

## Bleeding Disorders: Review Questions

*Richard S. Stein, MD, FACP*

### QUESTIONS

Choose the single best answer for each question.

**Questions 1 and 2 refer to the following case study.**

A 73-year-old woman who has been receiving 5 mg of warfarin daily for 3 months because of a pulmonary embolus with no known predisposing factor is seen for a routine outpatient visit; she is found to have an international normalized ratio (INR) of 3.5. There has been no recent change in her other medications. On physical examination, there is no evidence of bruising or bleeding.

- 1. Which of the following is the most reasonable approach to managing the patient's elevated INR?**
  - A) Administer 3 to 5 mg of vitamin K<sub>1</sub> orally to lower the INR
  - B) Stop warfarin therapy and administer 1 mg of vitamin K<sub>1</sub> subcutaneously to lower the INR
  - C) Stop warfarin therapy and administer 2 units of fresh frozen plasma to lower the INR
  - D) Stop warfarin therapy and do not resume, because 3 months is long enough to treat a pulmonary embolism
  - E) Stop warfarin therapy temporarily and recheck the INR every 1 to 2 days
- 2. The resident assigned to the case decides to evaluate the pulmonary embolus further by looking for a hypercoagulable state (ie, an increased predisposition to clotting). The work-up reveals the following results: protein C activity, 22% (normal, > 60%); protein S activity, 24% (normal, > 60%); factor V Leiden gene rearrangement test, mutation not detected; prothrombin 20210 gene rearrangement test, mutation not detected. Based on these results, which of the following best describes the patient's condition?**
  - A) The patient has protein C deficiency
  - B) The patient has protein S deficiency
  - C) The patient has both protein C and protein S deficiency
  - D) The patient has factor V Leiden deficiency
  - E) There is no evidence of a hypercoagulable state
- 3. A 37-year-old woman sees her physician because of calf pain; ultrasonography reveals a deep vein thrombosis in the calf. Which of the following is the most appropriate step in the initial management of her condition?**
  - A) Administer a low-molecular-weight heparin (LMWH) (eg, enoxaparin 1.0 mg/kg body weight twice daily) along with a 40-mg loading dose of warfarin, followed by warfarin 5.0 to 7.5 mg daily
  - B) Administer a LMWH (eg, enoxaparin 1.0 mg/kg twice daily) along with a 20-mg loading dose of warfarin, followed by warfarin 5.0 to 7.5 mg daily
  - C) Administer a LMWH (eg, enoxaparin 1.0 mg/kg twice daily) along with warfarin 5.0 to 7.5 mg daily
  - D) Start unfractionated heparin therapy at a bolus dose of 80 U/kg followed by 18 U/kg per hour, and then adjust based on the patient's partial thromboplastin time
  - E) Start warfarin therapy alone at a dose of 5.0 to 7.5 mg daily
- 4. The most appropriate treatment of heparin-induced thrombocytopenia with thrombosis in a patient receiving therapy with unfractionated heparin is to stop administering unfractionated heparin and perform which of the following steps?**
  - A) Start LMWH therapy
  - B) Start therapy with lepirudin, argatroban, or danaparoid
  - C) Start tissue plasminogen activator therapy
  - D) Start warfarin therapy
  - E) Wait for platelets to recover

*(turn page for answers)*

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*Dr. Stein is an Associate Professor of Medicine, Division of Hematology-Oncology, Vanderbilt University Medical Center, Nashville, TN.*

EXPLANATION OF ANSWERS

- 1. (E) Stop warfarin therapy temporarily and recheck the INR every 1 to 2 days.** The best approach to managing this patient's condition is to stop the warfarin temporarily, recheck the INR every 1 to 2 days, and resume warfarin at a lower dose when the INR is within the therapeutic range. Fresh frozen plasma has an immediate but brief effect and is only needed in patients with an elevated INR and critical bleeding; it also creates a risk of fluid overload. Vitamin K<sub>1</sub> (phytonadione) at any dose is effective as long as the physician is willing to wait 24 hours to correct the INR, but the administration of vitamin K<sub>1</sub> can make further anticoagulation difficult. Therefore, vitamin K<sub>1</sub> should be avoided in cases such as this one. If the INR was greater than 5, administration of low-dose vitamin K<sub>1</sub> subcutaneously could be considered, in addition to stopping the warfarin. For a markedly elevated INR (> 9), 3 to 5 mg of vitamin K<sub>1</sub> could be given orally, as well as stopping warfarin therapy. Although the optimal duration of anticoagulant therapy is unknown, most authorities recommend at least 6 months of anticoagulation for a pulmonary embolus unless there is an obvious predisposing factor, such as immobilization or surgery.
- 2. (E) There is no evidence of a hypercoagulable state.** Protein C and protein S are regulatory factors that decrease the risk for clotting. Deficiencies of protein C or protein S can increase the risk for clotting. A more common cause of the hypercoagulable state is factor V Leiden mutation. Protein C and protein S exert their effects via factor V. When the factor V Leiden mutation is present, this process does not occur. The case patient has low levels of protein C and protein S. However, one of the keys in obtaining laboratory measurements is understanding factors that invalidate the tests. Levels of protein C and protein S decrease in patients receiving warfarin; therefore, the low levels that are obtained are mean-

ingless. The only tests of significance are the genetic tests, because the DNA is unchanged by warfarin. Prothrombin 20210 is another mutation that can lead to hypercoagulability, but it is not detected in this case.

- 3. (C) Administer a LMWH (eg, enoxaparin 1.0 mg/kg twice daily) along with warfarin 5.0 to 7.5 mg daily.** There is never an indication for administering a loading dose of warfarin. Whereas a loading dose of warfarin can cause the INR to reach the therapeutic range more quickly, this occurs only because of a more rapid fall in factor VII. In that situation, the patient is not really anticoagulated, although the INR is in the therapeutic range, and there is an unnecessary risk of embolization that can only be eliminated by starting heparin (either low-molecular-weight heparin [LMWH] or unfractionated heparin) concurrently. Use of heparin alone creates immediate anticoagulation, but unless warfarin is started, the patient will likely be on long-term heparin. Whereas using heparin alone creates a minimal risk if LMWH is used, when unfractionated heparin is used, there is a 3% risk of heparin-induced thrombocytopenia with thrombosis (HITT). Therefore, simultaneous use of LMWH and warfarin is the most appropriate management. Using LMWH also eliminates the need for monitoring of the partial thromboplastin time.
- 4. (B) Start therapy with lepirudin, argatroban, or danaparoid.** HITT is life-threatening, and correct management is critical. In addition to stopping heparin, therapy must be initiated with a drug that acts directly on thrombin. Use of warfarin can increase the risk of venous limb gangrene and is not an acceptable option. There are no clinical data to support the use of tissue plasminogen activator therapy. Whereas the risk for HITT is less with LMWH than with unfractionated heparin, cross-reactivity can occur. As a result, LMWH is contraindicated in patients with HITT.

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