Case Reports on Preoperative Preparation
Heparin Induced Thrombocytopenia

Robert Groom and Jwana Ibsies

“Task of medical science falls in three buckets…”

1. Understanding disease biology
2. Finding effective therapies
3. Making sure those therapies are delivered effectively

“That third bucket has been almost totally ignored by researchers… a huge mistake.”
Session 2 and 4: Break out Sessions

- Three sessions where published reports will be used to fuel discussion on preoperative preparation.

Disclosures

- No financial disclosures related to this presentation (RCG JI)
- Bob Groom participated in The Medicines Company Angiomax Trials “Choose-on and Choose-off”
- Not hematologists (RCG JI)
Students using Flipped Classroom Scored 12% higher than controls.

“...the flipped classroom model is a highly effective means in which to disseminate key physiological concepts to graduate students.”
Welcome to Perfusion Methodology: Special CPB Procedures

Instructor: Alexandra Chester, MS, CCP and Dawn M. Oles, MHPE, CCP, LP

This course is the continuation of Perfusion Methodology: Special Procedures I. This course covers Sickle cell disease, Anemia, Hemophilia A & B, Methemoglobinemia, Heparin Resistance, AIDS patients, Malignant Hypothermia, Diabetic Patients, AT III Deficiency and HIT Patients.

Thank you to the original writers of the Ohio State Review Class.
Objectives

- Participants will learn about the pathophysiology, prevalence and clinical presentation of HIT.
- Participants will gain practical knowledge about preoperative preparation for treatment of patients requiring an alternative to heparin anticoagulation.
- Participants will review and critique case reports and case series from the medical literature.

Ideal drug for Anticoagulation during CPB

1). The agent should be effective in minimizing activation of coagulation during CPB.
2) A rapid and simple method of monitoring its anti-coagulating effects
3) Rapid and complete reversibility of the anti-coagulating effects

Warkenten-Heparin Induced Thrombocytopenia 3rd Edition
Have you ever provided CPB support for a patient with HIT?

1. Yes
2. No

What is the frequency of HIT cases that you are involved in each year at your center?

- _____ cases/year
HIT/HITTS: Our Experience, Nomogram, Patterns and Anticoagulation Algorithm

MMC Division of Cardiothoracic Surgery
Thrombocytopenia and Heparin-Induced
Thrombocytopenia and Thrombosis Syndrome (HITTS) 1/1/04 -12/31/09

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<th>Year</th>
<th>2004</th>
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<th>2007</th>
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<td>Rate of Thrombocytopenia*</td>
<td>18%</td>
<td>10.7%</td>
<td>19.7%</td>
<td>15.7%</td>
<td>13.75%</td>
<td>13.6%</td>
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<tr>
<td>DTI Use=15%</td>
<td>DTI Use=24%</td>
<td>DTI Use=20%</td>
<td>DTI Use=18%</td>
<td>DTI Use=17%</td>
<td>DTI Use=27%</td>
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<td>N=30/147</td>
<td>N=29/128</td>
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<td>N=31/115</td>
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<td>Rate of Clinical HITTS*</td>
<td>3.7%</td>
<td>7.2%</td>
<td>3.4%</td>
<td>3.9%</td>
<td>4.5%</td>
<td>7.8%</td>
</tr>
<tr>
<td>DTI Use=15%</td>
<td>DTI Use=24%</td>
<td>DTI Use=20%</td>
<td>DTI Use=18%</td>
<td>DTI Use=17%</td>
<td>DTI Use=27%</td>
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<td>N=32/208</td>
<td>N=27/111</td>
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<td>N=29/128</td>
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<td>N=31/115</td>
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<tr>
<td>HITTS Mortality Rate</td>
<td>57%</td>
<td>50%</td>
<td>80%</td>
<td>20%</td>
<td>20%</td>
<td>33%</td>
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<td>N=1/5</td>
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<td>N=3/9</td>
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### Four T'S of HIT/HITTS Post Op Cardiac Surgery Maine Medical Center

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<th>2 POINTS</th>
<th>1 POINT</th>
<th>0 POINTS</th>
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<td><strong>Thrombocytopenia</strong></td>
<td>Platelet count on POD# 1 (relative to last pre-op plat count)</td>
<td>&gt; 50% fall ONLY if after POD# 4</td>
<td>Any &gt; 50% fall</td>
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<td><strong>Timing</strong></td>
<td>consistent with HIT: Day 0 = day of surgery</td>
<td>Yes: If between POD# 5-10</td>
<td>Possible: After POD# 10</td>
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<tr>
<td><strong>Thrombosis</strong></td>
<td>If yes, add 2 → 4 points total</td>
<td>Possible or suspected</td>
<td>None</td>
</tr>
<tr>
<td><strong>Other causes of</strong></td>
<td>No explanation (besides HIT)</td>
<td>Possible other cause</td>
<td>Definite other cause</td>
</tr>
<tr>
<td><strong>Thrombosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
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</table>

HIT RISK: 0 – 3 Low, 4 – 5 Moderate, 6 – 8 High

Scoring system modified from Warkentin et al, 2003, revised 5/18/05, 6/24/10

### Platelet Patterns After CPB

Fig 1. Retrospective cohort. (A) Normal changes in PC after CPB in patients without antibodies to H-F9 (x = 145, mean ± 1 SD). (B, C) PC patterns associated with HIT. Patterns P1 and P2 were defined according to the evolution of PC (mean ± 1 SEM) in four and two HIT patients respectively.
Anticoagulation in Post-op Cardiac Surgical Patients

Platelet Count ≤50% of last pre-op platelet count or < 100

- HIT Score 4 or more (any thrombosis)
- Bivalirudin

Yes

- DVT prophylaxis

No

- Bridge to coumadin (e.g. valve, AF)

- DVT prophylaxis

- Heparin drip

- Renal function wnl

- Fondaparinux if normal renal function
  note: ½ life 17-24 h

- Bivalirudin

- Poor renal function

- Enoxaparin (Lovenox) (or unfractionated heparin)

Daily plat count on pts on heparin, enoxaparin, bival while in CTICU. QOD on R1.
Weekly extremity ultrasound exam on patients in CTICU 48 hrs or longer
All patients have intermittent pneumatic compression/sequential compression devices.

Check Multidisciplinary Rounds order set in SCM for all above options. rk.08.19.10

Has your team provided long term ECLS to a patient with HIT?

1. Yes
2. No
What is the frequency of ECLS cases where HIT is involved that you are involved in each year at your center?

- _____ cases/year

Which of the following alternative anticoagulants does your center currently use to for patients with HIT?

1. Argatroban
2. Bivalrudin
3. Prostaglandin
4. A and B
5. All the above
6. Other
Case Reports

Bivalirudin as an Alternative Anticoagulant for Cardiopulmonary Bypass During Adult Cardiac Surgery—A Change in Practice

Peter Gatt, MSc;* Samuel Anthony Galea, MD, MRCS (Ed);† Walter Busuttil, MD, FETCS;‡ Charles Grima, MSc;* Jeffrey Muscat, MSc;* Yvette Farrugia, BSc*

*Clinical Perfusion Services, Mater Dei Hospital, Msida, Malta; †Department of General Surgery, Mater Dei Hospital, Msida, Malta; and; ‡Department of Cardiac Surgery, Mater Dei Hospital, Msida, Malta

ACT Recommendations from the literature

- ACT cutoff to 480 seconds or $2.5 \times $ baseline ACT
- $2.5 \times $ baseline ACT cutoff
- 400 seconds target ACT
- APTTr > 5
- $2.5 \times $ patient baseline ACT, confirmed by an APTTr greater than 5.
“Alterations to an established protocol is a challenging task especially for a unit like ours that has been using heparin in adult cardiac surgery for more than 20 years. A positive outcome can be achieved with the involvement of all the professions associated with cardiac surgery.”
Figure 1. Results of coagulation analysis performed intra- and postoperatively until discharge from ICU. APTT reference range and 2.5 x baseline ACT limit are represented on the graph.

Use of Bivalirudin as an Anticoagulant During Cardiopulmonary Bypass

James J. Veale, CCP,* Harry M. McCarthy, CCP; George Palmer, MD; Cornelius M. Dyke, MD

Table 1. Dosing recommendation for cardiopulmonary bypass (CPB).

Before CPB  | During CPB  | After CPB
---|---|---
Patient | 1.0 mg/kg IV bolus  | 2.5 mg/kg IV infusion  | 2.5 mg/kg IV infusion until discontinuation
Flash solution | 0.1 mg/mL Angiomax  | (blood based) 1:12 CPD OR 0.1 mg/mL Angiomax in crystalloid solution  | 0.1 mg/mL Angiomax in crystalloid solution
Graft storage | (blood based) 1:12 CPD OR 0.1 mg/mL Angiomax in crystalloid solution  | (blood based) 1:12 CPD OR 0.1 mg/mL Angiomax in crystalloid solution  | (blood based) 1:12 CPD OR 0.1 mg/mL Angiomax in crystalloid solution
Cell saver | 1:12 sodium citrate/CPD  | 1:12 sodium citrate/CPD  | 1:12 sodium citrate/CPD
CPB pump | 50 mg priming dose  | 50 mg priming dose followed by 50 mg/h while recirulating  |
Argatroban

- Bolus to achieve 10 mcg/cc blood volume
- Maintenance drip to replace half q50(cold) and q30(warm)
- Prime- 20 mg

(Metabolized in liver therefore DTI of choice for patients with renal failure)

Closed vs Open
Do you use an open circuit or a closed circuit?

1. Open
2. Closed

Most standard CPB circuits do not require modifications.

- Requisites-
  - Method to collect excess volume from the venous reservoir in citrated collection bags.
  - Pericardial sump (weighted sump) to allow immediate collection of shed blood
  - Method to flash areas of stasis in the circuit
  - Method of reconnecting and recirculating the arterial and venous lines within 10 minutes of separation from CPB.
- **Requisites**-
  - Method to deploy V-V or A-V Modified Ultrafiltration
  - Citrate anticoagulation for collected shed blood (cell saver)
  - Alternate flush solution for harvested vein grafts
    (0.1mg/ml Bivalrudin in NaCl)

Gravlee GP et al., eds. Cardiopulmonary bypass: principles and practice, 2nd ed
Flash areas of Stasis

Filter Bridge

PRONTO Bridge

Recirculation Line

Gravlee GP et al., eds. Cardiopulmonary bypass: principles and practice, 2nd ed
My center uses bloodless cardioplegia when a patient has HIT or HITT?

1. Yes
2. No

“No incident of thrombosis within the oxygenator, arterial line, or cardioplegia line occurred in the study. In 2 patients receiving bivalirudin anticoagulation, clot formation was observed within the venous reservoir, with no adverse consequences.”
A Thrombus in the Venous Reservoir While Using Bivalirudin in a Patient with Heparin-Induced Thrombocytopenia Undergoing Heart Transplantation

Jim K. Wong, MD, Ying Tian, MD, Paul Shuttleworth, BSN, Anthony D. Caffarel, MD, Bruce A. Raiz, MD, and Christina T. Mora-Mangano, MD

(Anesth Analg 2010;111:609–12)
Rear view
Have you ever encounter thrombus in the circuit when using a Direct Thrombin Inhibitor for Anticoagulation?

1. Yes
2. No

Have any of your patients experienced a serious vascular thrombotic event when you used a Direct Thrombin Inhibitor for Anticoagulation for CPB or ECLS?

1. Yes
2. No
Thrombosis during off pump LVAD placement in a patient with heparin induced thrombocytopenia using bivalirudin

Hamdy Awad¹, Richard Bryant¹, Obaid Malik², Galina Dimitrova¹ and Chittoor Bhaskar Sai-Sudhakar³

UF effective removal of 45-69%

Koster Anes & Anal 96:2003

65K dalton Polysufanone
Use of Bivalirudin, a Direct Thrombin Inhibitor, and Its Reversal With Modified Ultrafiltration During Heart Transplantation in a Patient With Heparin-Induced Thrombocytopenia

Michael J. Mann, MD, Elaine Tseung, MD, Mark Ratcliffe, MD, Greg Strautman, MD, Atul De Silva, MD, Teresa DeMarco, MD, Nancy Achorn, CCP, William Moskalik, CCP, and Charles Hoopes, MD

J Heart Lung Transplant 2005;24:222-5

Modified Ultrafiltration

Figure 5. Modified Ultrafiltration circuit
At your center is Ultrafiltration used to reduce Bivalrudin levels

1. V-V Ultrafiltration
2. A-V Modified Ultrafiltration
3. Do not use Ultrafiltration for Bivalrudin removal
- Administer loading dose and start continuous infusion
- Initiate CPB when ACT ≥ 2.5 x baseline
- Use pericardial Sump
- Sequester excess volume in CPD collection bags

DTIs and TAH Implants

Use of Bivalirudin for Anticoagulation during Implantation of Total Artificial Heart
Myke Federman, MD; Douglas Dragomer; Stuart Grant; Brian Reemtsen, MD; Reshma Biniwale, MD
Ronald Reagan UCLA Medical Center, Los Angeles, California

This case was complicated by intra- and postoperative bleeding, which likely was the result of heavy cell saver use. We believe that the cell saver blood may have contained enough bivalirudin to have contributed to a profound coagulopathy that resulted in significant blood loss. (They returned 2,500 ml of washed RBCs from CS)
1. Suspicion index for HIT must remain high in these vulnerable patients
2. With any significant drop in platelet counts, heparin must be stopped and alternative anticoagulation with DTI should be started.
3. If clinically feasible, consider circuit change to a non-heparin-coated circuit, otherwise we recommend close monitoring to further decreases in platelet counts, thrombus formation, embolization, and ischemic changes.
4. Serosurveillance can be considered in critically ill thrombocytopenic patients at high risk.

In a patient with suspected HIT, I would change to a DTI and Switch to a non heparin coated ecmo circuit

1. Yes
2. No
The following types of ECMO Circuits are available at my center

1. Heparin coated circuit
2. Non-heparin coated circuit
3. Both