Cardiac Bypass Surgery in the Setting of Heparin Induced Thrombocytopenia (HIT)

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Heparin induced thrombocytopenia (HIT) is one of the most important adverse drug reactions that physicians encounter. If not recognized and without appropriate treatment, cardiac surgical patients with HIT have a 38 to 81% incidence of thrombosis and a 28% risk of death.(1)

Patients with known or suspected HIT who present for cardiac surgery represent a significant clinical dilemma. Frequently, patients are misdiagnosed and, probably more often, not all of the relevant information and studies that would help us clarify the situation are available. In the text that follows there will first be a discussion of useful facts about HIT followed by the current BIDMC, Division of Cardiac Anesthesia and Surgery guidelines for dealing with this subset of patients.

Useful Facts Regarding HIT

1. Heparin Antibodies

Heparin is a very immunogenic compound. When it complexes with platelet factor 4 (PF4), it induces an antibody response in up to 50% of patients. Not all of these antibodies cause HIT; HIT occurs in 1 to 5% of patients who receive unfractionated heparin and < 1% that receive low molecular weight heparin.(2)

These antibodies do not hang around for that long. Their median half-life is approximately 85 days but levels are clinically irrelevant in almost all patients by 100 days (median 50 days).(1,2) Furthermore, it appears that HIT antibody formation **does not** recur more quickly or, in fact, more often in patients with a history of HIT who are later re-exposed to heparin; i.e. there does not appear to be an immunologic memory.(1)

2. Diagnosis

A useful mnemonic for thinking about the diagnosis of HIT revolves around the four T's: **t**iming, **t**hrombocytopenia, **t**hrombosis, and o**t**her causes for thrombocytopenia.

The following table may be useful in scoring the pretest probability of HIT:

Table 1 Criteria for estimating the pretest probability of heparin-induced thrombocytopenia: the '4Ts' score according to Warkentin [3]

	2	1	0
Thrombocytopenia	> 50% fall or platelet nadir $20–100 \times 10^9\ L^{-1}$	30–50% fall or platelet nadir $10–20 \times 10^9\ L^{-1}$	Fall < 30% or platelet nadir < $10 \times 10^9\ L^{-1}$
Timing of fall in platelet count or other sequelae	Clear onset between days 5–10; or less than one day (if heparin exposure within past 100 days)	Consistent with immunization but not clear (e.g. missing platelet counts) or onset of thrombocytopenia after day 10	Fall in platelet count too early (without recent heparin exposure)
Thrombosis or other sequelae (e.g. skin lesions)	New thrombosis; skin necrosis; postheparin bolus acute systemic reaction	Progressive or recurrent thrombosis; erythematous skin lesions; suspected thrombosis not yet proven	None
Other cause for thrombocytopenia not evident	No other cause for fall in platelet count is evident	Possible other cause evident	Definite other cause present

Pretest probability score: 6–8 = high; 4–5 = intermediate; 0–3 = low.

From Pouplard et al.(3)

3. Laboratory Testing

Testing for antibodies to the heparin/PF4 complex is a sensitive but non-specific test for HIT that can be done in our laboratory. A call ahead to the lab can facilitate the process and can generally, unless off hours, lead to results within several hours. If the test comes back negative for antibodies, cardiac surgery can proceed with full, normal heparinization. A positive result is not as helpful since not all antibodies cause HIT. If the result is positive, the patient may or may not have HIT and, if time exists, more testing (serotonin release assay) should occur as below. In addition to knowing that the result is positive, it is also useful to know the titer of antibody.

The serotonin release assay does detect the HIT producing antibodies. It has both a high sensitivity and specificity. However, the test is very difficult to perform and is done only at a few large research centers. Our patient samples are sent to Wyoming once a week. From the practical stand point, this means that results may take a week or more to obtain. Many of our patients will have to come to the operating room before the results of this test are back.

Guidelines for the Management of Patients with Known or Suspected HIT Requiring Heparinization for Cardiac Surgery

This portion of the guidelines applies to patients who have active, diagnosed HIT, patients with heparin/PF4 antibodies present in their serum that have a clinical picture consistent with the possibility of HIT, and patients with thrombocytopenia that maybe related to HIT where there is no time for any testing.

Our current protocol calls for the use of **alprostadil** (PGE1), a potent reversible platelet inhibitor, with our standard heparin dosing protocol as follows:(4)

1. Establish if surgery can be postponed until the results of a serotonin release assay can be obtained or until heparin PF4 antibodies are no longer detectable. The serotonin assay takes about a week. The disappearance of antibodies will usually occur within 6 weeks but may take up to 6 months.
2. If the serotonin release assay is positive and surgery can be delayed, once it is established that the heparin PF4 antibodies are gone the patient can undergo surgery with normal heparinization. If it can not be delayed, proceed to step 3.
3. Contact OR pharmacy and inform them you will need alprostadil. It is not stocked in the OR pharmacy and will have to be obtained from the main pharmacy.
4. Dilute 2 vials of the alprostadil (1 mg total) in 50 mls of normal saline to make a solution of 20 mcg/ml.
5. After induction and placement of central access, begin infusion of alprostadil at **0.01 mcg/kg/min.**
6. Increase the rate of the alprostadil infusion incrementally over 30 to 40 minutes with the goal of reaching **0.1 mcg/kg/min.** This allows for the ability to keep up with decreases in vascular tone (see next).
7. Alprostadil is a potent vasodilator. Use norepinephrine (may want to quadruple concentrate) to maintain vascular tone and blood pressure as needed. **This may require large doses!**
8. Continue the alprostadil infusion until 15 minutes after the completion of protamine reversal.

There are several different protocols available for the management of these patients. Our current protocol is based on our institutional experience, review of the current literature, and consideration of the risks and benefits of the various available protocols.

Guidelines for the Management of Patients with a History of HIT Requiring Heparinization for Cardiac Surgery

This portion of the guidelines applies to patients with a known or suspected **history** of HIT.

1. Send blood for heparin/PF4 antibody testing.
2. If negative, proceed for surgery using standard heparinization protocols.
3. If positive, determine if surgery can be postponed until the antibodies have cleared (6 weeks to 6 months). Once cleared, surgery can proceed with normal heparinization.
4. If surgery can not be delayed or if there is no time for even heparin/PF4 antibody testing, use the alprostadil protocol outlined above.

References

1. Warkentin TE, Greinacher A. Heparin-induced thrombocytopenia and cardiac surgery. Ann Thorac Surg 2003;76:638-48.
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