PRACTICAL SUMMARIES IN

ACUTE CARE

A Focused Topical Review of the Literature for the Acute Care Practitioner

DVT: New therapeutic perspectives

Authors: **Donald H. Schrieber,** MD, CM, FRCPC, FACEP, Associate Professor of Emergency Medicine, Stanford University School of Medicine, Stanford, CA; and **Zoe Denée Howard**, BSc, The University of Chicago Pritzker School of Medicine, Chicago, IL.

Peer Reviewer: **Stephen Crabtree,** DO, FACEP, Staff Physician, Northside Emergency Associates, Atlanta, GA.

Introduction

Deep venous thrombosis (DVT) and its sequela, pulmonary embolism (PE), remain significant clinical challenges and the leading causes of preventable in-hospital mortality in the United States. Existing data probably underestimate the true incidence of DVT because it usually develops in the calf veins and resolves spontaneously without complication. Venous ulceration and chronic venous insufficiency are late complications of DVT and affect millions of patients. Treatment for DVT has evolved considerably since unfractionated heparin (UFH) was first introduced in 1937. This review will highlight current articles that review the major therapeutic strategies in the treatment of DVT, including the low molecular weight heparins (LMWHs), direct Factor Xa inhibitors, and oral direct thrombin inhibitors. The role of ambulation, vena caval filters, and catheter-directed thrombolytic therapy will be reviewed in a subsequent issue.

Anticoagulant therapy with LMWH

Source: Mismetti P, et al. Enoxaparin in the treatment of deep vein thrombosis with or without pulmonary embolism: An individual patient data meta-analysis. *Chest* 2005;128:2203-2210.

The efficacy and safety of LMWH for the initial treatment of DVT have been well established in several trials. The 7th American College of Chest Physicians (ACCP) conference on antithrombotic and thrombolytic therapy for venous thromboembolic disease has recommended short-term LMWH or UFH for the initial treatment of objectively confirmed DVT as vitamin K antagonist treatment is initiated. The original studies evaluating LMWH were conducted primarily on patients with DVT. The authors of this paper have conducted a systematic meta-analysis of the original source data to specifically address the question of whether the efficacy and safety of enoxaparin, a LMWH, is modified by the presence or absence of initial PE at baseline. It is recognized that PE is a sequela of DVT and most cases of PE arise from DVT of the lower extremities. Previous meta-analyses of published trials could not evaluate the efficacy and safety of LMWH if PE was present in addition to DVT because they reviewed only published summarized data. The authors reanalyzed the original individual source data from 1503 patients in three randomized controlled trials. Efficacy was assessed through objectively confirmed recurrence of DVT and/or PE. The authors also used a well-established margin of noninferiority for the treatment effect that

VOLUME II • NUMBER 5 • MAY 2007 • PAGES 37-45
AHC Media LLC Home Page—www.ahcmedia.com • CME for Physicians—www.cmeweb.com

Statement of Financial Disclosure: Executive Editor, Ann M. Dietrich, MD, FAAP, FACEP, reported that she receives research support from the National Institutes of Health and is the medical director for the Ohio Chapter of ACEP. Drs. Schrieber and Howard (authors) and Dr. Crabtree (peer reviewer) reported no financial relationships with companies having ties to this field of study.

AHC Media LLC

was calculated prior to data collection. Enoxaparin 1 mg/kg twice daily was found to be noninferior to UFH in the treatment of DVT with or without a coexisting PE. And, while not statistically significant, a trend favoring enoxaparin over UFH was also observed in the incidence of major bleeding and all-cause mortality at three months.

Subscriber Information

Customer Service: 1-800-688-2421.
Customer Service E-Mail: customerservice@ahcmedia.com
World-Wide Web: www.ahcmedia.com

Subscription Prices

United States
$299 per year (Student/Resident rate: $144.50).
Multiple Copies
Discounts are available for multiple subscriptions.
For pricing information, call Steve Vance at (404) 262-5511.
Outside the United States
$329 per year plus GST (Student/Resident rate: $159.50 plus GST).

Practical Summaries in Acute Care, ISSN 1930-1103, is published monthly by AHC Media LLC, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

SENIOR VICE PRESIDENT/GROUP PUBLISHER: Brenda L. Mooney
ASSOCIATE PUBLISHER: Lee Landenberger
SENIOR MANAGING EDITOR: Suzanne Thatcher
MARKETING MANAGER: Shawn DeMario
GST Registration Number: R128870672.
Periodical postage paid at Atlanta, GA.
POSTMASTER: Send address changes to ***Practical Summaries in Acute Care***, P.O. Box 740059, Atlanta, GA 30374.

Accreditation

AHC Media LLC is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media LLC designates this educational activity for a maximum of 20 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Approved by the American College of Emergency Physicians for 20 hours of ACEP Category 1 credit.

Practical Summaries in Acute Care has been reviewed and is acceptable for up to 12 Prescribed credits by the American Academy of Family Physicians. Term of approval is for one year from beginning distribution date of 06/01/06. Each semester (6 issues) is approved for 6 Prescribed credits. Credit may be claimed for 1 year from the date of this issue. The AAFP invites comments on any activity that has been approved for AAFP CME credit. Please forward your comments on the quality of this activity to cmecomment@aafp.org.

This CME activity is intended for emergency physicians. It is in effect for 24 months from the date of the publication.

Questions & Comments

Please E-mail **Suzanne Thatcher,** Senior Managing Editor, at suzanne.thatcher@ahcmedia.com.

AHC Media LLC

Commentary

In this meta-analysis, the authors' ability to use the original source data increased the statistical power and flexibility of their analysis. The authors confirmed the recommendations of the ACCP with respect to LMWH therapy for DVT. The primary outcome measure for efficacy of therapy in venous thromboembolic disease is the rate of venous thromboembolic (VTE) recurrence at three months. VTE recurrence is defined as the recurrence of DVT, PE, or both despite adequate therapy. Although LMWH is noninferior to UFH in the treatment of DVT, the emergency physician must recognize that despite adequate anticoagulant therapy, the recurrence rate for DVT and/or PE when enoxaparin was utilized was still 4.5%. With UFH, the recurrence rate for DVT, PE, or both was 4.4%, 1.8%, and 5.7%, respectively. The incidence of DVT and PE recurrence in patients presenting with DVT and an initial symptomatic PE is much higher, approaching 8.2% in the UFH group versus 4.8% in patients with DVT alone. When comparing the efficacy of enoxaparin versus UFH, there was no significant difference between patients with and without an initial symptomatic PE. However, the risk of recurrent PE was also higher in patients with an initial symptomatic PE despite adequate anticoagulant therapy. Therefore, a recurrent VTE must be considered in patients who present to the emergency department with recurrent symptoms despite adequate anticoagulant therapy. Incidentally, the group of patients presenting with DVT and symptomatic PE were found more often to be women with a previous history of VTE thus, they inherently were at greater risk for VTE recurrence.

Anticoagulant therapy with LMWH — another angle

Source: Wells PS, et al. A randomized trial comparing 2 low-molecular-weight heparins for the outpatient treatment of deep vein thrombosis and pulmonary embolism. *Arch Intern Med* 2005; 165:733-738.

Much has been studied in terms of the efficacy of the LMWHs, but this original trial aims to be the first head-to-head comparison within the class of LMWHs, while also exploring VTE therapy in the outpatient setting. The Canadian study compares tinzaparin to dalteparin, the former being the only LMWH to have demonstrated statistical superiority to UFH in the prevention of DVT recurrence. Dr. Wells and colleagues conducted a single-blind, randomized controlled trial of 505 outpatients with objectively proven DVT. In addition to subcutaneous LMWH, patients were simultaneously begun on warfarin using a standardized normogram.

After five days and an international normalized ratio (INR) of 2.0 or greater, the LMWH was stopped and oral anticoagulation was continued for three months. A composite endpoint, combining both the risk of recurrent thrombosis or PE and the risk of hemorrhage, was used as the most appropriate assessment of the two pharmacotherapies. The existing literature had predicted outcomes in favor of tinzaparin by a minimal, but clinically important, 4%

combined endpoint. However, with combined event rates of 4.8% and 5.4% for dalteparin and tinzaparin respectively, tinzaparin was not found to be superior to daltaperin and both therapies provided safe and efficacious outpatient treatment for acute DVT and PE. Given the study's unpredicted conclusion, it is also possible that there was insufficient power to detect a difference between the two LMWHs as a result of the small sample size.

Table 1. Exclusion criteria for outpatient therapy for DVT

MEDICAL EXCLUSIONS TO OUTPATIENT THERAPY	SOCIAL EXCLUSIONS TO OUTPATIENT THERAPY
• Concurrent suspected PE	• Unable to follow instructions
• Serious co-morbidity	• Unable to comply with follow-up
• Pregnancy	• Homeless
• Contraindications to anticoagulation	• No contact telephone
• Familial bleeding disorder	• Geographic – Too far from hospital
• ATIII, Protein C, Protein S deficiency, Factor V Leyden, Prothrombin 20210A, or other inherited clotting disorders	• Patient/family resistance to outpatient therapy

Key: DVT, deep venous thrombosis; PE, pulmonary embolism.

Source: Donald H. Schrieber, MD, CM, FRCPC, FACEP

Commentary

As the authors emphasize, not only is this the first trial to compare drugs within the LMWH class, but it is also the first study to treat patients with acute DVT and PE solely on an outpatient basis. In the United States, the U.S. Food and Drug Administration (FDA)-approved LMWH preparations are enoxaparin, tinzaparin, and dalteparin. The question of whether there is any significant clinical difference between these agents for the treatment of DVT or PE has only partially been answered. Clinical differences between these agents had previously been suggested based on the results of the original trials comparing them to UFH. However, this study was terminated early because a preliminary analysis revealed that the projected sample size that would be needed to detect any significant difference between dalteparin and tinzaparin would have exceeded 30,000 patients. This study showed that only very large clinical trials would be able to delineate any significant differences between the different LMWH compounds.

Other study limitations may have biased the results. The incidence of recurrent VTE and major bleeding complications would be affected by the adequacy of anticoagulation with warfarin. Whether or not the patients had therapeutic INRs during the follow-up period was not specifically reported. The authors also included major bleeding events in the composite outcome measure. This included bleeding events that occurred on warfarin therapy alone and may not be related at all to the bleeding complications associated with the LMWH compound that was used for initial anticoagulation.

This study confirms the safety and efficacy of outpatient therapy for DVT. Many emergency departments have instituted outpatient protocols that incorporate a LMWH agent overlapping with oral warfarin until a therapeutic INR has been reached. Apart from patient education to learn how to properly administer these drugs subcutaneously, an adequate follow-up mechanism must be in place to monitor the patient's clinical status and the INR. In general, there are a number of medical and social factors that would exclude a patient as a candidate for outpatient therapy and mandate admission to the hospital. These are outlined in **Table 1**.

Currently, outpatient treatment of PE with a LMWH compound is not FDA-approved and is considered to be off-label. Patients with serious pre-existing cardiorespiratory co-morbidities wherein a PE might be considered catastrophic are not good candidates for outpatient therapy. The LMWH medications have not been fully evaluated in pregnant patients and outpatient therapy is not FDA-approved during pregnancy. Patients with known genetic disorders of coagulation may be difficult to anticoagulate and hospitalization is recommended. The LMWH compounds are primarily cleared by the kidneys, so that patients with moderate to severe renal insufficiency (serum creatinine > 2.0 mg/dL) also are not good candidates for outpatient therapy.

Patients with social exclusions that preclude compliance with therapy or low likelihood of follow-up should be admitted to the hospital as well. In certain circumstances the patient may only require a short stay or observation unit admission until adequate social support and medical follow-up can be arranged.

Table 2. Therapeutic peak anti-Xa levels* with LMWH for treatment of DVT

Enoxaparin 1 mg/kg every 12 hrs	0.6–1.0 IU/mL
Enoxaparin 1.5 mg/kg daily	1.0–1.5 IU/mL
Tinzaparin 175 IU/kg daily	0.85–1.0 IU/mL
Dalteparin 100 IU/kg every 12 hrs	0.4–1.1 IU/mL
Dalteparin 200 IU/kg daily	1.0–2.0 IU/mL

* Via chromogenic anti-Xa assay drawn 4 hours after subcutaneous dose

Source: Donald H. Schrieber, MD, CM, FRCPC, FACEP

Treating VTE in special populations

Source: Michota F, et al. Anticoagulation in special patient populations: Are special dosing considerations required? *Cleve Clin J Med* 2005;72:S37-S42.

This paper reviews the efficacy, safety, and dosing of the LMWH compounds in DVT prophylaxis and in the treatment of VTE in special patient populations — morbid obesity, pregnancy, renal insufficiency, and cancer.

Given the prevalence of obesity, a problem that afflicts almost one-third of Americans, the authors reviewed its effect on enoxaparin dosing. Morbid obesity was defined as body weight greater than 150 kg or a body mass index (BMI) greater than 50. Dr. Michota and colleagues note that there is a paucity of morbidly obese patients represented in the major clinical trials evaluating the LMWH agents. The authors cite a British trial that demonstrated decreased anti-Xa activity with increased body weight when fixed, as opposed to weight-based, enoxaparin dosing was used. The relationship between intravascular volume, volume of distribution of the drug, and body weight is not linear. Therefore, there is concern that weight-based dosing in the morbidly obese patient population might lead to an excessive rate of bleeding complications. However, other studies have shown that there is no significant increase in anti-Xa activity when weight-based dosing of LMWH is used. In a cardiovascular trial, no increase in bleeding rates between obese and non-obese patients was documented when full weight-based dosing was used. In morbidly obese patients, the authors state that although the general consensus suggests that weight-based dosing without a cap is currently recommended, there is a paucity of data to support that recommendation. Therefore, they concluded that it is not unreasonable to initiate therapy with full weight-based dosing and monitor the anti-Xa levels. The therapeutic ranges for anti-Xa activity for the various LMWH compounds are listed in **Table 2.** Anti-Xa levels are drawn four hours after a subcutaneous dose.

Enoxaparin dosing also has been poorly studied in renal patients. Higher peak anti-Xa levels as well as half-life prolongation correlate with decreasing creatinine clearance as LMWH is renally cleared. Renal failure patients may be at increased risk for bleeding secondary to excessive anticoagulation. Several trials have substantiated increased bleeding rates with UFH and LMWH among patients with renal insufficiency (CrCl < 30 mL/min). Although UFH has a dual clearance mechanism and is less susceptible to drug accumulation in renal insufficiency than LMWH, its greater adverse effect on platelet function and capillary permeability leads to a similar rate of bleeding problems. There is a negative linear correlation between anti-Xa activity and CrCl. As a result, the FDA issued new dosing guidelines for enoxaparin of 1 mg/kg daily instead of twice a day (bid). There are no revised dosing guidelines for the other LMWH agents. The authors also conclude that monitoring of anti-Xa levels is the safest approach.

In pregnant patients with VTE, there are clear advantages to LMWH over UFH that include better bioavailability, lower incidence of heparin-induced thrombocytopenia and osteoporosis, and reduced monitoring requirements. Throughout pregnancy, the volume of distribution of LMWH is larger. Drug clearance is higher in early pregnancy and trends towards normal at delivery. Therefore, monitoring of anti- Xa levels is important. Drug therapy should be initiated at the same dose as for non-pregnant patients, but the dose may have to be increased if anti-Xa levels fall below the therapeutic ranges outlined in Table 2. Therapy should be held during delivery but then restarted postpartum and continued while the patient is crossed over to a vitamin K antagonist.

Cancer patients have a particularly higher rate of DVT recurrence than non-cancer patients. Long-term therapy for DVT is strongly recommended. Recent studies have shown a lower rate of

VTE recurrence without increasing the risk of bleeding with LMWH therapy. There have also been reports that the LMWH compounds may decrease the all-cause mortality rate as well. The authors recommend LMWH therapy alone without crossover to coumadin if the patient's insurance will cover it.

Commentary

The authors have presented a comprehensive review of anticoagulant therapy with the LMWH compounds — and, in particular, enoxaparin — in the special patient populations of obesity, renal insufficiency, pregnancy, and cancer. With a better understanding of the pharmacokinetics in these patients, the emergency physician is better able to initiate therapy with a LMWH agent provided that adequate monitoring of anti-Xa activity, where indicated, is available.

LMWH: Once or twice a day?

Source: van Dongen CJ, et al. Once versus twice daily LMWH for the initial treatment of venous thromboembolism. *Cochrane Database Syst Rev* 2005;Jul 20(3):CD003074.

The intent of this meta-analysis was to evaluate the safety and efficacy of once-daily versus twice-daily dosing of enoxaparin for DVT. The authors hypothesized that twice-daily dosing would be more effective and safer with fewer bleeding complications, and that higher frequency of dosing would allow more stability in anticoagulation. Therefore, Dr. van Dongen and colleagues expected fewer complications with this group. Using strict criteria for exclusion, they compared five randomized controlled trials with a total of 1508 patients. These trials all involved patients treated for initial VTE. When the data were pooled, the actual incidence of VTE recurrence between the two groups was not statistically significant, complying with the predetermined equivalence criteria. In assessing discrepancies in thrombus size, no statistical difference was noted. A lower mortality was calculated in the twice-daily group, while a lower incidence of hemorrhage was seen in the once-daily group, but again, neither of these differences were statistically significant. While admitting that the wide confidence interval lends decreased precision in these results, the authors concluded that once-daily dosing is as safe and efficacious as the standard twice-daily regimen.

Commentary

Despite an excellent meta-analysis, the optimal dosing regimen still, however, remains controversial. The two groups appeared equivalent in safety and efficacy, but, as mentioned, the confidence intervals were very wide: for risk of recurrent VTE the odds ratio was 0.82 (95% CI: 0.49-1.39), begging the question — Are these results meaningful? The authors acknowledged the possibility that once-daily dosing may present a greater risk of recurrent VTE than was represented in their article. The potential for lower efficacy may well offset the ease of only once daily dosing. The authors speak of the convenience of once-daily dosing, and we might add, the financial advantage of cutting the prescription in half, which, in and of itself, may entice greater compliance. But clearly, more investigation is required for greater precision in these results. Several aspects of anticoagulation were not considered in this analysis — namely, long-term therapy, the effect of different LMWH agents on dosing, as well as patients presenting with recurrent DVT. So until further evidence is demonstrated, in the specific setting of acute symptomatic initial DVT, once-daily dosing seems to be adequate, or, in familiar terms, "at least as effective and safe" as twice-daily dosing.

Fondaparinux, a Direct Factor Xa inhibitor

Source: Buller HR, et al. Fondaparinux or enoxaparin for the initial treatment of symptomatic deep venous thrombosis. *Ann Intern Med* 2004;140: 867-873.

Currently, enoxaparin and other LMWH agents are recommended for the treatment of DVT. However the data on once-daily or twice-daily dosing of enoxaparin are not clear. Second, the practical issues that surround the administration of a weight-based 1 mg/kg dose from fixed volume syringes of enoxaparin may be an issue for some patients. Third, the incidence of heparin induced thrombocytopenia, although reduced with enoxaparin, is not completely eliminated. Fondaparinux, a direct selective inhibitor of Factor Xa, overcomes many of these disadvantages. Pharmacokinetic studies reveal that only a single daily subcutaneous dose is required. Furthermore, a single dose of 7.5 mg may be effective

over a wide range of patient weights between 50 and 100 kg. Daily doses of 5 mg or 10 mg are appropriate for patients who weigh less or more than that weight range. Heparin-induced thrombocytopenia has not been reported. Therapeutic monitoring of laboratory parameters such as the prothrombin time or partial thromboplastin time is not required.

In this article, the authors on behalf of the Matisse Investigators present the results of their 2205 patient randomized, double-blind, international trial of fondaparinux versus enoxaparin in objectively confirmed DVT. The efficacy and safety of fondaparinux was compared to enoxaparin. Patients were randomly assigned to receive fondaparinux or enoxaparin therapy. Fondaparinux was administered as a 7.5 mg daily dose, with adjustments made for those patients weighing less than 50 kg (5 mg) or greater than 100 kg (10 mg). Enoxaparin was given 1 mg/kg twice daily. Both agents were bridged with a vitamin K antagonist until a therapeutic INR was achieved. Anticoagulation with a vitamin K antagonist was continued for three months. Efficacy was measured by the rate of recurrent venous thromboembolism in the three-month follow-up period after enrollment. Safety was assessed by the incidence of major bleeding and mortality over the same interval.

The recurrence rate showed a nonsignificant trend in favor of fondaparinux (3.9%) as compared to enoxaparin (4.1%). (Absolute difference = 0.15%, 95% CI: 1.8% to -1.5%). The conservative noninferiority margin was attained and fondaparinux was determined to be equally as effective as enoxaparin for the treatment of DVT. Major bleeding rates were essentially identical and mortality rates were also comparable. In a subgroup analysis, the authors also evaluated the relationship between the recurrence rate, the bleeding risks and the patients' body weight. In general, the safety and efficacy of fondaparinux were independent of body weight. However, patients with mild renal insufficiency and a low creatinine clearance had the same risk of bleeding in both the LMWH and fondaparinux groups. Overall, the authors concluded that once-daily fondaparinux was as effective and as safe as twice-daily, weight-adjusted enoxaparin.

Commentary

The Matisse DVT trial confirms that fondaparinux and enoxaparin have similar safety and efficacy for the initial treatment of DVT. Only one fixed-dosage regimen is required for patients who weigh between 50 kg and 100 kg and only one subcutaneous dose per day is required. This greatly simplifies the treatment of DVT and facilitates outpatient therapy. In the original study, about one third of the patients were treated partially or entirely as outpatients without any increased risk when compared to those treated as inpatients.

In renal insufficiency with a creatinine clearance < 30 mL/min, major bleeding occurred in 2/25 (8.0%) patients on fondaparinux versus 1/18 (5.6%) patients treated with enoxaparin (P = NS). Because of the small sample size and the higher risk of bleeding, fondaparinux is contraindicated in patients with renal insufficiency and a creatinine clearance of < 30 mL/min.

In the event of a major bleed, protamine sulfate partially reverses the anticoagulant effect of enoxaparin. However, there is no specific antidote to fondaparinux. A recent study revealed that a bolus dose of 90 mcg/kg of recombinant Factor VIIa reversed the anticoagulant effect of fondaparinux, at least in healthy volunteers given a larger, 10 mg dose.

In some regions, the cost of therapy with fondaparinux is less than enoxaparin when it is being used to bridge therapy to a vitamin K antagonist.

Emergency physicians should consider fondaparinux for the treatment of DVT.

Conclusion

Therapy for DVT continues to evolve. The transition to outpatient therapy based on LMWH has been affirmed. The emergency physician must be cognizant of those special patient populations where outpatient therapy is not recommended. There is no consensus on any clinically relevant distinction among the LMWH agents that are currently approved in the United States. Once-daily dosing of enoxaparin seems to be as effective and safe as twice-daily dosing. Literature was presented that reviewed the dosing schedules in special patient populations. Enoxaparin may still be administered using full, unadjusted, weight-based dosing even in the morbidly obese, but monitoring of anti-Xa levels is suggested. Patients with renal insufficiency and a creatinine clearance rate of less than 30 mL/min need a reduction in their enoxaparin dose to 1 mg/kg daily. Ideally, anti-factor Xa levels should be moni-

tored, as well. Pregnant women require close monitoring of anti-Xa levels, as drug clearance is increased in pregnancy. Cancer patients have a particular high risk of recurrent DVT and long-term anticoagulation is strongly recommended. Enoxaparin seems to confer a survival advantage over oral vitamin K antagonists in cancer patients for reasons that are unclear.

Innovative drug therapy with direct Factor Xa inhibition such as fondaparinux has been shown to be as safe and as effective as traditional anticoagulant therapy with enoxaparin/warfarin. Fondaparinux only requires once daily administration and dosing is fixed over a wide weight range.

Increasingly, emergency physicians will assume primary responsibility for managing patients with acute DVT. It is imperative that they understand the risks and benefits of outpatient anticoagulant therapy, the pharmacology of the LMWHs, the indications for monitoring anti-Xa levels, and the availability of new anticoagulant drug therapies.

CME OBJECTIVES

Upon completing this program, participants will be able to:

- Summarize the most recent significant studies in emergency medicine/urgent care related to a single topic;
- Discuss up-to-date information about new drugs, techniques, equipment, trials, studies, books, teaching aids, and other information pertinent to the stated topic;
- Evaluate the credibility of published data and recommendations about the stated topic.

CME QUESTIONS

26. A patient with DVT and symptomatic PE on initial presentation:

a. will require lifelong anticoagulation.
b. has a higher incidence of VTE recurrence than patients with DVT alone.
c. should be treated with UFH rather than a LMWH.
d. will only have a DVT and/or PE recurrence if not adequately anticoagulated.

27. Fondaparinux is:

a. safe in renal insufficiency with a creatinine clearance of < 30 mL/min because it is cleared by the liver.
b. administered twice daily.
c. as safe and effective as enoxaparin for acute DVT.
d. a low molecular-weight heparin product.

28. Monitoring of anti Xa levels while on anticoagulant therapy with a low molecular-weight heparin is recommended for which of the following patients?

a. All patients with acute DVT who require admission to the hospital
b. Patients with chronic renal failure and an acute DVT
c. Patients with cancer who are at higher risk of recurrent VTE
d. Patients with a history of GI bleeding

29. Outpatient therapy for acute DVT is recommended in:

a. patients with acute recurrent DVT.
b. patients who are resistant to self-administering subcutaneous injections.
c. patients with a familial history of recurrent DVT.
d. patients with no primary care provider and no medical follow-up.

30. Which of the following is true?

a. The risk of recurrent PE was higher in patients with an initial symptomatic PE, despite adequate anticoagulation.
b. VTE does not need to be considered in a patient who is adequately anticoagulated.
c. The FDA has not approved the LMWH enoxaparin.
d. Outpatient therapy should never be considered for DVT.

Answers: 26. b, 27. c, 28. c, 29. b, 30. a

CME INSTRUCTIONS

Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (May and November) and return it in the reply envelope provided to receive a credit letter. When an evaluation form is received, a credit letter will be mailed to the participant.