

Clinical Use

- Diagnose heparin-induced thrombocytopenia (HIT) type II

Clinical Background

HIT, the most common form of drug-induced thrombocytopenia, may develop in up to 5% of patients treated with heparin. The clinical course of HIT is varied, but can include catastrophic outcomes such as amputation and death secondary to sudden arterial or venous thrombosis. HIT usually results from the formation of antibodies that react with a trimolecular complex between platelet factor 4 (PF4), heparin, or other glycosaminoglycans and the platelet membrane receptor Fc(gamma)RIIa, leading to reduced platelet count and paradoxically increased thrombosis. Thrombocytopenia typically develops after 5 days in naive patients and can develop within minutes to hours post-exposure in those who have received heparin therapy within the past 6 months.

A presumptive diagnosis of HIT can be based on a >50% reduction in platelet count more than 5 days after initiation of heparin therapy, a platelet count <150,000/ μ L, or the development of thromboembolic complication(s). Laboratory confirmation is important, but withdrawal of all heparin sources should *not* be delayed while awaiting confirmatory results.

The ¹⁴C-serotonin release assay (SRA) is considered the gold standard for laboratory diagnosis because of its high sensitivity and specificity. An enzyme-linked immunosorbent assay (ELISA) detecting antibodies to the platelet factor 4 (PF4)/PVS complex offers rapid and sensitive detection, but lower specificity than the SRA. Physicians often order the 2 assays together. Quest Diagnostics offers the SRA and ELISA separately and as a panel.

Method

SRA: This assay is performed using Fc(gamma)RIIa receptor-phenotyped platelets from highly reactive donors. After incubation of donor platelets with ¹⁴C serotonin, bovine heparin (0.1, 0.5, and 100 U) is added along with patient serum. False-positive results are excluded by running a parallel study with anti-Fc(gamma)RIIa. Results are reported as percent serotonin released; values <20% are considered negative. Specimens with borderline results are re-tested

the next day with fresh platelets from a different donor. Positive results are called in to the ordering physician and consultation is available.

CPT code*: 86022

ELISA: This assay utilizes the PF4/PVS complex as the capture antigen and an alkaline phosphatase-labeled anti-human globulin as the detection antibody. The optical density (OD) is reported: OD values >0.41 are considered positive and indicate the presence of heparin-induced antibodies.

CPT code*: 86022

Interpretive Information

SRA: A positive result strongly suggests HIT; consider substituting heparin with an appropriate direct thrombin inhibitor. A negative result suggests the absence of HIT.

ELISA: A positive result indicates the presence of heparin-induced antibodies but is not diagnostic of HIT; other clinical and laboratory findings should be considered prior to diagnosis. The presence of immune complexes or other immunoglobulin aggregates may cause false-positive results. A negative result suggests the absence of heparin-induced antibodies, although this assay may not detect low-titer, low-avidity antibodies.

Panel: Although SRA is the gold standard for diagnosis of HIT, caution may be warranted when interpreting discrepant ELISA and SRA results (Table 1).

Table 1. Interpretation of Heparin-Induced Platelet Antibody (ELISA) and SRA Results in the Presence of Thrombocytopenia

SRA	ELISA	Interpretation
+	+	HIT II confirmed
-	-	HIT II unlikely*
+	-	HIT II likely
-	+	HIT II unlikely*†

HIT II = heparin-induced thrombocytopenia type II

*Look for other causes of thrombocytopenia.

†Consider repeat SRA if clinically warranted.

Specimen Requirements

SRA: 1 mL frozen serum; 0.4 mL minimum.

Heparin-Induced Platelet Antibody assay: 1 mL frozen serum; 0.5 mL minimum.

HIT Panel: two 1-mL aliquots frozen serum; 1 mL minimum.

*The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

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