

Heparin-Induced Thrombocytopenia: Review Questions

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QUESTIONS

Choose the single best answer for each question.

1. **What is the incidence of immune-mediated heparin-induced thrombocytopenia (HIT type II) in patients exposed to heparin for more than 4 days?**

(A) 10%–20%
(B) 5%–10%
(C) 3%–5%
(D) 0.3%–3%
(E) 0.05%–0.1%

2. **What is the median platelet count nadir in HIT type II?**

(A) $100 \times 10^3/\text{mm}^3$
(B) $80 \times 10^3/\text{mm}^3$
(C) $60 \times 10^3/\text{mm}^3$
(D) $20 \times 10^3/\text{mm}^3$
(E) $10 \times 10^3/\text{mm}^3$

3. **Which of the following manifestations of HIT leads to the most frequent complications in HIT?**

(A) Arterial thrombosis
(B) Venous thrombosis
(C) Thrombocytopenia
(D) Heparin-induced skin lesions
(E) Acute systemic reactions (ie, fevers, chills, rigors, tachycardia, hypertension)

Questions 4 and 5 refer to the following case study.

A 45-year-old man with diabetes, chronic atrial fibrillation, and chronic renal insufficiency is admitted to the hospital with 3 days of cough and fever. Physical examination demonstrates right lung base rales and consolidation. Routine laboratory tests demonstrate the following: serum electrolytes, normal levels; blood urea nitrogen, 36 mg/dL; serum creatinine, 3.1 mg/dL (patient's baseline is 2.6 mg/dL); leukocyte count, $14.5 \times 10^3/\text{mm}^3$; platelet count, $170 \times 10^3/\text{mm}^3$; and international normalized ratio, 1.2. A chest radiograph shows a right lower lobe infiltrate, and a diagnosis of pneumonia is made. The patient is started on ceftriaxone and azi-

thromycin. He is placed on unfractionated heparin and warfarin for treatment of his atrial fibrillation. On hospital day 5, the patient complains of right calf pain and swelling. Duplex ultrasonography demonstrates venous thrombosis in the right lower extremity. Platelet count is now $54 \times 10^3/\text{mm}^3$. HIT is suspected.

4. **Which of the following statements about the diagnosis of HIT is CORRECT?**

(A) Diagnosis of HIT is most reliably made when both clinical and pathologic criteria are met
(B) Diagnostic testing for HIT has a quick turnaround time and is almost always immediately available at most medical centers
(C) Enzyme immunoassays (ie, detection of antibodies against the heparin/PF4 complexes that contribute to HIT) are considered the "gold standard" in the diagnosis of HIT
(D) The concordance between activation assays (those in which heparin "activates" normal donor platelets in the presence on the patient's serum) and enzyme immunoassays is approximately 100%
(E) The advantage of the ^{14}C -serotonin release assay is its low cost

5. **In addition to the immediate cessation of all unfractionated heparin products, the next appropriate step in the treatment of HIT in this patient is the addition of which one of the following?**

(A) Low-molecular-weight heparin (LMWH)
(B) Aspirin
(C) Lepirudin
(D) Argatroban
(E) Ancrod

(turn page for answers)

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EXPLANATION OF ANSWERS

1. **(D) 0.3%–3%.** HIT type II is thought to occur in approximately 0.3 to 3% of patients exposed to heparin for more than 4 days. Approximately 10% to 20% of patients receiving unfractionated heparin experience a fall in platelet count to less than the normal range or a 50% fall in platelet count within the normal range. However, most of these cases are thought to be secondary to HIT type I, or nonimmune-mediated disease.
2. **(C) $60 \times 10^3/\text{mm}^3$.** The thrombocytopenia in HIT type II is mild to moderate in severity. The median platelet count nadir is $60 \times 10^3/\text{mm}^3$, and spontaneous bleeding is rare. It is important to recognize that a drop in platelet count of 50% or greater within the normal range still can be indicative of HIT.
3. **(B) Venous thrombosis.** Deep venous thrombosis, pulmonary embolism, venous limb gangrene, and adrenal hemorrhage are examples of potential complications due to the venous thrombotic state in HIT. Complications from arterial thrombosis include limb ischemia, stroke, and myocardial infarction. However, in one study, pulmonary embolism was observed more frequently than all arterial thrombotic events combined.¹ Thrombocytopenia is the most common clinical manifestation of HIT, but it is rarely severe, and spontaneous bleeding is unusual. Heparin-induced skin lesions and acute systemic reactions are less common complications of HIT.
4. **(A) Diagnosis of HIT is most reliably made when both clinical and pathologic criteria are met.** The first step in diagnosing HIT is recognizing the possibility that HIT exists by assessing clinical and laboratory data. While the diagnosis should be confirmed by pathologic testing, the initiation of treatment should begin prior to obtaining test results. Most tests available for detecting HIT are time-consuming. Many of the tests are not available at all medical centers, adding to the length of time needed for pathologic

diagnosis. The ¹⁴C-serotonin release assay is considered the “gold standard” in HIT testing due to its high specificity and sensitivity. Disadvantages of the test include high technical demand, use of radioactivity, and high cost. The concordance between the two types of testing for HIT (ie, activation assays, enzyme immunoassays) is only approximately 80% to 90%, making “cross-verification” necessary (ie, confirmation of a borderline result with one test by using a second test).

5. **(D) Argatroban.** Argatroban is a direct thrombin inhibitor that is metabolized by the liver, making it useful for treating HIT patients with renal failure. Lepirudin also is a potent antithrombin agent; however, it is metabolized and excreted by the kidneys, which makes it less than ideal for the patient described. Although LMWH is much less likely to cause or worsen HIT than unfractionated heparin, it has been shown to be 100% cross-reactive with HIT antibodies. It should therefore never be used in the treatment of HIT. Aspirin is considered to be of marginal therapeutic benefit in HIT but can be started in those patients judged to be at high risk for arterial thrombosis. Ancrod is defibrinogenating snake venom that has had some benefit in HIT patients in uncontrolled studies.¹ However, it is not ideal for treatment for several reasons. First, it may actually increase thrombin generation (which is the underlying pathophysiologic problem in HIT). Second, its effects are unpredictable and highly patient specific. Finally, it must be administered slowly. Of particular note is that the most important factor in the treatment of HIT is the immediate cessation of all heparin-containing products and treatments (including heparin flushes).

REFERENCE

1. Warkentin TE. Heparin-induced thrombocytopenia: a ten-year retrospective. *Annu Rev Med* 1999;50:129–47.

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