

PRACTICE MANAGEMENT

Thomas L. Forbes, MD, Section Editor

Call to action to prevent venous thromboembolism

Thomas W. Wakefield, MD,^a Robert B. McLafferty, MD,^b Joann M. Lohr, MD,^c Joseph A. Caprini, MD,^d David L. Gillespie, MD,^e and Marc A. Passman, MD,^f on behalf of the Executive Committee of the American Venous Forum, *Ann Arbor, Mich; Springfield, Ill; Cincinnati, OH; Chicago, Ill; Rochester, NY; and Birmingham, Ala*

Deep venous thrombosis and pulmonary embolism, together called venous thromboembolism, remain a serious national health problem. Estimates suggest that over 900,000 cases occur in the United States per year, with 300,000 deaths per year. Because of the significant and serious nature of this problem, a workshop was held in May of 2006, which resulted in the Acting U.S. Public Health Service Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism. On September 15, 2008, Acting Surgeon General, Rear Admiral Steven K. Galson, MD, MPH, and Elizabeth Nabel, MD, Director National Heart, Lung, and Blood Institute, announced the Call to Action. The Call to Action highlights public awareness about the risk factors, triggering events, and symptoms of venous thrombosis and pulmonary embolism, and encourages the development of evidence based practices for screening, prevention, diagnosis, and treatment of venous thrombosis and pulmonary embolism. It is designed to encourage new scientific investigation in an effort to obtain needed evidence to fill in the gaps of knowledge about venous thrombosis and pulmonary embolism. This knowledge should be quickly and easily disseminated to the public and put into practice by health professionals. The Surgeon General's Call to Action represents one of the most important advances in the field of venous thromboembolism and sets the stage for multidisciplinary efforts to combat this serious national health problem. (*J Vasc Surg* 2009;49:1620-3.)

Deep venous thrombosis (DVT) and pulmonary embolism (PE), together called venous thromboembolism (VTE), remain a serious health care problem. The best estimates suggest that there are over 900,000 cases of VTE per year in the United States of which 300,000 individuals die of PE every year.¹ Deaths from PE are five times more common than deaths from breast cancer, motor vehicle accidents, and AIDS combined. After heart disease and stroke, VTE is the third most common vascular disease. The major sequel of DVT, the post-thrombotic syndrome, leads to pain and leg swelling after thrombosis. Patients with this syndrome suffer poor quality of life due to these chronic symptoms. The incidence of post-thrombotic syndrome is as high as 30% over eight years, although some suggest that the incidence is even higher, especially for iliofemoral venous thrombosis.²

A number of risk factors for VTE have been identified, and new factors are currently being investigated. Those factors considered to be acquired include age, malignancy,

surgery and trauma, immobilization, oral contraceptive use, hormone replacement therapy, pregnancy and the puerperium, obesity, neurological and cardiac diseases, and antiphospholipid antibodies.³ Those factors considered genetic include deficiencies of antithrombin, protein C and S; factor V Leiden and prothrombin 20210A gene variants; blood group non-O, hyperhomocystinemia, dysfibrinogenemia, dysplasminogenemia, reduced heparin cofactor II activity, elevated levels of clotting factors such as factors XI, IX, VII, VIII, X, and II, and elevation in plasminogen activator inhibitor-1.⁴ Among hematologic diseases associated with an increased risk of DVT, heparin-induced thrombocytopenia (HIT) and antiphospholipid antibody syndrome are most likely to be treated by vascular specialists.⁵ For venous thrombosis, indications for procoagulant screening include venous thrombosis in unusual locations (ie, mesenteric venous, portal venous, etc), idiopathic venous thrombosis, recurrent venous thrombosis, thrombosis while taking oral contraceptives, and superficial venous thrombophlebitis in a non varicose long saphenous vein. It is the significant nature of the VTE problem noted above that prompted the Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism.⁶

From the Section of Vascular Surgery, University of Michigan Medical Center,^a Southern Illinois University Medical Center,^b Good Samaritan Hospital,^c Feinberg School of Medicine, Northwestern University,^d University of Rochester School of Medicine,^e University of Alabama at Birmingham.^f

Competition of interest: none.

Reprint requests: Thomas W. Wakefield, MD, S. Martin Lindenauer Professor of Surgery Section, Head of Vascular Surgery, Department of Surgery, 1500 E. Medical Center Dr., CVC 5179 – SPC 5867, Ann Arbor, MI 48109 (e-mail: thomasww@umich.edu).

0741-5214/\$36.00

Copyright © 2009 by the Society for Vascular Surgery.

doi:10.1016/j.jvs.2009.01.058

HISTORY OF THE CALL TO ACTION

The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism grew out of a Workshop on DVT/PE held in May 2006 at the National Institute of Health in Bethesda, Maryland. At that time,



Fig 1. A, Dr. Steven Galson addressing the Call to Action. Photograph courtesy of the Vascular Disease Foundation. B, Dr. Elizabeth Nabel addressing the Call to Action. Photograph courtesy of the Vascular Disease Foundation.

over 40 experts on behalf of themselves and their organizations presented findings regarding the prevention, diagnosis and treatment of VTE. The workshop was co-chaired by Thomas L. Ortel, MD, PhD, Duke University Medical Center and Samuel Z. Goldhaber, MD, Harvard Medical School. The workshop was hosted by former Surgeon General, Vice Admiral Richard H. Carmona, MD, MPH, FACS; the Deputy Surgeon General and Workshop Chair RADM Kenneth P. Moritsugu, MD, MPH; and the Director of National Heart, Lung and Blood Institute Elizabeth G. Nabel, MD. Members of the American Venous Forum were well represented at this workshop, including Joseph A. Caprini, MD, Robert B. McLafferty, MD, and Thomas W. Wakefield, MD. The workshop highlighted the tremendous gap in understanding and knowledge that exists regarding these thrombotic disorders despite the advances in the prevention, diagnosis, and treatment for these disorders that have been made. Conclusions from that workshop included the need to disseminate information more widely about the availability of effective interventions to prevent and treat DVT/PE, the need to invest in basic scientific, clinical, and epidemiological research related to DVT/PE,



Fig 2. Picture of all the representatives from the AVF (from left to right); Robert McLafferty, David Gillespie, Thomas Wakefield, Joann Lohr, Joseph Caprini, Marc Passman.

and the need to encourage translational research to allow for the latest information to be put into practice. The Surgeon General's Call to Action was proposed by Dr. Carmona at the conclusion of the workshop to provide a mechanism for the development of a coordinated plan to address these issues as listed above. This Call to Action occurred September 15, 2008 and was delivered by Acting Surgeon General, Rear Admiral Steven K. Galson, MD, MPH (Fig 1, A), and Elizabeth G. Nabel, MD, Director National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH; Fig 1, B). Again, the American Venous Forum was well represented with members present Joann M. Lohr MD, Joseph A. Caprini, MD, Marc A. Passman, MD, David L. Gillespie, MD, Robert B. McLafferty, MD, and Thomas W. Wakefield, MD (Fig 2). Additionally, to aid attendees in the work of education in venous disease, the American Venous Forum had a National Venous Screening Program booth setup on site (Fig 3). As Dr. Nabel stated, "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. . . 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." In fact, the NIH has just funded eight new research projects in an RFA entitled "Deep Vein Thrombosis and Venous Disease (R01)." Topics funded are wide ranging and encompass many areas of new research. They include aspects of malignancy and venous thrombosis including the role of tissue factor, procoagulant microparticles and other basic mechanisms of thrombosis in cancer-associated venous thrombosis, new treatment paradigms for childhood venous thrombosis, and new therapeutic targets for venous thrombosis prophylaxis and treatment. Additionally, studies of recurrent venous thrombosis, chronic thrombotic venous disease, and new imaging biomarkers for the prognosis of pulmonary embolism are included.



Fig 3. Dr. Steven Galson at the screening booth with Robert McLafferty and Marc Passman.

What follows is a summary of the Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism (U.S. Department of Health and Human Services). It is divided into a number of sections (which are reproduced in the current review) and concludes with a vision for the future.

DEFINITIONS OF DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM

The call to action begins with a definition of DVT and PE. Important points made in this section include the fact that half of all DVT produce few if any symptoms, 30% of patients go on to suffer additional symptoms such as pain and swelling, recurrent skin breakdown, and painful leg ulcers, and that patients who have suffered a DVT are at increased risk of developing subsequent episodes throughout the remainder of their lives.⁷⁻¹¹ Regarding PE, which occur in over one-third of patients with DVT, this is a serious life-threatening condition that can not only produce symptoms of shortness of breath, tachycardia, sweating, and sharp chest pain but can also lead to sudden death.¹¹ This occurs when one or more of the vessels that supply blood to the lungs are completely blocked by clot. Although most of the time these PE lyse on their own, in some instances they do not lyse completely, leading to chronic pulmonary hypertension.

DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM AS MAJOR PUBLIC HEALTH PROBLEMS

In this section of the Call to Action document, much of the epidemiology of VTE is discussed. As stated, "While the precise incidence and prevalence remain 'elusive' and a matter of some debate, one thing is undeniably clear – DVT/PE are major national health problems that have a dramatic, negative input on the lives of hundreds of thousands of Americans each year." The mortality and morbidity of VTE is emphasized, which for PE is death and for DVT includes recurrence and the development of post-

thrombotic syndrome (chronic venous insufficiency). Factors that raise the risk of VTE are next discussed, including genetic risk factors (deficiencies of anticoagulant protein C, protein S, and antithrombin); mutations in Factor V Leiden and prothrombin G20210A, and the concept that genetic risk factors and the environment interact. Acquired risk factors are discussed including exposure to estrogen containing agents, pregnancy, cancer, surgery (especially in cancer patients), and obesity. The concept of triggering events such as hospitalization, major surgery, trauma, and prolonged immobility is discussed. Hospitalization for acute medical illness, trauma, and major surgery are next discussed in detail, as is the fact that nursing home residency increases the risk as well. Finally, travel is discussed as a risk factor for thrombosis. Although the economic impact is introduced, there is a lack of hard data on this topic.

REDUCING THE RISK FOR DVT/PE

The Call to Action document discusses the pharmacological agents and mechanical devices that are available for VTE prophylaxis. Regarding guidelines to prevent DVT and PE, a search conducted June 27, 2006 revealed more than 100 such guidelines. The Agency for Healthcare Research and Quality (AHRQ) has ranked the effectiveness of 79 safety practices based on the strength of evidence and found prevention to be the highest ranked of all the practices evaluated.¹² Based on this information, the National Quality Forum (NQF) now recommends that all hospitalized patients be evaluated upon admission and regularly thereafter for VTE prophylaxis. The American College of Chest Physicians (ACCP) consensus document provides detailed recommendations on what regimes to use and when to use them in prophylaxis.¹³ In 2006, the NQF endorsed a set of 20 national voluntary consensus standards related to the prevention and care of VTE. This set of standards includes a policy statement 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 and two performance measures . . . which relate to ordering and providing preventive treatment to hospitalized patients. These measures are "Surgery patients with recommended prophylaxis orders; and Surgery patients who receive appropriate prophylaxis within 24 hours prior to surgery to 24 hours after surgery." In this section of the Call to Action is a plea that all stakeholders come together to develop a "more unified, synthesized, and clear set of guidelines related to the prevention, diagnosis, and treatment of DVT/PE in specific patient populations.

GAPS IN APPLICATIONS AND AWARENESS OF EVIDENCE-BASED INTERVENTIONS

Despite the availability of effective agents for the prophylaxis of VTE, evidence-based guidelines are not being routinely followed. This is true across all age groups, in both academic and community hospitals, and throughout all regions of the country and even in Canada. Women are even more likely than men not to receive prophylaxis.¹⁴

Not only is there a problem with proper adherence to prophylaxis guidelines, there is also a lack of adherence to proper treatment guidelines.¹⁵ Recommendations to improve proper adherence to guidelines includes a multipronged approach.¹⁶ The public awareness of DVT is even more problematic – 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.”

A CALL TO ACTION: A PUBLIC HEALTH RESPONSE TO REDUCING DVT AND PE/A CATALYST FOR ACTION

The next two sections of the Call to Action basically list key actions organized in a framework of communication, action, research, and evaluation from the 2006 Workshop. The settings for these actions included communities, the health care system, policymakers, and governments. These sections make recommendations on how to move ahead on these processes. As an example of the response of the American Venous Forum (AVF) to these recommendations, developing tools and materials that patients can use when talking with their physicians and other health care workers is being championed by the AVF screening program. The AVF’s guidelines effort is developing standardized, evidence-based guidelines in those areas where multiple and/or conflicting guidelines currently exist. Finally, the AVF is supporting actions that lead to enhanced public awareness about DVT/PE among health professionals and greater adherence to evidence-based practices through active membership and participation in organizations such as the Venous Disease Coalition. Additionally, the Call to Action emphasizes the formation of partnerships between the government and providers, the government and professional societies, and the public and private sectors.

A VISION FOR THE FUTURE

As stated in the final section, 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.”

AUTHOR CONTRIBUTIONS

Conception and design: TW
Analysis and interpretation: TW
Data collection: TW
Writing the article: TW
Critical revision of the article: TW, RM, JL, JC, DG, MP
Final approval of the article: TW
Statistical analysis: N/A
Obtained funding: N/A
Overall responsibility: TW

REFERENCES

1. Heit JA, Cohen AT, Anderson FJ. Estimated annual number of incident and recurrent, non-fatal venous thromboembolism (VTE) events in the US. *Blood* 2005;106:267A.
2. Prandoni P, Lensing AW, Prins MR. Long-term outcomes after deep venous thrombosis of the lower extremities. *Vasc Med* 1998;3:57-60.
3. Bauer KA, Rosendaal FR, Heit JA. Hypercoagulability: too many tests, too much conflicting data. *Hematology Am Soc Hematol Educ Program* 2002:353-68.
4. Henke PK, Schmaier A, Wakefield TW. Vascular thrombosis due to hypercoagulable states. In: Rutherford RB, editor. *Vascular Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2005. p. 568-78.
5. Andreotti F, Becker RC. Atherothrombotic disorders: new insights from hematology. *Circulation* 2005;111:1855-63.
6. The Surgeon General’s Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism. U.S. Department of Health and Human Services, 2008. Located at: <http://www.surgeongeneral.gov/topics/deepvein/calltoaction/call-to-action-on-dvt-2008.pdf>. Accessed date: .
7. Piazza G, Goldhaber SZ. Acute pulmonary embolism: part II: treatment and prophylaxis. *Circulation* 2006;114:e42-7.
8. Mohr DN, Silverstein MD, Heit JA, Petterson TM, O’Fallon WM, Melton LJ. The venous stasis syndrome after deep venous thrombosis or pulmonary embolism: a population-based study. *Mayo Clin Proc* 2000; 75:1249-56.
9. Prandoni P, Lensing AW, Cogo A, Cuppini S, Villalta S, Carta M, et al. The long-term clinical course of acute deep venous thrombosis. *Ann Intern Med* 1996;125:1-7.
10. Heit JA, Mohr DN, Silverstein MD, Petterson TM, O’Fallon WM, Melton LJ 3rd. Predictors of recurrence after deep vein thrombosis and pulmonary embolism: a population-based cohort study. *Arch Intern Med* 2000;160:761-8.
11. Heit JA, Silverstein MD, Mohr DN, Petterson TM, O’Fallon WM, Melton LJ 3rd. Predictors of survival after deep vein thrombosis and pulmonary embolism: a population-based, cohort study. *Arch Intern Med* 1999;159:445-53.
12. Shojania KG, Duncan BW, McDonald KM, Wachter RM, Markowitz AJ. Making health care safer: a critical analysis of patient safety practices. *Evid Rep Technol Assess (Summ)* 2001;i-x, 1-668.
13. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, Colwell CW; American College of Chest Physicians. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; 133(6 Supp):381S-453S.
14. Kucher N, Tapson VF, Quiroz R, Mir SS, Morrison RB, McKenzie D, Goldhaber SZ. Gender differences in the administration of prophylaxis to prevent deep venous thrombosis. *Thromb Haemost* 2005;93:284-8.
15. Caprini JA, Tapson VF, Hyers TM, Waldo AL, Wittkowsky AK, Friedman R, et al. Treatment of venous thromboembolism: adherence to guidelines and impact of physician knowledge, attitudes, and beliefs. *J Vasc Surg* 2005;42:726-33.
16. Toother R, Middleton P, Pham C, Fitridge R, Rowe S, Babidge W, Maddem G. A systematic review of strategies to improve prophylaxis for venous thromboembolism in hospitals. *Ann Surg* 2005;241:397-415.

Submitted Jan 14, 2009; accepted Jan 24, 2009.