

Prevention of Thromboembolism in Spinal Cord Injury

Second Edition



Consortium for Spinal Cord Medicine

Administrative and financial support provided by Paralyzed Veterans of America

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This guideline has been prepared based on scientific and professional information available in September 1999. Users of this guideline should periodically review this material to ensure that the advice herein is consistent with current reasonable clinical practice.

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Foreword

Clots in the leg veins and pulmonary arteries occur frequently in persons with spinal cord injuries (SCI) and are a major cause of death and disability. Unfortunately, there does not appear to be a decline in either the rate of deep vein thrombosis (DVT) or of fatalities from pulmonary embolism (PE). Because a variety of methods have been recommended for thromboprophylaxis, some practitioners feel uncertain as to which method should be implemented and under what circumstances. As a result, considerable confusion exists in the medical community.

Prevention of these diseases requires both an awareness of the problem and implementation of safe and effective deterrents. To this end, panelists from a variety of disciplines—including medical specialties, physical therapy, and nursing—met under the auspices of the Paralyzed Veterans of America (PVA) to draft recommendations for the prevention of thromboembolism. This group, which consisted of representatives from 17 organizations concerned with the health of patients with spinal cord injury, commissioned a group of experts to develop clinical practice guidelines (CPGs), with recommendations specifically for thromboprophylaxis. The panel was assisted by a methodologist, who searched the medical literature for relevant articles on this topic. These publications then were reviewed, evaluated, and placed in a database to support development of the recommendations.

The guidelines that grew out of this process are designed to focus attention on the issues of awareness and prevention and to provide the best medical and scientific knowledge available to those entrusted with the care of patients who are at special risk. The guidelines include a statement on the prevalence of venous thromboembolism and on the impact of thrombotic disease on rehabilitation and recovery, as well as on mortality. Recommendations are provided on the use of local measures, such as passive leg motion, elastic hose, compression boots, and vena cava filters. Other recommendations concern the use of anticoagulants, such as the low molecular weight heparins, and combined modalities.

The concept of selecting prophylactic measures on the basis of risk is introduced, with risk being defined in terms of such factors as obesity, age, location of lesion, completeness of motor paralysis, prior history of thromboembolism, concurrent surgical procedures, and use of agents to decrease spasticity. Recommendations for when prophylaxis should be initiated as well as discontinued are provided. Finally, future directions for investigation are delineated, because informational gaps in the literature became evident through the process of developing the guidelines.

The panelists recognize that these guidelines are but a first draft in what must be an ongoing dialogue among patients, members of the medical community, and researchers and practitioners who prepare documents such as this. Although every effort has been made to provide a comprehensive statement of the problem, some issues may have been overlooked or not dealt with completely. Some areas are controversial and clearly require further study. And some of the recommended devices and medications may soon become obsolete as other, safer, more effective agents take their place. In 1999, the panel considered three new references in the literature and modified appropriate recommendations accordingly. It is our fervent hope that these guidelines will stimulate new research into the pathophysiology, management, and prevention of thromboembolism in spinal injury and will lead to improved patient outcomes.

David Green, MD, PhD
Chairman
Guidelines Development Panel

Preface

Thromboembolic disorders continue to be a significant threat to the person with a recent spinal cord injury. Less well recognized is the threat of recurrent thromboembolic disorders in people who are living with the after effects of SCI. New research and publications have expanded the state of our knowledge since the publication of the first edition of *Prevention of Thromboembolism in Spinal Cord Injury* in February 1997.

Since its inception the Steering Committee of the Consortium for Spinal Cord Medicine has been committed to publication of clinical practice guidelines and their periodic updating, so that the health-care providers who serve people with SCI will have access to the current thinking, while maintaining the benefits of established scientific evidence. The second edition of *Prevention of Thromboembolism in Spinal Cord Injury* presents such an update in our attempt to disseminate the current concepts of prevention of this deadly complication.

Controversies remain in this field. What about new approaches to anticoagulation? As risk stratification is further refined, how long should prophylaxis be continued in specific clinical circumstances? What is the most cost-effective protocol that combines the use of the various agents that are available?

The recent increase in use of inferior vena cava filters, both temporary and permanent, may yield benefits in prevention of pulmonary emboli, but the long-term consequences of their use in people with spinal cord injury must be monitored. Will assisted coughing with abdominal compression (AKA “quad cough”) dislodge a filter or cause further trauma to the inferior vena cava? Should prophylaxis be continued indefinitely, since the presence of the filter may increase the risk of lower body thrombosis? It is my hope that prospective studies will be published that address these questions. Then there will be new material for incorporation in future editions of this important guideline.

Once again I must express my gratitude to David Green, MD, PhD, for his willingness to lead and champion this cause for the specific population that we serve. He and his panel have proved that endurance and effort bring continued success by publishing this, the first of our second editions. I am also grateful to Dawn M. Sexton and J. Paul Thomas at PVA as they continue to shepherd the process that leads to our publications. Their excellence is manifested daily! For the leadership, membership, and supporters of the Paralyzed Veterans of America, I reserve my highest praise: without you all, this would not have been possible.

Kenneth C. Parsons, MD
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Acknowledgments

The chairman and members of the panel wish to express special appreciation to the individuals and the professional organizations that were involved in the spinal cord medicine consortium, to the expert health care providers who reviewed the draft documents, and to the consumers, the advocacy organizations, and the staffs of the numerous medical facilities and spinal cord injury rehabilitation centers who contributed their time and expertise to the development of these guidelines.

Kit N. Simpson, Andrea K. Biddle, and their fine staff in the Health Policy and Administration Department at the University of North Carolina at Chapel Hill masterfully conducted the initial and secondary-level literature searches, evaluated the quality and strength of evidence of the scientific investigations, constructed evidence tables, and performed meta-analyses of the benefits and effects of the various preventive and therapeutic modalities and interventions.

Members of the Consortium Steering Committee, representing 17 professional organizations, were joined by 50 expert reviewers in providing outstanding scientific and clinical analysis. Through their valuable comments, they helped to refine the recommendations and to identify additional supporting evidence from the scientific literature. The quality of the technical assistance from these dedicated reviewers contributed significantly to the professional consensus building that is hopefully achieved through the guidelines development process.

The guidelines development panel is grateful for the many technical support services provided by the various departments of the Paralyzed Veterans of America. In particular, the panel recognizes the organizational and managerial skills of J. Paul Thomas and Dawn M. Sexton in the Research, Education, and Practice Guidelines Department; the guidance in writing, formatting, and art work provided by James A. Angelo, Patricia E. Scully, and Christine Campbell in the Communications Department; the excellent technical review of the clinical practice guidelines provided by medical writer Joellen Talbot; and the intensive efforts of both PVA staff and consultants who developed the glossary, standardized the nomenclature, and indexed the guidelines. Appreciation is expressed for the steadfast commitment and enthusiastic advocacy of PVA's senior officers, including National President Joseph L. Fox, Sr., Executive Director Delatorro L. McNeal, Deputy Executive Director John C. Bollinger, and the entire PVA Board of Directors. Their generous financial support has made the CPG consortium and guidelines development process a successful venture.

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Summary of Treatment Recommendations

Mechanical Methods of Prophylaxis

1. Whenever possible, compression hose or pneumatic devices should be applied to the legs of all patients for the first 2 weeks following injury. External pneumatic compression devices may be knee or thigh length with single or sequential chamber compression. The effectiveness of these devices may be enhanced by combining them with pharmacologic antithrombotic agents.
2. During every nursing shift, compression modalities should be inspected for proper placement and the underlying skin examined for evidence of abrasions, ecchymoses, or injury. In patients whose thromboprophylaxis has been delayed for more than 72 hours after injury, tests to exclude the presence of leg thrombi should be performed prior to applying compression devices.
3. Vena cava filter placement is indicated in SCI patients who have failed anticoagulant prophylaxis or who have a contraindication to anticoagulation, such as active or potential bleeding sites not amenable to local control (e.g., the central nervous system, gastrointestinal tract, or lungs). Filters should also be considered in patients with complete motor paralysis due to lesions in the high cervical cord (C2, C3),

with poor cardiopulmonary reserve, or with thrombus in the inferior vena cava despite anticoagulant prophylaxis. However, filter placement is not a substitute for thromboprophylaxis, which should be commenced as soon as feasible. Furthermore, filter placement may increase the risk of future development of deep vein thrombosis, so the use of removable filters should be considered.

Anticoagulant Prophylaxis

4. Anticoagulant prophylaxis with either low molecular weight heparin or adjusted dose unfractionated heparin should be initiated within 72 hours after SCI, provided there is no active bleeding or coagulopathy.
5. Anticoagulants should be continued until discharge in patients with incomplete injuries, for 8 weeks in patients with uncomplicated complete motor injury, and for 12 weeks or until discharge from rehabilitation for those with complete motor injury and other risk factors (e.g., lower limb fractures, a history of thrombosis, cancer, heart failure, obesity, or age over 70). This recommendation also applies to those with inferior vena cava filters, because such persons are at increased risk for deep vein thrombosis.

TABLE 1
Guidelines for the Prevention of Thromboembolism in Spinal Cord Injury

Clinical Decision Table

Level of Risk	Motor Incomplete	Motor Complete	Motor Complete With Other Risk*
Intensity of Prophylaxis			
Low	Compression hose Compression boots	Compression hose Compression boots	Compression hose Compression boots
Intermediate	and UH ⁺ : 5000 U q 12h; or LMWH ⁺⁺⁺	and UH ⁺ : Dose adjusted to high normal aPTT ⁺⁺ ; or LMWH ⁺⁺⁺	and UH ⁺ : Dose adjusted to high normal aPTT ⁺⁺ ; or LMWH ⁺⁺⁺
High	—	—	and Inferior vena cava filter in certain situations
Duration of Prophylaxis			
	Compression boots: 2 weeks; Anticoagulants: while in hospital for ASIA class D and up to 8 weeks for ASIA class C	Compression boots: 2 weeks; Anticoagulants: at least 8 weeks	Compression boots: 2 weeks; Anticoagulants: 12 weeks or until discharge from rehabilitation

*Other risk factors: lower limb fracture, previous thrombosis, cancer, heart failure, obesity, age over 70
⁺UH—Unfractionated heparin
⁺⁺activated partial thromboplastin time
⁺⁺⁺LMWH—Low molecular weight heparin, prophylactic dose as recommended by the manufacturers.

Prophylaxis Based on Patient Stratification for Risk

6. Patients with complete motor and/or incomplete non-functional motor involvement should be on prophylactic measures for venous thromboembolism as early as possible.
7. Spinal cord injured patients with functional motor movements or with no significant motor/neurological deficits should be on prophylactic measures as early as possible.
8. The duration of the prophylaxis for thromboembolism should be individualized, depending on the need, medical condition, functional status, support services, and risk of the patient.
9. Reinstitution of prophylactic measures should be considered in chronic SCI patients if they are immobilized with bed rest for a prolonged period of time, are readmitted for medical illnesses or altered medical conditions, or undergo surgical procedures.

Failure of Prophylaxis

10. In symptomatic patients, perform ultrasound of the lower extremities and/or tests for pulmonary emboli. If clinical suspicion is strong but the tests are negative or indeterminate, obtain venography of the legs, spiral computerized tomography of the lungs, or magnetic resonance/contrast angiography.

Exercise, Passive Movement, and Early Mobilization

11. Early mobilization and passive exercise should be initiated as soon as the patient is medically and surgically stable. These activities should be coordinated with other preventative modalities. With documented DVT, mobilization and exercise of the lower extremities should be withheld 48 to 72 hours until appropriate medical therapy is implemented.

Educational Priorities for Health Care Professionals

12. Health care professionals should be aware of the signs and symptoms of DVT and should perform physical assessment to detect this complication. Appropriate prophylactic measures, including application of mechanical devices and administration of anticoagulant agents, should be implemented. Patients, family members, and significant others should be educated in the recognition and prevention of DVT.

Introduction

The high incidence, insidious onset, and potentially lethal consequences make venous thromboembolic disease a leading cause of mortality and morbidity following acute spinal cord injury. The major factors predisposing persons with acute SCI to venous thromboembolism include venostasis due to failure of the venous muscle pump with paralysis (Seifert et al., 1972) and a transient hypercoagulable state (Rossi et al., 1980).

Alterations in hemostasis seen after acute SCI have included reduced fibrinolytic activity (Petaja et al., 1989) and increased blood factor VIII activity (Myllynen et al., 1987), despite normal values on routine coagulation measures. This situation may be aggravated by dehydration, administration of blood products, and concomitant injury to the soft tissue or long bones. Because deep vein thrombosis (DVT) may progress proximally in 20 percent of cases (Davies and Salzman, 1979) and may embolize in up to 50 percent (Carabasi et al., 1987), it is important to regard venous thromboembolism as a continuum of pathology, of which DVT and pulmonary embolism (PE) are subgroups. PE has been found to lead to death in as many as 35 percent of patients not treated for thrombosis (Davies and Salzman, 1979). The need for aggressive medical prophylaxis for thromboembolic disease has become increasingly apparent, and to this end the term "thromboprophylaxis" has been suggested to refer to all measures, medical and otherwise, that act to prevent thromboembolic disease.

Studies examining the incidence of venous thromboembolism in acute SCI vary greatly, principally due to variation in surveillance technique (table 2). Studies based on clinical parameters alone typically estimate the incidence of DVT in acute SCI at 14 to 16 percent (Watson, 1978–79; Myllynen et al., 1985; Waring and Karunas, 1991). The advent of newer technology in the detection of DVT, particularly noninvasive measures, combined with protocols of routine surveillance of acute SCI patients have led to a new appreciation of the high frequency of thromboembolic disease in acute SCI without medical prophylaxis for DVT.

Using sensitive measures such as doppler ultrasonographic imaging and 125-I fibrinogen scan, coupled with the traditional contrast dye venography, studies employing serial examination have shown the incidence of DVT in acute SCI to be from 47 to 100 percent (Myllynen et al., 1985; Merli et al., 1988; Geerts et al., 1994; Clagett et al., 1995). Myllynen et al. (1985) reported on a limited series of 9 patients, all of whom developed DVT when examined using 125-I fibrinogen scans confirmed with venography. The study of a placebo control group by Merli et al. (1988) documented DVT in 47 percent (8 of 17) of acute SCI patients without prophylactic measures.

More recently, Geerts et al. (1994) presented a series of 26 acute unprophylaxed SCI patients, 81 percent of whom developed DVT confirmed on venography. Clagett et al. (1995) published a meta-

TABLE 2
Incidence of objectively diagnosed DVT in patients with acute spinal cord injury

Source and Year	Number of Patients	Number of Patients With DVT	Incidence (%)	Endpoint
Bors et al. (1954)	99	58	59	Venography
Silver (1974)	100	18	18	FUT*
Brach et al. (1977)	10	9	90	FUT*/IPG+
Rossi et al. (1980)	18	13	72	FUT*
Myllynen et al. (1985)	9	9	100	FUT*
Merli et al. (1988)	17	8	47	FUT*
Petaja et al. (1989)	9	7	78	FUT*
Yelnik et al. (1991)	127	29	23	Venography
Gunduz et al. (1993)	30	16	53	Venography
Overall incidence	419	167	40	

Notes: Reprinted with permission from Clagett, G.P., F.A. Anderson, Jr., and J. Heit et al., Prevention of venous thromboembolism, *Chest* 108 (4 Suppl) (1995): 312S–345.

*FUT—Fibrinogen uptake test, confirmed by venography where positive
+IPG—Impedance plethysmography

analysis of 9 studies examining the incidence of objectively measured (using venography or 125-I fibrinogen scan) DVT following acute SCI; of 419 unprophylaxed patients, 167 showed DVT, for an overall incidence of 40 percent.

Several studies have examined the occurrence of DVT relative to time postinjury. DVT has been reported as soon as 72 hours postinjury; however, risk prior to this time appears to be low (Green et al., 1990). In studies of unprophylaxed patients, researchers have found that over 80 percent of DVTs occur within the first 2 weeks of injury (Rossi et al., 1980; Merli et al., 1993). Evidence documenting the duration of this heightened risk is less clear. Incidence of DVT declines after week 2, and one report suggests a 6-percent incidence of DVT at week 8 with discontinuation of medical prophylaxis (Green, 1994).

Studies of longer term risk for venous thromboembolism are rare, but overall suggest a much lower rate of occurrence. Data from the federally designated Model Spinal Cord Injury Systems suggest that the risk for DVT among chronic SCI patients (1–6 years postinjury) is much lower than that for acute SCI patients (1.1 percent), and the risk for PE is even lower (0.3 percent). However, the sample size decreases dramatically, from 2791 at year 1 to 45 for year 6, suggesting significant data loss (Ragnarsson et al., 1995). Kim et al. (1994) looked prospectively at 22 asymptomatic chronic SCI patients and found that only 1 patient (7.0 percent) had chronic DVT. Interestingly, among 21 admissions of chronic SCI patients with clinical signs suggestive of DVT, only 6 turned out to have DVT on venography, yielding an incidence of 28.6 percent among symptomatic patients.

Other clinical factors have been associated with the onset of DVT. Reporting on 2186 acute admissions, Ragnarsson et al. (1995) found a higher rate of occurrence of DVT among those with motor complete injuries (16.6 percent) and lower rates of occurrence among those with incomplete injuries (12.5 percent) and with minimal deficit (6.4 percent). Considering the level of injury as it influences venous thromboembolism risk, Ragnarsson reported that those with paraplegic SCI have a greater risk for DVT than tetraplegic patients (16 and 11.9 percent, respectively). Furthermore, he found that the incidence of PE was not influenced by the degree or level of injury. The same study described the effects of age on the onset of venous thromboembolism, with DVT showing a relatively uniform incidence over the years (15–17 percent), while PE displayed a marked peak in years 61–75. Additionally, both PE and DVT exhibited preferential occurrences in males (M:F roughly 5:3). Finally, a significant association was seen between heterotopic ossification and DVT in a limited retrospective study (Colachis and Clinchot, 1993).

It is not uncommon for DVT to evolve to a chronic stage—postthrombotic syndrome, evidenced by degrees of chronic edema, induration, pain, and skin ulceration. Although clinicians generally agree that postthrombotic syndrome is prevalent among the chronic SCI population, it remains poorly studied among persons with SCI. Prospective studies of unselected patients reveal that DVT progresses to postthrombotic syndrome in one-half to two-thirds of patients (Monreal et al., 1993). These investigators found that 12 percent of patients followed for a 3-year period after DVT were disabled due to postthrombotic syndrome alone. Chronic skin breakdown, pain, refractory edema, recurrent DVT, frequent hospitalization, and at times pulmonary hypertension and cor pulmonale have all been seen in conjunction with postthrombotic syndrome (Davies and Salzman, 1979).

The most striking evidence for the necessity of effective prevention of thromboembolic disease comes from studies of mortality in the first year after SCI. Autopsy investigations into the deaths of acute SCI patients have shown as high as a 37-percent incidence of death due to PE (Tribe, 1963). Reporting on the first years of Model Systems care of SCI, Stover and Fine (1986) reported that PE ranked as the fifth leading cause of death from 1973 to 1985, accounting for 8.5 percent of deaths. In the 1995 Model Systems report, DeVivo and Stover (1995) reported that PE was the third leading cause of death among those with paraplegia, and it was tied for second leading cause of death in those with Frankel D (neurologically incomplete) lesions. Furthermore, PE was found to be the third leading cause of death for all SCI patients in the first postinjury year, accounting for 14.9 percent of deaths in this group. For those with acute SCI, the risk of death due to PE is 210 times greater than that of a similar healthy population. This risk decreases to 19.1 times normal for years 2–5 and further decreases to 8.9 for those who survive more than 5 years.

The toll exacted by thromboembolic disease on society is difficult to calculate, particularly for those with SCI. As a whole, the economic cost of SCI in the United States has been estimated at \$7.2 billion per year (DeVivo et al., 1995). In a conservative investigation, Tator et al. (1993) found that thromboembolic disease can increase length of hospital stay by 46 percent and costs by 35 percent. The development of DVT can mean an additional 1 to 2 weeks of acute hospital care, with costs ranging from \$19,000 to \$38,000 (DeVivo et al., 1995). Given an annual incidence rate for SCI of 30 to 40 cases per million (DeVivo et al., 1995), and a conservative incidence of clinically significant DVT of 47 percent, annual direct costs for hospital care alone can run as high as \$178 million. These figures do not take into account the economic cost of lives lost to throm-

boembolic disease. For the individual person with a spinal cord injury, thromboembolic disease causes considerable discomfort and a delay in recovery. Weeks are lost from physical rehabilitation, an unwelcome interruption in an era when physical rehabilitation time is doled out parsimoniously. In summary, venous thromboembolism causes chronic disfigurement, disability, pain, and too often, death. Knowledgeable medical practitioners can play a significant role in reducing the incidence of this disease.

The Spinal Cord Medicine Consortium

Clinical practice guidelines are a new trend in medicine. They are derived from the National Institutes of Health Consensus Conference format, which enables scientists and clinicians to make statements about clinical conditions based on evidence published in the scientific literature. In June 1995, 17 organizations joined the Paralyzed Veterans of America to create a formal consortium for the development of clinical practice guidelines in spinal cord medicine. After studying the guidelines development process, the PVA Health Policy Department recognized that the success of its CPG process would require that all disciplines and specialties involved in clinical decisionmaking, including payers and consumers, participate and that the development process would have to be based on scientific evidence in order to be credible in the community of practice.

The consortium asked each participating organization to select a representative with guidelines development experience to sit on a steering committee. That committee serves as the consortium governance. To ensure a standardized frame of reference for all organizational representatives, PVA conducted an orientation workshop featuring experts from a number of leading professional organizations with extensive guidelines development experience. The workshop faculty included senior staff members from the Academy of Family Practice, the Academy of Pediatrics, the Agency for Health Care Policy and Research (AHCPR), the American Academy of Otolaryngology—Head and Neck Surgery, the American College of Cardiology, and the American Medical Association.

After extensive study of the processes used to develop numerous types of guidelines, the consortium steering committee unanimously agreed on a new, modified scientific evidence-based model derived from AHCPR. The model was:

- Interdisciplinary, to reflect the multiple information needs of the spinal cord medicine practice community.
- Responsive, with a time line of 12 months for the completion of the guidelines.
- Reality-based, to make the best use of the time and energy of the busy clinicians who were serving as panel members and field reviewers.

Both administrative and financial support were provided by PVA.

The Spinal Cord Medicine Consortium was unique to the practice guidelines field in that it employed highly effective management strategies based on the availability of resources in the health

care community, it was coordinated by a recognized national consumer organization with a reputation for providing effective service and advocacy for persons with spinal cord injury and disease, and it included third-party and reinsurance payer organizations in every level of the development and dissemination process.

Goals of the Guidelines

The primary goal of these guidelines is to improve outcomes for individuals with spinal cord injury by decreasing the frequency and severity of thromboembolic complications. The specific goals are to:

- Provide a rationale for the implementation of thromboprophylaxis.
- Make available to providers the best current knowledge and expert consensus regarding safe and effective prophylaxis procedures.
- Encourage providers to reexamine their practice patterns and to individualize treatment based on patient characteristics.
- Stimulate future research to fill gaps in knowledge regarding thromboprophylaxis for spinal cord injury.

The focus is on persons who have sustained a spinal cord injury and who require appropriate interventions to prevent deep vein thrombosis and pulmonary embolism. The guidelines apply not only to the period immediately following injury, but also to the months and years when longer term prophylaxis is needed. Attempts are made to tailor the approaches to persons with a broad variety of risk factors for thrombosis, such as complete motor paralysis, advanced age, obesity, or a prior history of thrombosis. It is hoped that the recommendations have been optimized by combining published evidence with clinical experience.

Need for the Guidelines

Concerns about thromboembolism arise during the care of nearly every patient with acute spinal cord injury. Centers collecting data on the incidence of deep vein thrombosis and pulmonary embolism continue to report high rates of these complications. Methods of prevention vary widely—from the simple application of elastic hose to the insertion of mechanical filters in the vena cava. Such broad variations in clinical practice reflect the uncertainty and confusion among health care providers regarding optimal management. Thus, there is a need for clinical guidelines based on the best available scientific evidence.

Framework for the Guidelines

The outcome measures used in preparing these guidelines included the endpoints of deep vein thrombosis—pulmonary embolism, hemorrhagic episodes, and mortality. Quality-of-life considerations were also included. The scope of the guidelines covers all patients with spinal injury, although the focus is predominantly on persons with spinal cord injury.

Methodology

To prepare the guidelines, a panel of nine persons was selected: three specialists in internal medicine, two in physical medicine and rehabilitation, and one specialist each in nursing, physical therapy, pharmacology, and radiology. All of the panelists had extensive clinical experience working with persons either with spinal cord injury or venous thrombosis.

In addition, a methodologist, Kit N. Simpson, of the Department of Health Policy and Administration, University of North Carolina School of Public Health, Chapel Hill, conducted an extensive literature search. Sources included MEDLINE and several other databases and covered materials published in English as well as in most European languages. The search strategy included MeSH heading and key word searches and focused on SCI and DVT or other thromboembolic (TE) events. The time period from 1975 to 1999 was examined; more than 126 articles were reviewed. Information was extracted from each article and compiled into summary tables according to epidemiology of DVT/TE, diagnosis of DVT/TE, prophylactic therapy for DVT/TE, and therapy/management approaches for DVT/TE. A separate search was conducted for vena cava filter; some 30 articles published from 1990 to 1999 were retrieved and reviewed.

Nearly seventy articles are cited in these guidelines. The primary emphasis is on experimental studies, although review articles and observational studies also are included if they provide information critical to understanding the natural history of thromboembolism in SCI. This database was sent to all members of the panel, who were asked to prepare a brief summary of the issues in their areas of expertise based on the published literature and on their own clinical experience. Next, a meeting of the panel was convened, and the summaries drafted by each panelist were thoroughly discussed. These discussions led to specific recommendations for management. Over a period of 2 months, panelists revised their drafts and recommendations, which were then forwarded to the Chair to be edited and incorporated into the complete document. Copies of the full draft guidelines were then submitted to representatives of each Consortium member organization for critique and amendment. As a result, the recommendations are based on the best current knowledge, although they undoubtedly will undergo revision as new information becomes available.

Evidence Analysis

Each guideline recommendation is justified in terms of the level of evidence supporting it, with level I being the strongest evidence and level V the weakest. Unfortunately, randomized, controlled clinical trials—level I evidence—have been conducted infrequently in patients with SCI. However, such studies have been done in patients undergoing joint replacement surgery, hip fracture, and stroke so that surrogate evidence for safety and efficacy is available. In addition, observational studies and clinical experience do provide important, though by no means infallible, support for some recommendations. The levels of evidence used in these guidelines (Sackett, 1989) are as follows:

- I. Large randomized trials with definite results.
- II. Small randomized trials with uncertain results.
- III. Nonrandomized studies with concurrent controls.
- IV. Nonrandomized studies with historic controls.
- V. Case series with no controls.

Next, each of the guideline recommendations was classified depending upon the level of scientific evidence supporting the specific recommendations. The schema used by the panel is:

- A Guideline recommendation is supported by one or more Level I studies
- B Guideline recommendation is supported by one or more Level II studies
- C Guideline recommendation is supported only by Level III, IV, or V studies

In situations where no published literature existed, consensus of the panel members and outside expert reviewers was used to develop the guideline recommendation and is indicated as “expert consensus.”

After deliberation and discussion of each guideline recommendation and the supporting evidence, the level of panel agreement with the recommendation was assessed as either low, moderate, or strong. In this assessment, each panel member was asked to indicate his or her level of agreement on a 5-point scale, with 1 corresponding to “neutrality” and 5 representing “maximum agreement.” The scores were aggregated across the panel members and an arithmetic mean was calculated. This mean score was translated into low, moderate, or strong, as follows:

- Low—1.0 to less than 2.33
 Moderate—2.33 to less than 3.67
 Strong—3.67 to 5.0

Treatment Recommendations

Mechanical Methods of Prophylaxis

1. **Whenever possible, compression hose or pneumatic devices should be applied to the legs of all patients for the first 2 weeks following injury. External pneumatic compression devices may be knee or thigh length with single or sequential chamber compression. The effectiveness of these devices may be enhanced by combining them with other antithrombotic agents.** (Scientific evidence—level I; Grade of recommendation—A; Strength of panel opinion—strong)
2. **During every nursing shift, compression modalities should be inspected for proper placement and the underlying skin examined for evidence of abrasions, ecchymoses, or injury. In patients whose thromboprophylaxis has been delayed for more than 72 hours after injury, tests to exclude the presence of leg thrombi should be performed prior to applying compression devices.** (Scientific evidence—NA; Grade of recommendation—expert consensus; Strength of panel opinion—strong)

A number of mechanical modalities have been shown to be effective in reducing the incidence of deep vein thrombosis in acute SCI. These modalities improve lower extremity venous return, which reduces stasis, a major cause for thrombus development in this patient population. Active and passive range of motion reduces lower extremity stasis by simulating flexion and extension of the gastrocnemius and soleus muscle groups, resulting in emptying of the calf veins. Centripetal massage also enhances venous drainage by manual compression. A level III study compared active and passive range of motion twice per day (group A) with lower extremity massage plus elastic bandages (group B) (Van Hove, 1978–79). The incidence of clinical DVT was 40 percent in group A and 0 percent for group B. Because the efficacy of these modalities was assessed by clinical examination, conclusions about the effectiveness of this intervention are not firm.

Several mechanical methods are available for improving lower extremity venous return. A level II study of 15 patients evaluated the rotation of treatment tables as a modality for reducing stasis and preventing DVT (Becker et al., 1987). Although the authors concluded that the method was effective, their mode of assessing the endpoint of thrombosis was limited and their sample size was small, suggesting that the results must be interpreted with caution. Gradient elastic stockings (GES) reduce venous capacitance by applying a uniform distribution of pressure over the extremity. Calf-length stockings are

the most frequently prescribed because of their ease of application. No study indicates a difference in the incidence of DVT with thigh-length versus calf-length GES. This modality has been shown to be effective in low-risk surgery (Wells et al., 1994).

Electrical stimulation (ES) was developed to mechanically simulate dorsi and plantar flexion of the lower extremity (Merli et al., 1988). To accomplish this, stimulation at a pulse duration of 50 μ s and a frequency of 10 HZ was required. The contractions were 4 seconds, with a rest period of 8 seconds. The muscle groups were activated 5 times per minute for 23 hours daily. This modality was evaluated in a level I trial comparing a saline placebo, low-dose heparin, and ES plus low-dose heparin. Patients had acute SCI; were in American Spinal Injury Association (ASIA) class A, B, and C; and were treated during the first 30 days following trauma. The incidence of DVT was 47 percent, 50 percent, and 6.7 percent in the placebo, heparin, and heparin plus ES group, respectively. Despite the effectiveness of ES, it has not been further developed because the stimulation is painful in sensate patients and difficult in patients with lower extremity edema. Additionally, frequent maintenance of the equipment is required.

External pneumatic compression offers a more sustained method of augmenting lower extremity venous return (Salzman et al., 1987). Various devices are commercially available. External pneumatic compression sleeves (EPCS) may be thigh and/or knee length, and the mode of compression may be either graded sequential, multicompartiment uniform, or single-chamber uniform pressures. Although the multichambered sequential pressure devices show improved flow velocity, volume flow rate, shear stress, residual volume, and stimulation of fibrinolysis (Salzman et al., 1987), greater antithrombotic effectiveness has not been demonstrated clinically.

EPCS and EPCS plus antiplatelet agents (aspirin 300 mg twice daily and dipyridamole 75 mg 3 times daily) were studied in ASIA A, B, and C acute SCI by Green et al. (1982). Thrombosis was detected by radiolabeled fibrinogen leg scanning; a previous study by the authors using this method recorded a 72-percent frequency of DVT in patients not treated with EPCS or antiplatelet agents. The incidence of DVT was 40 percent in the EPCS group and only 25 percent in the combination therapy group, but bleeding occurred in some patients receiving aspirin. Merli et al. (1992) demonstrated a reduction in DVT in a similar population by combining EPCS with GES and low-dose heparin (5,000 U subcutaneously every 8 hours).

Another mechanical device is the venous foot pump. It functions by rapidly flattening the plantar arch, which causes an increase in venous return, as well as turbulence in the valve pockets, as demonstrated by video phlebography. In a study of patients having total hip replacement, Fordyce and Ling (1992) demonstrated DVT in 40 percent of a control group compared to 5 percent in those using the venous foot pump. Wilson et al. (1992) evaluated the efficacy of this same device in total knee replacement, but found no significant differences in the incidence of DVT (68.7 percent for the control group versus 50 percent for the venous foot pump group). These were small level II studies, and larger trials will be required to justify the use of these devices in the SCI population.

Only a few studies have examined the safety and effectiveness of combining pneumatic compression devices with anticoagulants. In a very recent trial, more than 2000 patients undergoing cardiac surgery were fitted with pneumatic compression boots on a random basis (Ramos et al., 1996); all were treated with unfractionated heparin (UH), 5000 U every 12 hours. Pulmonary emboli occurred in 1.5 percent of those with boots, as compared to 4 percent without boots ($p < 0.01$). The investigators concluded that the addition of the devices to standard heparin prophylaxis was of significant benefit.

- 3. Vena cava filter placement is indicated in SCI patients who have failed anticoagulant prophylaxis or who have a contraindication to anticoagulation, such as active or potential bleeding sites not amenable to local control (e.g., the central nervous system, gastrointestinal tract, or lungs). Filters should also be considered in patients with complete motor paralysis due to lesions in the high cervical cord (C2, C3), with poor cardiopulmonary reserve, or with thrombus in the inferior vena cava despite anticoagulant prophylaxis. However, filter placement is not a substitute for thromboprophylaxis, which should be commenced as soon as feasible. Furthermore, filter placement may increase the risk for future development of deep vein thrombosis.** (Scientific evidence—level IV; Grade of recommendation—C; Strength of panel opinion—moderate)

No randomized controlled trials of vena cava filters in SCI patients have been reported, and very few studies have specifically addressed the use of filters in these patients. In one prospective series of 63 high-risk trauma patients prophylactically treated with filters (Rogers et al., 1995), the incidence of symptomatic pulmonary embolus was significantly reduced, compared with historical controls treated with heparin and/or venous compression boots. This trial included 25 SCI patients. In a consecutive series of 15 SCI patients treated prophylactically with filters (Wilson et al., 1994), there were no symptomatic pulmonary emboli, compared to an incidence of 6.3

percent in a historical group of 111 SCI patients treated with heparin and/or venous compression boots (with no statistical difference). Some or all of these patients may have been included in the above study. In a third level IV study (Khansarinia et al., 1995), 108 patients with severe trauma were treated prospectively with filter placement as well as with continued DVT prophylaxis. This group was compared to a matched historical series of 216 patients. There was no clinical evidence of pulmonary embolism in the filter treated group, compared to 13 in the historical control group, including 9 PE-related fatalities. This difference was statistically significant. Although SCI patients were included in this study, the specific numbers were not noted.

Recently, 400 patients with deep vein thrombosis considered at risk for pulmonary embolism were randomized to receive a vena cava filter or no filter (Decousus et al., 1998). All patients were given heparin or LMWH acutely and continued on warfarin for at least three months. Evaluation at day 12 showed a significant reduction in the frequency of pulmonary emboli (1.1 percent in those with filters; 4.8 percent in those without filters). However, at two years, 20.8 percent of those with filters, but only 11.6 percent of those without filters, had experienced recurrent deep vein thrombosis. There was no difference in mortality between the two groups. The investigators concluded that the beneficial effect of the vena cava filters was counterbalanced by the excess of deep vein thrombosis.

Adverse experiences reported with vena cava filters include cava thrombosis, filter migration, perforation of the vena cava, and complications at the skin insertion site. The frequency of these problems using the newer small caliber systems and percutaneous insertion is low. Filter malposition is usually due to poor insertion technique, but also can be related to anomalies involving the cava or renal veins or to the presence of intracaval thrombus. This complication can be largely eliminated by the use of routine preinsertion inferior vena cavagrams and fluoroscopic guidance, which should be a prerequisite to filter placement. A followup plain film of the abdomen should always be obtained immediately after the procedure to document filter position. Recurrent pulmonary embolism (defined as embolization with the filter in place) is reported in 2 percent to 5 percent of patients (Balshi et al., 1989; Becker et al., 1992).

Anticoagulant Prophylaxis

- 4. Anticoagulant prophylaxis with either low molecular weight heparin (LMWH) or adjusted dose unfractionated heparin should be initiated within 72 hours after SCI, provided there is no active bleeding or coagulopathy.** (Scientific evidence—one level II study; Grade of recommendation—B; Strength of panel opinion—strong)

5. **Anticoagulants should be continued for 8 weeks in patients with uncomplicated complete motor injury and for 12 weeks or until discharge from rehabilitation for those with complete motor injury and other risk factors (e.g., lower limb fractures, a history of thrombosis, cancer, heart failure, obesity, or age over 70). This recommendation also applies to those with inferior vena cava filters, because such persons are at increased risk for deep vein thrombosis.** (Scientific evidence—level IV studies; Grade of recommendation—C; Strength of panel opinion—strong)

The evidence that low-dose unfractionated heparin (5000 U 2 or 3 times a day) may be beneficial comes from small studies, some retrospective, with inadequate outcome measures. To determine whether higher doses of unfractionated heparin would be more effective, Green et al. (1988) conducted a level I unblinded trial comparing UH 5000 U every 12 hours, with doses of heparin adjusted to prolong the activated partial thromboplastin time (aPTT) into the upper normal range. Doses averaging 13,200 U every 12 hours were required to maintain the aPTT at 1.5 times control values. One-third of patients receiving low-dose UH had thrombosis, compared to 7 percent receiving adjusted dose UH ($p < 0.05$). However, not only was the adjusted dose UH difficult to implement logistically, but 7 of 29 patients had bleeding sufficient to require withdrawal of the heparin.

Green et al. (1990) then compared low molecular weight heparin (tinzaparin) 3,500 U once daily with a higher fixed dose of UH (5000 U 3 times daily), also in a level I trial. This trial was blinded for thrombosis but not for bleeding. The regimens were commenced within 72 hours of injury. Thrombi detected by noninvasive tests were confirmed venographically. The trial was stopped after 41 patients because 7 patients in the UH group but no one in the tinzaparin group had an event ($p = 0.006$). These events included 5 incidents of thrombosis (2 involving fatal pulmonary emboli) and 2 incidents of bleeding.

Subsequent uncontrolled experience with tinzaparin in 60 patients suggested that thrombosis developed at a rate of 10 percent over 8 weeks but bleeding was infrequent; only 1 patient bled in the immediate postoperative period (Green et al., 1994). Experience with another low molecular weight heparin, enoxaparin, has been similar. This anticoagulant was given to 105 spinal injury patients in a dose of 30 mg subcutaneously every 12 hours (Harris et al., 1996). No patient developed clinical evidence of thromboembolism, and bleeding attributed to the low molecular weight heparin was reported in only 3 patients.

Geerts et al. (1995) compared the safety and effectiveness of low-dose UH (5000 U twice daily) and LMWH (enoxaparin, 30 mg twice daily) in patients with major trauma, including a few with SCI. Treatment was initiated 36 hours after injury. The overall rate of

TABLE 3
Thromboembolism after acute spinal cord injury

Agent, Author, and Year	Untreated Controls	Treated	Endpoint
Low-Dose Heparin			
Frisbie and Sasahara (1981)	1/17 (6%)	1/15 (7%)	IPG
Green et al. (1988)	None	N9/29 (31%)	IPG
Merli et al. (1988)	8/17 (47%)	8/16 (50%)	FUT
Green et al. (1990)	None	5/21 (24%)	IPG
Intermittent Pneumatic Compression			
Green et al. (1982)	None	6/15 (40%)	FUT, IPG
Adjusted Dose Heparin			
Green et al. (1988)	None	2/29 (7%)	IPG
Low Molecular Weight Heparin			
Green et al. (1990)	None	0/20 (0%)	IPG
Green (1994)	None	5/60 (8%)	IPG, DU, VEN
Geerts et al. (1996)	None	4/8 (50%)	VEN
Combined Prophylaxis With IPC, ASA, and DIP			
Green et al. (1982)	None	4/12 (33%)	FUT, IPG
Combined Prophylaxis With IPC, ES, and LDUH			
Merli et al. (1992)	6/17 (35%)	1/19 (5%)	FUT

Notes: Modified with permission from Clagett, G.P., F.A. Anderson, Jr., and J. Heit et al., Prevention of venous thromboembolism, *Chest* 114 (Suppl) (1998): 531S–560S.

ASA—Aspirin
DIP—Dipyridamole
DU—Duplex ultrasound
ES—Elastic stockings
FUT—Fibrinogen uptake test
IPC—Intermittent pneumatic compression
IPG—Impedance plethymography
LDUH—Low-dose unfractionated heparin
VEN—Venography

venous thrombosis (44 percent versus 31 percent; $p = 0.014$) and proximal vein thrombosis (15 percent versus 6 percent; $p = 0.009$) was significantly higher in the UH group. Furthermore, there was 1 nonfatal PE and 2 episodes of heparin-induced thrombocytopenia in this group. Major bleeding occurred in 2.9 percent of patients receiving LMWH and 0.6 percent receiving UH. Thus, LMWH was significantly more effective with a relatively low rate of bleeding. There were 23 patients with spinal injury in this study; 10 of 15 (67 percent) receiving UH but only 4 of 8 (50 percent) treated with LMWH developed deep vein thrombosis. Table 3 summarizes the results of preventive anticoagulant regimes in patients with acute spinal cord injury.

At the time these guidelines were prepared, LMWHs were approved by the U.S. Food and Drug Administration for prophylaxis of thrombosis in patients undergoing surgical procedures on the abdomen, pelvis, hip, and knee.

Prophylaxis Based on Patient Stratification for Risk

6. **Patients with complete motor and/or incomplete nonfunctional motor involvement should be on prophylactic measures for venous thromboembolism as early as possible.** (Scientific evidence—

level I; Grade of recommendation—A; Strength of panel opinion—strong)

Many studies have shown that the risk of thromboembolism in SCI increases rapidly following injury and is maximal between days 7 and 10 (Geerts et al., 1994; Green et al., 1982; Merli et al., 1988). Anticoagulants may be withheld during the first 24 to 48 hours after injury because of concern for bleeding complications and for potential neurological deterioration. The incidence of venous thromboembolism within the first 72 hours is probably small, but measures such as mechanical devices and physical modalities should be implemented to prevent thromboembolism. If surgical intervention such as spinal stabilization is required, heparin or low molecular weight heparin may be withheld the morning of the procedure and resumed the next day. Physical modalities, including compression devices, should be continued if possible during this period.

- 7. Spinal cord injured patients with functional motor movements or with no significant motor/neurological deficits should be on prophylactic measures as early as possible.** (Scientific evidence—level I; Grade of recommendation—A; Strength of panel opinion—strong)

Because of prolonged bed rest and concomitant injuries, these patients should be on prophylactic measures, at least until they are ambulatory (Geerts et al., 1994).

- 8. The duration of the prophylaxis for thromboembolism should be individualized, depending on the need, medical condition, functional status, support services, and risk of the patient.** (Scientific evidence—level II; Grade of recommendation—B; Strength of panel opinion—strong)

The duration of prophylaxis after SCI is controversial. Many practitioners continue prophylactic measures for about 3 months postinjury (Green et al., 1994). Although some evidence of decreased incidence of thromboembolism after 3 months exists in this patient population, there are many clinical reports of the incidence of thromboembolism after 3 months (Perkash et al., 1993). With changes in the provision of health care and improvements in management throughout acute and rehabilitation settings, many patients are discharged from the hospital setting before 3 months. If a minimum of 3 months for prophylactic measures is recommended, many issues need to be addressed regarding patients who are being discharged from institutional settings earlier than 3 months. The patient's functional ability, level of neurological injury, access to nursing and medical care at home and other sites and family support, cost, appropriate use of recommended measures, and patient and family education and training are just some of the issues that need to be considered before recommending continuation of prophylactic measures.

Is there a need for prophylactic measures after 3 months? The role of spasticity in the reduction of inci-

dence of venous thromboembolism in this population is not clear. Spasticity of muscles of lower extremities in the spinal cord injured may cause increased venous flow, which may reduce the development of venous thromboembolism. Theoretically, treatment of spasticity could increase the risk of venous thromboembolism. Other factors, such as limited participation in therapy programs, recurrent infections, heterotopic ossification, or history of thromboembolism, may suggest the need to continue prophylactic measures beyond 3 months (Perkash and Perkash, 1990). The benefits of continuing prophylactic measures versus the risks—including bleeding complications and the development of osteoporosis with long-term use of heparin—as well as the cost should be considered. Some of the nursing measures and physical modalities, including turning, use of stockings, physical therapy, and range-of-motion exercises, could be continued without significant risk or cost, although it is not clear whether these measures decrease the development of thromboembolism in SCI patients.

- 9. Reinstitution of prophylactic measures should be considered in chronic SCI patients if they are immobilized with bed rest for a prolonged period of time, are readmitted for medical illnesses or altered medical conditions, or undergo surgical procedures.** (Scientific evidence—level I; Grade of recommendation—A; Strength of panel opinion—strong)

SCI patients who have acute medical illnesses or who require surgical procedures are at similar or increased risk for the development of venous thromboembolism as any other patient (Kim et al., 1994). Prophylaxis with either mechanical devices or anticoagulants may be appropriate, depending on the clinical situation.

Failure of Prophylaxis

- 10. In symptomatic patients, perform ultrasound of the lower extremities and/or tests for pulmonary emboli. If clinical suspicion is strong but the tests are negative or indeterminate, obtain venography of the legs, spiral computerized tomography of the lungs, or magnetic resonance/contrast angiography.** (Scientific evidence—level I; Grade of recommendation—A; Strength of panel opinion—strong)

Failure of prophylaxis should be suspected in individuals with unexplained fever; unilateral leg swelling, pain, or erythema; or sudden onset of hypotension, tachycardia, tachypnea, chest pain, cardiac arrhythmia, or hypoxemia. Although ultrasound examination of the lower extremities is highly sensitive and specific in symptomatic persons, it is less sensitive in those who are asymptomatic, and venography may be necessary to establish a diagnosis.

Ventilation/perfusion lung scans are interpreted as normal or high, intermediate, or low probability of

pulmonary embolism. Only normal or high probability lung scans are regarded as definitive; scans in the other categories offer no assurance that patients have or do not have thromboses, and therefore further evaluation, such as spiral computerized tomography of the chest or pulmonary angiography, is required if there is strong clinical suspicion of thromboembolism.

Exercise, Passive Movement, and Early Mobilization

- 11. Early mobilization and passive exercise should be initiated as soon as the patient is medically and surgically stable. These activities should be coordinated with other preventative modalities. With documented DVT, mobilization and exercise of the lower extremities should be withheld 48 to 72 hours until appropriate medical therapy is implemented.** (Scientific evidence—Grade of recommendation—expert consensus; Strength of panel opinion—strong)

Physical therapy has been a routine part of acute SCI treatment for decades. The physical therapy assessment and treatment focuses on respiratory function, muscle strength, joint range of motion, and skin condition. Orientation to the vertical position and initiation of functional activities begin when spinal stability has been established. In terms of prevention of deep vein thrombosis, it is widely held that early mobilization and movement of the extremities are essential parts of treatment (Frost, 1993; Keppler, 1987).

In the acute phase of SCI management, physical therapy intervention can begin immediately in the intensive care unit (McBride and Rodts, 1994). The goal of range-of-motion activities is to prevent joint contractures. However, because of spinal instability, certain precautions may be necessary. Range-of-motion activities of the shoulder and arms must be limited in patients with cervical injuries. Similarly, hip flexion and extension should be limited in individuals with low thoracic and lumbar injuries. Movement of the extremities occurs passively or, if possible, actively. With incomplete injuries, active muscle contraction may be possible. Movement and strengthening activities can become more vigorous as the patient is cleared for more functional activity and as he or she moves into the postacute phase.

The role of physical therapy intervention in the prevention of deep vein thrombosis has not been examined rigorously. Because physical therapy is routinely applied, controlled studies examining the specific effects of early mobilization activities have not been undertaken. In addition, in studies that have examined other treatment modalities, little if any mention is made of the type and frequency of these routine procedures. No mention is made as to whether exercise, passive movement, or early mobilization activities have been controlled by proper randomization and control groups.

Some evidence suggests indirectly that a vigorous program of passive and, if possible, active exercise could be beneficial in the prevention of DVT. Myllynen et al. (1985) compared the incidence of DVT in individuals immobilized due to spinal fractures. The group without paralysis had no detectable DVT, whereas nearly 80 percent of the paralyzed individuals developed DVT. This would suggest that either preserved motor function or preserved sympathetic input to the veins was responsible for the decreased incidence of DVT in the nonparalyzed patients. If inherent muscle tone and small spontaneous movements were responsible for the decreased incidence, then one might extrapolate that a persistent passive exercise program might produce a significant reduction in DVT. However, the intact sympathetic system may play the more significant role. These factors need further investigation.

In addition to improvements in venous return as a result of changes in intrathoracic pressure, elevation of the lower extremities utilizes the effects of gravity to reduce venous stasis. Positioning of the lower extremities higher than the level of the heart could prove beneficial and very cost effective. Close monitoring of arterial perfusion would be necessary in those individuals with hypotension and bradycardia. This intervention would require no equipment, and the legs could be positioned for specified periods of time and comparisons made to electrical stimulation (Merli et al., 1988) and to external compression stockings and boots (Green et al., 1982; Merli et al., 1992). Unfortunately, use of this simple intervention has not been formally examined.

In summary, very few controlled studies have been performed examining the effectiveness of early mobilization, and many areas need research. It would be of benefit to more closely monitor and document the type, duration, and frequency of physical therapy intervention. Given the absence of side effects and complications (except for the precautions mentioned above), early mobilization and physical therapy deserve closer attention.

Educational Priorities for Health Care Professionals

- 12. Health care professionals should be aware of the signs and symptoms of DVT and should perform physical assessment to detect this complication. Appropriate prophylactic measures, including application of mechanical devices and administration of anticoagulant agents, should be implemented. Patients, family members, and significant others should be educated in the recognition and prevention of DVT.** (Scientific evidence—NA; Grade of recommendation—expert consensus; Strength of panel opinion—strong)

With an understanding of the rate of incidence, risk factors, pathophysiology, clinical presentation,

and treatment strategies, health care professionals can be instrumental in preventing and treating DVT. Physical assessment should be performed on each patient twice daily (Herzog, 1992). All extremities should be inspected for the following signs of DVT:

- An increase in the circumference of the calf or thigh (unilateral edema).
- An increase in the venous pattern of collateral veins in the affected extremity.
- Pain, tenderness, and/or heaviness of the affected extremity.
- A low-grade fever of unknown origin.

The patient also should be monitored for clinical manifestations of pulmonary embolus, which include chest pain, breathlessness, apprehension, fever, and cough. The neurovascular status of the extremities also should be assessed. The physician should be notified if there is a change in baseline signs and symptoms, and the patient should be immobilized until seen by a physician.

Because patients are frequently asymptomatic, health care professionals need to understand what factors increase the risk of developing a thromboembolism. In persons with SCI, immobilization due to paralysis or to concomitant injuries, such as lower limb fractures, greatly increase the risk of thrombosis. Other risk factors include dehydration, obesity, age over 40, malignancy, congestive heart failure, estrogen therapy, pregnancy, and a history of thrombosis.

Additional interventions should include the performance of active and passive range-of-motion exercises and the application of elastic support hose and mechanical devices (Fowler, 1995; Spoltore and O'Brien, 1995). Elastic support—such as elastic bandages or compression stockings—should be worn to promote venous return and to control edema. The devices should be removed twice daily and the legs and feet carefully inspected for signs of erythema, ecchymoses, or skin breakdown. Hose must be applied so that tight bands around the limb are avoided. If pneumatic compression systems are implemented, they must be monitored regularly to assure correct placement of the sleeves and proper function of the pump. The extremities must be examined before and after the application of stockings and sleeves to make certain that the integrity of the underlying skin is not compromised from pressure exerted by the devices. Pneumatic compression systems—intermittent or sequential—are contraindicated in patients with severe arterial insufficiency.

A baseline partial thromboplastin time, prothrombin time, and platelet count should be obtained

before heparin and/or warfarin therapy are initiated. Patients receiving heparin should be observed for signs of heparin-induced thrombocytopenia, which usually appear 5 to 7 days after initial exposure to heparin, or sooner with reexposure to heparin (Fahey, 1994). The diagnosis is suspected if the platelet count declines by 50 percent or more and/or if signs of venous or arterial occlusion occur: stroke, myocardial infarction, or acute arterial or venous thrombosis. Patients also should be monitored for signs of bleeding, including epistaxis, hematoma, hematuria, melena, and/or decrease in hemoglobin and hematocrit.

Intake and output should be monitored and fluids administered as needed to maintain fluid balance and avoid dehydration (Fahey, 1994). The legs should be elevated above the level of the heart. Elevation of the knees—using either pillows or the bed adjustment—should be avoided, as this creates a jackknife position that can promote venous obstruction, venous hypertension, and thrombus formation. If elevation of the foot gatch is required, the knee section of the bed also should be raised to prevent hyperextension of the leg.

Comprehensive patient and staff educational programs should include information about the signs and symptoms of thromboembolism, the importance of physician notification if thrombosis is suspected, and the common risk factors that increase the likelihood of clotting (Fowler, 1995). Interventions that protect against thrombosis should be emphasized:

- Exercise
- Weight loss
- Cessation of smoking
- Good elastic support
- Avoidance of constricting garters, leg bag straps, tight knee-high boots, girdles, or overly tight pantyhose or slacks

If the patient is receiving anticoagulant therapy, instructions should include the purpose of the drug, the side effects (e.g., bleeding), potential drug and food interactions, and the need for regular laboratory monitoring and medical followup. Written instructions should be provided whenever possible, and documentation of drugs, dose, and instructions in the medical record is always advisable.

Directions for Future Research

Our review of the literature of the past decade identified many areas in need of further study. The factors leading to thromboembolism remain incompletely understood. Fatal pulmonary emboli may occur even in patients thought to be at low risk. The interplay of clotting factor activation and inhibition, vessel wall injury, and fibrinolytic activity needs careful examination using contemporary methods such as measurement of molecular markers of coagulation, studies of platelet-derived microvesicles, and assessment of endothelial cell integrity.

Another understudied area is the detection of thromboembolism. Because of impaired sensation and horizontal leg position, clinical signs of deep vein thrombosis such as leg pain and swelling are usually lacking, and signs associated with pulmonary embolization such as shortness of breath are usually attributed to atelectasis or lung infection. Although the clinician may have a high index of suspicion for thromboembolism, studies such as venous ultrasound and ventilation/perfusion scanning are less sensitive in asymptomatic patients. Therefore, laboratory methods with adequate sensitivity for the detection of thrombosis, such as some of the newer d-dimer tests, need to be studied in the SCI population. Positive results obtained with these tests will need to be confirmed by advanced imaging modalities such as spiral computerized tomography (CT) and ultrafast CT and magnetic resonance imaging.

Evaluation of methods of prophylaxis is incomplete. Randomized controlled trials of various physical modalities used for thrombosis prevention, such as advanced models of sequential compression

devices and foot pumps, have not been done, nor are there randomized studies of vena cava filters, although these are in widespread use. The risks and benefits of such filters and their appropriate use in SCI require urgent attention. With regard to anticoagulant therapy, there is a multicenter, randomized trial comparing low-dose heparin, 5000 U every 8 hours plus compression boots with low molecular weight heparin, 30 mg twice daily for 2 weeks. For the next 6 weeks, patients continue on either the low-dose heparin or on low molecular weight heparin, 40 mg once daily. This study, by Geno Merli, MD, at Jefferson Medical College, Philadelphia, has been submitted for publication.

The optimal duration of thromboprophylaxis also needs to be clarified. Clearly, patient characteristics are important and such factors as location of the cord lesion; extent of paralysis; associated injuries, especially to the long bones; age; obesity; and concomitant illnesses need study. If a leg thrombus is detected, when is it safe to resume physical and other therapies? No data on thrombus stability exist, to our knowledge. Treatment for thromboembolism has traditionally been intravenous heparin and warfarin. However, the benefits of low molecular weight heparins for thrombosis therapy are now being recognized; these include administration by the subcutaneous route, no requirement for monitoring, and fewer complications such as bleeding, osteoporosis, and heparin-induced thrombocytopenia. Whether low molecular weight heparins or other new anticoagulants will be as safe and effective in the management of SCI as in other indications needs to be examined.

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Glossary of Terms

- Abrasion:** an excoriation or circumscribed removal of the superficial layers of skin or mucous membrane.
- Anticoagulant:** a drug or substance that prevents clotting, the process of changing from a liquid to a solid, said especially of blood.
- Antithrombotic agent:** a drug that prevents occlusion of blood vessels by clots.
- aPTT (activated partial thromboplastin time):** a test used to monitor the activity of anticoagulant medications such as heparin.
- Arterial perfusion:** the flow of blood through arteries to organs.
- ASIA class C:** incomplete: motor function is preserved below the neurological level, and the majority of key muscles below the neurological level have a muscle grade less than 3.
- ASIA class D:** incomplete: motor function is preserved below the neurological level, and the majority of key muscles below the neurological level have a muscle grade greater than or equal to 3.
- Atelectasis:** absence of gas from a part or the whole of the lungs, due to failure of expansion or resorption of gas from the alveoli.
- Blood factor VIII activity:** a clotting protein important in blood coagulation.
- Bradycardia:** slowness of the heartbeat, usually defined (by convention) as a rate under 60 beats per minute.
- Clot:** coagulate, said especially of blood; or, a soft, nonrigid, insoluble mass formed when a liquid gels.
- Collateral vein:** a vein that forms to convey blood around an occluded blood vessel.
- Contrast dye venography:** radiographic demonstration of a vein after the injection of contrast medium.
- Cor pulmonale:** failure of the right side of the heart, usually due to obstruction of blood flow through the lungs.
- Deep vein thrombosis:** displacement of thrombi (clots) from the leg veins to the arteries of the lung (pulmonary embolism). If there is a hole in the heart, the clots may cross into the arterial circulation and deposit in the brain, causing a stroke.
- Dipyridamole:** a coronary vasodilator that also has a weak action to reduce platelet aggregation; commonly used in place of exercise for radionuclide studies of the myocardium.
- Doppler ultrasonographic imaging:** application of the Doppler effect in ultrasound to detect movement of scatterers (usually red blood cells) by analysis of change in frequency of the returning echoes.
- Early mobilization:** exercising as soon as possible after surgery or injury.
- Ecchymosis (plural, ecchymoses):** a purplish patch caused by extravasation of blood into the skin, differing from a petechia only in size (larger than 3 mm diameter).
- Electrical stimulation (ES):** electrical charge to cause muscle contraction.
- Erythema:** redness of the skin due to capillary dilatation
- Evidence table:** a chart prepared by methodologists that reports the strength of evidence of literary cited in practice guideline development.
- Fibrinolysis:** dissolution of an elastic filamentous protein derived from fibrinogen by the action of thrombin, which releases fibrinopeptides A and B from fibrinogen in coagulation of the blood.
- Fibrinolytic activity:** denoting, characterized by, or causing fibrinolysis.
- Frankel D (neurologically incomplete) lesion:** a level of injury under the Frankel method of classifying spinal cord injury based on severity of nerve damage; D indicates persisting neurological function.
- FUT (fibrinogen uptake test):** a test which uses fibrinogen with a radioactive tag (^{125}I) to detect blood clots in the lower extremities.
- Gradient elastic stockings (GES):** rubberized hose applied snugly to provide uniform compression of the veins of the lower limb.
- Hemostasis:** the arrest of bleeding, the arrest of circulation in a part.
- Heterotopic ossification:** deposition of calcium in the muscles, usually occurring after injury and nerve damage.
- Hypercoagulable state:** characterized by abnormally increased coagulation.
- Hypotension:** subnormal arterial blood pressure, reduced pressure or tension of any kind.
- Hypoxemia:** subnormal oxygenation of arterial blood, short of anoxia.
- I-125 fibrinogen scan:** a test that uses fibrinogen with a radioactive tag (^{125}I) to detect blood clots in the lower extremities.
- Impedance plethysmography:** a technique used to determine whether there are clots blocking the major veins of the legs.
- Inferior vena cava:** the main vein of the abdomen, transporting blood from the lower extremities to the heart.
- Joint contractures:** usually permanent deformity of a joint causing limited mobility.

Low molecular weight heparin (LMWH): a fragment of heparin prepared by enzymatic or chemical processing, having many advantages over heparin including better absorption after injection, longer persistence in the blood, and fewer side effects.

Meta-analysis: a statistical technique for combining the results of many studies, giving greater weight to the final conclusion.

Methodologist: an individual who reviews published data and retrieves the salient information.

Microvesicle: a fluid-filled space formed within the epidermis that is too small to be recognized as a blister.

Morbidity: the ratio of sick to well in a community.

Mortality: pertaining to death or causing of death.

Paraplegic: relating to or having paralysis of both lower extremities and generally the lower trunk.

Passive exercise: movement of an extremity by someone other than the patient.

Pathophysiology: derangement of function seen in disease; alteration in function as distinguished from structural defects.

Placebo: an inert compound identical in appearance to material being tested in experimental research, which may or may not be known to the physician and/or patient.

Placebo control group: a group of patients to which a placebo is administered in experimental research, to distinguish between drug action and suggestive effect of the material under study.

Pneumatic compression devices: bladders that are intermittently filled with air and are applied to an extremity to rhythmically compress the veins.

Postthrombotic syndrome: a complication of deep vein thrombosis consisting of chronic swelling of the leg, cramping, itching, skin discoloration, and often skin ulceration.

Potential bleeding sites: breaks in the lining of blood vessels in various organs such as the brain, lung, stomach, or bladder that may bleed when a patient is treated with anticoagulant drugs.

Pulmonary arteries: the two terminal branches of the pulmonary trunk, which pierces the pericardium to enter the hilus of the lungs. Branches are distributed with the bronchi, frequent variations occurs.

Pulmonary angiography: radiography of vessels in the lungs after the injection of a radiopaque contrast material; usually requires percutaneous insertion of a radiopaque catheter and positioning under fluoroscopic control.

Pulmonary embolism: obstruction or occlusion of a vessel by an embolus of the pulmonary arteries, most frequently by detached fragments of thrombi from a leg or pelvic vein, commonly when thrombosis has followed an operation or confinement to bed.

Pulmonary hypertension: an increase in the blood pressure in the arteries of the lung, often due to clots in the smaller branches of these arteries.

Randomized: by chance; method for allocation of individuals to groups for experimental and control regimens.

Range of motion: a statistical measurement of a dispersion or variation of change of place or position.

Refractory edema: an accumulation of an excessive amount of watery fluids in cells, tissues, or serous cavities that is resistant to treatment.

Spasticity: an state of increased muscular tone with exaggeration of the tendon reflexes.

Tachycardia: rapid beating of the heart, conventionally applied to rates over 100 per minute.

Tachypnea: rapid breathing.

Tetraplegic: pertaining to the paralysis of all four limbs.

Thrombocytopenia: a condition in which there is an abnormally small number of platelets in the circulating blood.

Thromboembolism: displacement of thrombi (clots) from the leg veins to the arteries of the lung (pulmonary embolism). If there is a hole in the heart, the clots may cross into the arterial circulation and deposit in the brain, causing a stroke.

Thrombotic disease: a disorder of body functions caused by a clot in the cardiovascular system formed during life from constituents of blood.

Ultrasound: a technique for visualizing thrombi in the veins, usually using Doppler methodology.

Vena cava filter: a device that is introduced into the vena cava to prevent thrombi from passing from the legs to the lungs.

Venography: radiographic demonstration of a vein after the injection of contrast medium.

Venostasis: abnormally slow motion of blood in veins, usually with venous distention.

Venous thromboembolism: embolism from a clot in the cardiovascular system formed during life from constituents of blood relating to the veins.

Ventilation/perfusion lung scanning: using a combination of tracers to measure airflow and blood flow in the lungs. The demonstration of airflow in tissue that is not receiving blood flow suggests that the blood vessels to the tissue are blocked by clots (pulmonary emboli).

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