intervention group (i.e., patients whose physicians received an alert) and 1,251 in the control group (i.e., patients whose physicians did not receive an alert) [92]. The study found that 33.5 percent of high-risk patients in the intervention group received DVT prophylaxis, compared to 14.5 percent in the control group. While both figures are too low, the computerized system clearly helped improve adherence dramatically. More importantly, this improved adherence led to a 41 percent lower incidence of symptomatic disease among patients in the intervention group, as compared to those in the control group. Subsequent monitoring of the alert system has found that physicians are now ordering prophylaxis in response to the alert 40 percent of the time, suggesting that further improvement in physician adherence has occurred. Additional testing and analysis of strategies to further improve adherence rates are warranted.

It is important to note that the beneficial effect of the electronic alert system can potentially be replicated without computer support. A nurse, physician, or pharmacist could conduct patient rounds on all overnight admissions, review their charts, and determine whether specific patients are at high risk for developing DVT/PE during hospitalization. They could then review the written physician orders to determine whether prophylaxis had been instituted. For high-risk patients not receiving prophylaxis, the reviewer could page the responsible physician, point out the patient's high risk, note the absence of prophylaxis orders, and suggest implementation of preventive measures.

tions, with less than a quarter of respondents having heard of the disease, compared to 93 percent who had heard of diabetes and allergies and 91 percent who had heard of stroke. Even colitis—at 42 percent awareness levels—was better known than DVT. Males, those under the age of 35, and those with lower levels of education were more likely to be unaware of DVT [93].

Among the one-quarter of the queried population with at least some awareness of the disease, less than half were familiar with any signs or symptoms of the disease (46 percent), had any knowledge of risk factors (43 percent), or knew that DVT could be prevented (25 percent) [93]. In other words, only about 1 in 10 Americans know about DVT and are familiar with its symptoms and/or risk factors, and only about six percent of Americans know what it is and that it can be prevented.

The Importance of Educating the Public: David Bloom's Story

David Bloom died in April 2003 at the age of 39 while covering the war in Iraq as a reporter for NBC News. An avid tennis player who was in great health, he was subject to prolonged periods of immobility and dehydration in Iraq, often having to spend many hours inside a cramped tank. Unknown to David, he had an inherited blood coagulation disorder along with other acquired risk factors for DVT. Two nights before his death, David spoke with his wife, Melanie, on the telephone, telling her that his legs hurt because they had been cramped up inside the tank for too long. He told her that he was planning to sleep outside that night because he could not bear to be cooped up for another night. Having heard that he planned to sleep out in the open naturally made Melanie fear for his safety.

Two days later, as a result of DVT, a massive blood clot traveled from David's leg to his lungs resulting in a PE that killed him almost instantly. He was a victim not of the war's violence, but rather of a lack of awareness about DVT. Had he, his loved ones, or those around him been aware of the risk factors and warning signs, and had he known about his genetic predisposition to the disease, his life might have been saved. Melanie has now made it her mission to educate the public about DVT so that others will not die unnecessarily.

SECTION IV

A Call to Action: A Public Health Response to Reducing DVT and PE

DVT and PE are major public health problems in the United States. Much is known about how to reduce their burden, yet this knowledge is not being applied systematically today. Without a concerted effort to stem this public health crisis, the incidence and burden of these diseases will only grow larger as the population ages.

In May 2006, the Surgeon General hosted a workshop on DVT. This meeting began a developmental process that led to this "Surgeon General's Call to Action." A menu of important actions has been assembled from the presentations, discussion, and comments that were made during that Surgeon General's Workshop. This menu, which is presented in the following section, highlights areas that received significant attention during the workshop and in background papers prepared by scientists and clinicians who participated in the workshop [94]. Although not meant to be prescriptive recommendations, the menu should establish useful starting points for consideration as individuals and groups focus their own skills, creativity, and inspiration on reducing the public health crisis of DVT and PE.

The discussions at the Surgeon General's Workshop centered on research, activities, and interventions in three settings: communities, the health care system, and governments. The key actions discussed are presented for each of these settings, although many of these actions can be applied in all of the settings.

The key actions are organized by a framework called CARE: Communication, Action, Research, and Evaluation.

- Communication refers to the provision of information and tools to motivate and empower decisionmakers within the various settings to create change that will lead to more effective prevention, diagnosis, and treatment of first-time and recurrent DVT/PE.
- Action refers to interventions and activities that will assist various stakeholders in preventing, diagnosing, and treating the diseases more effectively.
- Research and evaluation refers to scientific investigations that will allow for a better understanding of issues that are currently not well understood related to the prevention, diagnosis, and treatment of these conditions.

Setting 1: Communities

Individuals, families, and their communities need to understand DVT and PE, the risk factors for these diseases, and how to reduce these risks. They also need to recognize the signs and symptoms and know about available treatments. Patients and family members should proactively discuss these conditions when interacting with their health care providers. The goal is to raise awareness among patients and family members and empower them to ask their physicians about preventive treatment during hospitalization, after a traumatic event, or in other high-risk situations.

A broad-based communications program can play a major role in raising awareness. From a public education and social marketing standpoint, communications programs can disseminate health messages aimed at educating individuals about DVT/PE and the fact that anyone can be at risk for them. These messages

can highlight the symptoms, warning signs, triggering events, and risk factors associated with these conditions.

One approach that an outreach effort can take is to work with various media, including the Internet, to help fill an important gap that exists today in the availability of appropriate educational materials.

A recent survey found that individuals and family members of those who have had a clot or who suffer from thrombophilia are interested in a variety of topics, most notably prevention, treatment, insurance issues; signs and symptoms of the disease; risk factors; genetics; general information on clots; and local, national, and regional resources to support those at risk or who have DVT/PE [95]. An evaluation of available educational materials found that very few, if any, appropriate materials on these high-interest topics exist [96].

Community-based and national advocacy organizations can potentially play a critical role in helping individuals become more knowledgeable and empowered. Many of these organizations are already actively involved in this effort, and their work needs to be supported and expanded. Emphasis should be placed on family and community opportunities for communication and actions that will raise awareness of DVT/PE among the public at large and among specific, high-risk groups.

Initiating a Communications Campaign: A Case Example

The Coalition to Prevent DVT (The Coalition) established March 2004 as the first DVT Awareness Month. This month-long campaign included a celebrity spokesperson in conjunction with print media coverage, a satellite media tour, and a television public service announcement (PSA) that reached millions of Americans. The following year, the U.S. Senate passed Resolution 56, declaring March as DVT Awareness Month. In March 2005 representatives from The Coalition were seen on "Larry King Live," the "Today Show," and the "Jane Pauley Show." A campaign PSA reached an additional 37 million people. Patient stories were the focus for DVT Awareness Month 2006, and the Coalition is currently preparing a book of patient stories for release by primary author Melanie Bloom, widow of NBC journalist David Bloom who died suddenly of a PE while covering the war in Iraq.

Communication

- Raise consumer awareness about DVT/PE and the magnitude of the burden caused by these conditions.
- Educate consumers about symptoms, risk factors, and triggering events, especially surgery, hospitalization, and trauma.
- Raise consumer awareness about genetic predispositions to DVT/PE
- Promote the use of messages in news reports that educate the public by sharing informa-

tion on the magnitude of the problem, both in terms of incidence and mortality/morbidity.
- Disseminate to the public through news outlets and the Internet individual patient stories, as these stories can often have more impact than statistics alone.
- Emphasize the fact that there exists a large gap between what is known about how to prevent and treat DVT/PE and what is happening in practice today.
- Facilitate the development and dissemination of uniform messages about DVT/PE that are consistent with existing guidelines.

Action

- Form community coalitions to sponsor public awareness campaigns.
- Develop tools and materials that patients can use when talking with their physicians and other health professionals.
- Create local networks and peer support programs for patients and their family members.
- Work with volunteer groups, professional societies, and the media as part of a national awareness campaign intended to educate both the public and health professionals about the incidence of the disease, along with its symptoms and risk factors.
- Make available to the media accurate messages about DVT/PE for news stories and media programming, including television shows.
- Encourage community-based advertising campaigns.
- Consider using a celebrity spokesperson to deliver messages about these conditions, especially a celebrity who may have had a personal experience related to either DVT or PE.

Research and Evaluation

- Gain a better understanding of what the public already knows about DVT/PE, gaps in their understanding, and how best to address those gaps.
- Develop and test messages to determine which approaches work best to educate the public, inform them of when they are at risk, and empower them to raise issues proactively with their clinicians.
- Investigate, in a culturally and linguistically appropriate manner, why certain ethnic groups are more or less likely to develop these conditions.
- Investigate the causes of age- and gender-based variations in the incidence and recurrence of these diseases, including why men are more susceptible to a recurrence.
- Research the role that behavior modification (e.g., smoking cessation, increased physical activity, better diet, weight loss) plays, if any, in reducing risk.
- Conduct research to better understand why obesity increases risk.
- Investigate the role that prolonged immobility due to travel (air, car, rail), hospitalization, or nursing home confinement plays in increasing risk.
- Conduct an analysis of the economic toll of DVT/PE on individuals, families, communities, and the nation as a whole. This analysis should include not only the direct costs (i.e., healthcare expenditures), but also indirect costs such as lost productivity and wages due to time away from work.
- Evaluate the impact of communication and social marketing programs, including pre- and post-evaluation levels of consumer awareness and knowledge.
- Conduct formative research to ensure that media messages are positive, realistic, relevant, consistent, and effective.

Setting 2: The Health Care System

The health care system is uniquely positioned to implement interventions aimed at reducing the incidence and burden of DVT/PE. The majority of cases occur within the health care system, for example, during surgery, hospitalization, or treatment for trauma. Although much is known about effiective prevention and treatment, this evidence is not being applied in a systematic way.

Hospitals, health systems, medical schools and residency programs, researchers, universities, primary care and specialty group practices, physicians, nurses, and allied health professionals have a critical role to play in preventing and reducing the burden of DVT/PE. There is much work to be done—both to better apply evidence-based medicine in real-world settings today, and to investigate the many gaps in knowledge related to the basic and clinical science surrounding these diseases. Insurers, health plans, and other public and private purchasers also have a critical role to play in establishing payment policies that encourage the provision of high-quality, evidence-based care.

Communication

- Inform health care professionals and administrators about the problem of DVT/ PE in terms of mortality, morbidity, and direct and indirect costs.
- Promote evidence-based practice by sharing existing guidelines with appropriate professionals on the prevention, diagnosis, and treatment in specific populations.
- Promote the findings and recommendations from groups such as the IOM, AHRQ, Joint Commission, and NQF related to the importance of screening all hospitalized patients for risk for these diseases, and providing appropriate preventive treatment based on those screenings.
- Raise awareness of current agency and organizational guidelines in relation to preferred practices and performance measures.
- Educate health professionals about the availability of genetic testing, when it may be appropriate to discuss with and test patients, and the importance of counseling for those who test positive.
- Educate primary care physicians and specialists about the true, relative risks of excessive bleeding from properly managed anticoagulation therapy versus the risks of not using such therapy.
- Inform health care providers about the availability and appropriate use of treatment options, including anticoagulation therapy and clot-dissolving/clot-removal therapies.

Action

- Convene cross-disciplinary forums to forge consensus on a single set of clear, standardized, evidence-based guidelines in those areas where multiple and/or conflicting guidelines currently exist.
- Institute formal systems related to risk assessment and the provision of preventive therapy (prophylaxis) to appropriate high-risk individuals in the hospital and community.
- Consistently track performance on current and future DVT measures that are endorsed by NQF, and develop quality improvement initiatives designed to improve performance on these measures over time.
- Develop and improve easy-to-use tools (e.g., reminder systems) that provide ready access to relevant data and information at the point of care. These tools help practitioners to follow existing evidence-based guidelines.
- Develop and/or refine tools and/or algorithms

to determine who should undergo diagnostic imaging tests for DVT/PE. These tools could incorporate clinical manifestations, biomarkers and genetic profiles, patient and family history, the results of simple mechanical tests, and other information to determine who should be screened.
- Identify and support physician champions who can encourage their peers to provide evidence-based preventive, diagnostic, and therapeutic care.
- Encourage the development of new pharmaceutical agents that have fewer drawbacks than existing medications. The goal is to find agents with faster onset, a wider therapeutic range (thus reducing the need for frequent testing or monitoring of dosage), and fewer food and drug interactions.
- Encourage medical, nursing, and pharmacy schools, and residency programs to provide adequate classroom education and training to ensure that new physicians, nurses, and pharmacists are aware of the magnitude of the problem and how to prevent, diagnose, and treat DVT/PE in accordance with the latest scientific evidence.
- Encourage medical, nursing, and pharmacy schools, and residency programs to develop more formalized programs for training students and residents who might be interested in becoming thrombosis specialists.
- Encourage medical, nursing, and pharmacy schools, and other organizations to incorporate training into continuing medical education, certification, and recertification processes.
- Review payment policies to ensure that they provide appropriate reimbursement for high-quality, evidence-based care.
- Support the development of hospital- and community-based support programs for patients with DVT/PE and their family members.
- Analyze the merits of innovative approaches to anticoagulation therapy management, including, but not limited to, anticoagulation clinics and patient self-testing/management.
- Develop and/or encourage physicians, nurses, and other health professionals to attend education programs related to all aspects of DVT/PE.
- Support the training of investigators and providers by sponsoring fellowships and other training opportunities.

Research and Evaluation

- Conduct further research into the benefits and risks associated with various strategies (pharmacological, mechanical, and surgical) for dissolving or removing clots, and to determine which patients, if any, would benefit from these approaches (as an alternative to anticoagulation therapy).
- Conduct further research into the pathophysiology of DVT/PE, including the roles of inflammation, obesity, stasis, and the basic endothelial cell biology and vessel response to stasis and thrombosis. This research can lead to the development of novel prevention and treatment strategies.
- Investigate whether biomarkers can be identified that will allow for the development of individualized risk profiles for primary and recurrent DVT/PE, and chronic venous insufficiency. These biomarkers can be used to help predict an individual's response to therapy.
- Investigate the role of prolonged air, car, or rail trips (and other situations causing long periods of immobility) on raising risk, both for the general population and certain high-risk groups, such as women on oral contraceptives or individuals with a genetic predisposition to DVT/PE.

- Investigate the role of compression ultrasonography (CUS) in diagnosing isolated calf DVT, and study the benefits and costs associated with treatment.
- Study the effectiveness of the D-dimer test in diagnosing recurrence of the disease.
- Investigate the safety and effectiveness of various approaches to diagnosing DVT/ PE in pregnant women.
- Conduct further research into the best drugs, dosing strategies, and treatment regimens for anticoagulation therapy for certain patient populations, including children (from infancy through adolescence), obese individuals, and those with renal insufficiency.
- Conduct further research on the benefits and risks of preventive and therapeutic anticoagulation therapy for certain patient populations, including children, pregnant women, individuals with a genetic predisposition to DVT/PE (with or without prior events), cancer patients, and the elderly. Such research should also address how to treat individuals with multiple risk factors, such as pregnant women or children with genetic predisposition.
- Conduct further research into the appropriate duration of anticoagulation therapy in specific patient populations, including whether some high-risk groups should remain on the therapy indefinitely.
- Investigate the role that pharmacogenetics can play in determining optimal warfarin dosing in individuals.
- Investigate the role of inferior vena caval (IVC) filters as a primary means of preventing PE, and research the risks and benefits related to permanent versus retrievable placement of IVC filters.
- Investigate and evaluate the various approaches (e.g., pharmacological, mechanical, and/or a combination) to reducing the risk and impact of chronic venous insufficiency.
- Investigate the risks and benefits of using clot-dissolving medications in patients with PE.
- Conduct research into when genetic testing is appropriate, including whether and when to test the asymptomatic family members of those with a genetic predisposition to DVT/PE.
- Conduct further research into the optimal therapy for those with genetic predisposition, and how that therapy might vary depending upon the number of genetic and other acquired risk factors or triggering events. Research should focus on the impact of specific thrombophilic disorders on anticoagulant therapy management and the identification of optimal prophylactic strategies for asymptomatic individuals during high-risk situations.
- Conduct research into how upper extremity DVT—a less common and less studied form than DVT in the legs—should best be evaluated, diagnosed, and managed.

Setting 3: Policymakers and Governments

Policymakers and various branches of local, tribal, state, and national governments also have a critical role to play in raising awareness and encouraging the development and use of evidence-based guidelines.

Communication

- Raise policymakers' awareness of DVT/PE and the magnitude of the problems caused by the disease, as well as the need to support research, infrastructure, and payment policies that are consistent with the provision of evidence-based care.
- Support public awareness campaigns, including DVT Awareness Month activities.
- Support the education of health professionals,

including the dissemination of evidence-based guidelines.

Action

- Review reimbursement policies to ensure that they encourage the provision of evidence-based prevention, diagnosis, and treatment.
- Support the formation of community-based, regional, and national multistakeholder coalitions dedicated to raising awareness about these diseases.
- Form task forces, steering committees, or advisory committees dedicated to addressing the problems resulting from these conditions.
- Support actions that lead to enhanced public awareness about DVT/PE among health professionals and greater adherence to evidence-based practices.

Research and Evaluation

- Support basic, clinical, and epidemiological research that is intended to fill critical gaps in today's knowledge about DVT/PE.
- Support translational research and the development of other tools that are intended to speed the adoption of new scientific knowledge into the everyday practice of medicine.
- Support the training of scientific investigators and providers who are interested in these diseases.

SECTION V

A Catalyst for Action

This "Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism" is intended to serve as a catalyst for the development of coordinated efforts to prevent and treat these diseases. Translating the ideas raised in this report will require a great national commitment. Collectively identifying current gaps in knowledge and action, and developing and initiating programs to fill those gaps are necessary. Public and private partnerships will be critical to this task. While the magnitude of the problem is great, the range of potential solutions is even greater. The design of successful interventions and actions for prevention and appropriate diagnosis and treatment of DVT/PE will require the careful attention of many individuals and organizations working together at multiple levels.

The Power of Partnerships

Partnerships and collaborations can be powerful vehicles for stimulating positive change. These collaborations can play a critical role in any or all of the following:

- educating the public, patients, and healthcare providers
- assessing the true educational needs and evaluating educational efforts through formal research
- creating and distributing educational messages and materials for the public and patients through seminars, printed material, Web sites, and the media
- educating various health care provider groups
- encouraging the development of scientific studies for at-risk populations
- promoting the development of evidence-based standards related to prevention, diagnosis, and treatment
- making existing standards accessible and easy to use for all providers
- participating in the development of national treatment guidelines and endorsing them.

Fortunately, there are already successful partnerships on which to build. A number of them are included in the presentations given at the Surgeon General's Workshop on Deep Vein Thrombosis (www.surgeongeneral.gov/topics/deepvein/). The following are three examples.

Government-Provider Collaboration

The Thrombosis and Hemostasis Centers Pilot Program was initiated in 2001 as a collaborative program between the Division of Blood Disorders of the Centers for Disease Control and Prevention and eight Thrombosis and Hemostasis Centers. The intended purpose of the program is to:

- determine the efficacy of integrated multidisciplinary care and prevention services for persons with hemostatic disorders to reduce morbidity and mortality associated with bleeding and clotting diseases
- assess unmet needs for service delivery and identify outreach strategies designed to improve access to care
- develop effective messages aimed at disease management and prevention; and
- foster the development of training programs to enhance provider skills for the delivery of hemostasis and thrombosis care.

During the first five years of this pilot program, the collaborative program has established a patient registry that includes over 3,300 patients (as of October 2006) and has published a manuscript on essential components for a multidisciplinary program in support of patients with thrombotic and hemorrhagic disorders [97]. In July of 2007, the Thrombosis and Hemostasis Centers Research and Prevention Network was established to further epidemiologic and clinical research investigations in thrombosis and thrombophilia (and their associated complications). For more information, please see www.cdc.gov/ncbddd/hbd/clotting.htm.

Government-Professional Society Collaboration

In February 2003, the APHA and CDC convened 60 of the nation's leading medical experts and patient advocates in Washington, DC for a Public Health Leadership Conference on DVT. The purpose of the conference was to highlight the urgency of increased diligence related to disease prevention on the part of the healthcare community, as well as the need to raise awareness of DVT/PE and its complications among the general public. The conference identified several areas in need of immediate attention for education about these conditions:

- Create a national coalition to advocate for greater awareness of DVT/PE among health care professionals and the general public.
- Enlist the support of medical, professional, and patient advocacy organizations to make awareness part of their agendas.
- Develop a public awareness campaign and communication tools to educate consumers about the risk factors, symptoms, and prevention measures.
- Encourage state medical licensing boards to include DVT/PE in their CME/CE licensing renewal requirements.
- Close the gap between clinical practice guidelines for prophylaxis and actual practice through the creation and implementation of institutional standards.
- Encourage academic centers to incorporate education into curricula for all medical professionals.
- Ask accreditation and "standardization" institutions to ensure that healthcare providers and institutions implement clinical practice guidelines for prevention.
- Encourage the Joint Commission to make adherence to prevention guidelines part of its accreditation process.
- Educate policymakers about the cost-effectiveness of prevention and treatment of these conditions.

Public-Private Sector Collaboration

The Centers for Medicare and Medicaid Services (CMS) and the Joint Commission have joined together to adopt standardized performance measures for hospitals to report. The DVT/PE quality measures initiative is expected to become a CMS required reportable item, thus allowing CMS to benchmark hospitals' care of these diseases against best performance.

Other examples can be found in the proceedings of the Surgeon General's Workshop on Deep Vein Thrombosis.

CONCLUSION

A Vision for the Future

As the previous section illustrates, there is no shortage of interest in grappling with the problem of DVT/PE. High-profile individuals and organizations with substantial resources are committed to the task. The key for these stakeholders is to come together to build a coordinated plan that can lead to a dramatic reduction in the incidence and burden of these diseases in this nation.

This Call to Action is for all who can have an impact on the incidence and burden of DVT and PE in the United States. It calls for these stakeholders to take effective action to create a future where:

- The public at large is knowledgeable about the risk factors, triggering events, and symptoms of these diseases, and individuals feel empowered to talk with their clinicians about them whenever appropriate.
- Evidence-based practices for the screening, prevention, diagnosis, and treatment of DVT/PE are clearly understood and routinely applied by all medical professionals in all settings.
- New scientific evidence is routinely being discovered to fill gaps in knowledge, and these findings are quickly and easily disseminated to the public and put into practice by health professionals.

The overall results of this action agenda will be to save tens of thousands of lives each year and to reduce the suffering for many more. Implementing this vision will not be an easy task, and progress will take time. Many barriers stand in the way, but solutions must be found and, more importantly, set into motion. We will need the energy and commitment of individuals, families, the health care system, private sector organizations, and government at all levels to work together to build solutions that will bring better health to Americans. With these dedicated efforts we can make this vision a reality.

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