\*The intent of this product is to be a resource; not a replacement for institutional protocols. Standard 1 of AmSECT’s Standards and Guidelines for Perfusion Practice.1 These Standards and Guidelines may also be superseded by the judgement of the healthcare professional taking into account the facts and circumstances of the individual case.

|  |  |  |
| --- | --- | --- |
| **SUBJECT/TITLE** | **Heparin-Induced Thrombocytopenia** | |
|  |  |  |
| **PURPOSE:** | To provide a guideline and resource for patients unable to acceptunfractionated heparin. To minimize risk in the conduct of CPB inpatients suspected or diagnosed with HIT/HITT, specialconsiderations should be taken during cardiac surgery. Thissituation requires careful preparation of the patient and all devicesthat are used in the surgical procedure, such as the extracorporealcircuit, cardioplegia solution, and administration system,pharmacologic management, arterial lines and autotransfusionsystems. | |
|  |  |  |
| **TARGET POPULATION:** | Patients unable to accept unfractionated heparin. | |
|  |  |  |
| **DEFINITIONS:** | Heparin‐Induced Thrombocytopenia (HIT) is a life threatening immune response to heparin. Caused by anti‐platelet factor 4 (PF4)/heparin antibodies that activate platelet and serotonin‐release. (2)  ● PF4 is released from platelets in circulation  ● Heparin binds to PF4 to form a complex.  In some patients, this complex causes development of heparin- PF4 IgG antibodies and immune complex formation.(3)  ● Leads to a cycle of additional platelet activation, thrombocytopenia, and clot formation (HIT). (3)  For HIT patients undergoing surgical or cardiac surgical procedures, NO approved anticoagulant is available. | |
|  |  |  |

**POLICY:**

1. The surgeon should determine the anticoagulation management with the surgical team prior to the day of surgery.
2. (Insert Hospital name) supports the use of (insert appropriate anticoagulant for your institution) for patients unable to accept heparin.
3. The (Insert Hospital name) Standard tubing pack and oxygenator without a heparin surface coating should be considered on all HIT positive patients.
   1. Most manufactures provide CPB components with surface modified additives aimed to provide reduced platelet activation and adhesion and preserve platelet function without heparin.

**Preoperative Diagnosis of HIT: is it *true* HIT**

1. General description of what happens before patient enters OR
   1. Note that HIT “does not recur more quickly or more often in a patient with previous HIT who is re-exposed to heparin if the antibody and activation assay are negative.”7
   2. The decision to perform platelet count monitoring, and the intensity of such monitoring, depends on the patient’s risk factors, particularly the type of heparin, duration of heparin therapy, and the type of patient.
   3. It is appropriate to perform platelet count monitoring in certain clinical situations, and to focus platelet count monitoring during those times when HIT usually occurs.4
   4. What clinicians need to understand is that the diagnosis of a “true” HIT situation comes from “a combination of clinical evaluation and laboratory testing to best ensure the accuracy of the diagnosis.”2
   5. The answers cannot be found in just one lab value.
2. **Clinical Assessment**: 4T score (or 4Ts)
   1. Thrombocytopenia - platelet count less than 15,000
   2. The Timing of the platelet fall - how soon the platelets fall after heparin exposure
   3. The presence of Thrombosis - arterial or venous thrombosis, anaphylactic reaction
   4. The oTher potential causes of thrombocytopenia.
   5. The 4Ts provides a pre-test probability score of the likelihood of HIT.
      1. 0–3 low probability for HIT
      2. 4–5 intermediate probability for HIT
      3. 6–8 high probability for HIT
   6. Low 4Ts
      1. Low probability of HIT, then the lab tests are omitted and the patient is treated as if they don’t have HIT.4
      2. Low 4Ts usually excludes HIT (\*not always\*)
   7. High 4Ts
      1. High probability of HIT, then conduct further tests
      2. High 4Ts does not always\* prove HIT.4
   8. “Empiric clinical judgement is still required, and should clinical suspicion still be high, despite low 4Ts, then immunological testing may resolve the discrepancy. 4
   9. In general terms, most patients under suspicion of HIT do not have HIT.”4

**Preoperative Testing:**

If HIT is suspected based on the 4T’s there are two types of further testing:

1. Immunological screenings
   1. An immunoassay is a chemical test used to detect or quantify a specific substance, the analyte, in a blood or body fluid sample, using an immunological reaction.5
   2. STiC – lateral flow assay
   3. AcuStar – (HIT-IgG) Automated chemiluminescence based assay
   4. Elisa – Enzyme linked immunosorbent Assay \*the best test for excluding HIT
      1. This test is sensitive for clinical HIT (about 99%)
      2. A negative test essentially rules out the diagnosis.2
      3. A positive test, is then followed by a confirmatory ‘functional’ assay
2. Functional Assays
   1. An assay is the determination of the purity of a substance or the amount of any particular constituent of a mixture.5
   2. SRA – Serotonin Release Assay
   3. Multiplate – whole blood
   4. LTA – platelet rich plasma4
3. **Why isn’t every patient tested for HIT?**
   1. The issue with the actual tests for HIT is that they are not always readily available and/or possible at an in-hospital laboratory.
   2. Many of these tests are sent off to larger institutions with the proper equipment for results
   3. Results are not available in a timely enough manner to assist in making clinical decisions regarding the management of HIT.4

**PERFUSION PUMP CONSIDERATIONS:**

The following CPB system and components should be considered:

1. Autotransfusion System
2. Non-Heparin coated circuit
3. Cardiopulmonary Bypass Pump setup: Closed system with no additional cardiotomy (if available)
4. Cardioplegia: Blood or Crystalloid
5. No hemoconcentration
6. MUF
7. Diligent anticoagulation monitoring- ACT every 15-20 minutes

More detail on each topic below

1. **Autotransfusion system**
   1. Highly recommended
   2. Should be continued until chest closure occurs.
   3. Anticoagulant Citrate Phosphate Dextrose Solution (ACDA) should be used instead of heparin.
2. **Non- Heparin coated circuit:**
   1. Use of a non-heparin coated circuit
   2. Arterial blood gas sensor may be heparin coated
   3. Beware that some of the following may contain heparin:
      1. vein flush on field
      2. IABP flush line
      3. Dialysis flush lines and heparin coated swans
      4. Arterial flush line should be 10mg bivalirudin per 1000ml crystalloid 2,3
3. **Cardiopulmonary Bypass Pump Setup:**
   1. Use of Bivalirudin anticoagulation for cardiopulmonary bypass requires some modification to conventional bypass circuit setup
   2. Both open and closed system setups may be used for cardiopulmonary bypass in this protocol
   3. ***Open versus Closed System for Bypass***
      1. A **closed** system may offer some benefits.
      2. In general, there are less low-flow areas in a closed system circuit versus an open circuit with a cardiotomy.
      3. If you don’t have a closed system, increased monitoring is necessary due to the additional risks involved with possible areas of stagnation.
   4. ***Cardiotomy***
      1. If an open circuit with cardiotomy suction and a reservoir is being used, continuous drainage and/or frequent emptying of the reservoir into the bypass circuit is recommended, in order to avoid the possibility of localized Bivalrudin depletion in the isolated blood volume.
      2. Extra blood volume can be placed in CPD bags temporarily to be anticoagulated during CPB.
4. **Cardioplegia** 
   1. The use of Bivalirudin during cardiac surgery does not require a specific type of cardioplegia (either crystalloid or blood cardioplegia may be used).
   2. When using Bivalirudin just be aware of the additional risks involved with possible areas of stagnation.
   3. **Crystalloid cardioplegia**
      1. No anticoagulant needs to be added to crystalloid cardioplegia solution.
   4. **Blood cardioplegia:** 
      1. Several methods whereby blood cardioplegia can be used with Bivalirudin anticoagulation.
      2. Modify the system so that the risk of flow-isolated areas is minimized in the cardioplegia circuit:
      3. ***Flushing*** *of cardioplegia circuit:*
         1. Any non-circulating portions of line between the pump and the patient should be flushed prior to cardioplegia administration
         2. Freshly collected blood is delivered to the patient each time with successive cardioplegia doses
         3. This flushed blood can be sent to the cell saver and washed free of additives prior to re-administration to the patient.
      4. ***Recirculation*** *of cardioplegia solution:*
         1. The cardioplegia can be circulated continuously by use of a “Y” cardioplegia connector added to the setup.
         2. The prime volume of the cardioplegia circuit is typically 250 mL
      5. ***Concurrent*** *use of blood cardioplegia and crystalloid cardioplegia:*
         1. Blood cardioplegia is used to arrest the heart.
         2. After initial delivery is completed, use crystalloid cardioplegia solution to chase out remaining blood in the cardioplegia circuit to prevent stagnation.
         3. The modality for purge may vary between institutions.
5. **Hemofiltration**
   1. Hemofiltration is **not** recommended during CPB because the plasma concentration of Bivalrudin will be reduced with hemoconcentration.
   2. If medically indicated, hemofiltration may be used, but frequent monitoring of anticoagulation effect is suggested.
   3. An additional bolus administration of Angiomax (0.1-0.5 mg/kg) may be prudent prior to beginning hemofiltration.
6. **Modified Ultrafiltration**
   1. The use of Modified Ultrafiltration (MUF) following termination of CPB will facilitate the removal of Bivalirudin from the patient.
   2. Clinicians may choose to use MUF at their discretion. Institutional practice should be followed.
   3. MUF should be carefully monitored since it will lower the concentration of Angiomax and possibly allow formation of thrombosis in the MUF circuit
   4. Careful and frequent monitoring of the amount of anticoagulant should be performed while using MUF.

**PROCEDURE: see Perfusion Pump Considerations above**

**CLINICAL ASSESSMENT/SCREENING:**

1. Contraindications: None

# RELATED DOCUMENTS:

1. Angiomax/Bivalirudin

# REFERENCES:

1. Baker RA, Bronson SL, Dickinson TA, et al. Report from AmSECT’s International Consortium for Evidence-Based Perfusion: American Society of Extracorporeal Technology Standards and Guidelines for Perfusion Practice: 2013. J Extra Corpor Technol. 2013;45(3):156-66.
2. Shuster TA., Silliman WR, Coats RD, Mureebe L, Silver D. Heparin-induced thrombocytopenia: twenty-nine years later. J Vasc Surg 2003;38(6):1316-22.
3. Slaughter TF, Bennett-Guerrero E, Su Z, El-Moalem H, Klemp KF, Greenberg CS, et al. Anti-heparin/PF4 antibodies detected prior to cardiac surgery identify patients at high risk for adverse perioperative outcomes [Society of Cardiovascular Anesthesiologists 24 th annual meeting abstract]. Anesth Analg 2002; 93:SCA28.
4. 4. Favaloro, E. J., Mccaughan, G., Mohammed, S., Lau, K. K., Gemmell, R., Cavanaugh, L., . . . Pasalic, L. (2018). HIT or miss? A comprehensive contemporary investigation of laboratory tests for heparin induced thrombocytopenia. Pathology,50(4), 426-436. doi:10.1016/j.pathol.2017.11.089
5. Definition of Assay. (n.d.). Retrieved from <https://www.medicinenet.com/script/main/art.asp?articlekey=8412> on July 20, 2020

# DISCLAIMER:

In emergency situations, immediate life support measures of whatever appropriate nature come first with attention turning to measures described in this protocol/process as soon as possible and practical.

This is a minimal protocol/process that may be exceeded at any time based on the judgment of the involved patient care personnel.

This protocol/process encourages high quality patient care but observing it cannot guarantee any specific patient outcome.

This protocol/process is subject to revision from time to time, as warranted by the evolution of technology and practice.

Review period: Review as changes occur or per institutional protocol.

Original hard copies and computer copies of this protocol are stored under the supervision of the Chief Perfusionist, Department of Cardiovascular Perfusion.

Documents relating to patient care standards are developed according to the accepted hospital standards.

# APPROVED BY: *(signature of CMO and CNE only required)*

|  |  |  |  |
| --- | --- | --- | --- |
| Source: | (originating department/committee) | | |
| Effective Date: | (can use ‘created date’ for this) | | |
| Version Number: | (should match # of revisions, use 1.0 if new document) | | |
| Date Revised: | MM/YYYY; all dates any content changes were made | | |
| Date Reviewed: | Amb. Care PPP:  QSOS: | | |
|  |  | | |
|  | | Date: |  |
| <Insert Name>  *<Insert Title>* | |  |  |
|  | | Date: |  |
| <Insert Name>  *<Insert Title>* | |  |  |
|  | | Date: |  |
| <Insert Name>  <Insert Hospital Name> Chief Medical Officer | |  |  |
|  | | Date: |  |
| <Insert Name>  <Insert Hospital Name> Chief Nursing Executive | |  |  |