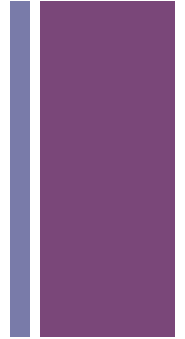


**Mot de passe du 22 novembre 2013 : rein2211**  
**Password, November 22nd, 2013 : rein2211**

**Heparin-Induced  
Thrombocytopenia  
Causing Graft  
Thrombosis and  
Bowel Ischemia post  
Endovascular  
Aneurysm Repair**



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# **Potential conflict of interests**

**Société des sciences vasculaires du Québec (SSVQ)**

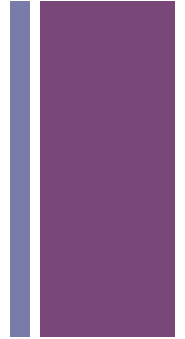
**Journée d'Actualités en sciences vasculaires**

**22 novembre 2013**

**Dr. Abdulmajeed Altoijry, Presenter**

**No conflict of interests to declare**



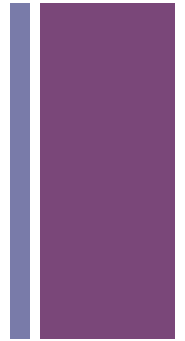


## Introduction

### Heparin

- Commonly used as an anticoagulant.
- Prevention and treatment of thromboembolism.
- Vascular and cardiac surgery procedures.
- Bleeding and thrombosis may occur.

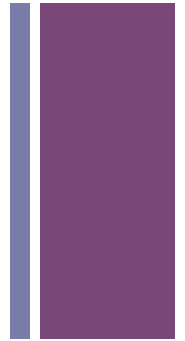




## Introduction. Cont,

- Heparin-induced thrombocytopenia (HIT).
- Known complication of heparin therapy.
- Sudden fall in the platelet count and usually appears a few days after the start of heparin.
- Slight decrease in platelet count (HIT-I)
- Complicated by thrombotic events (HIT-II).
- Vascular procedures; endovascular interventions, ? literature for HIT.





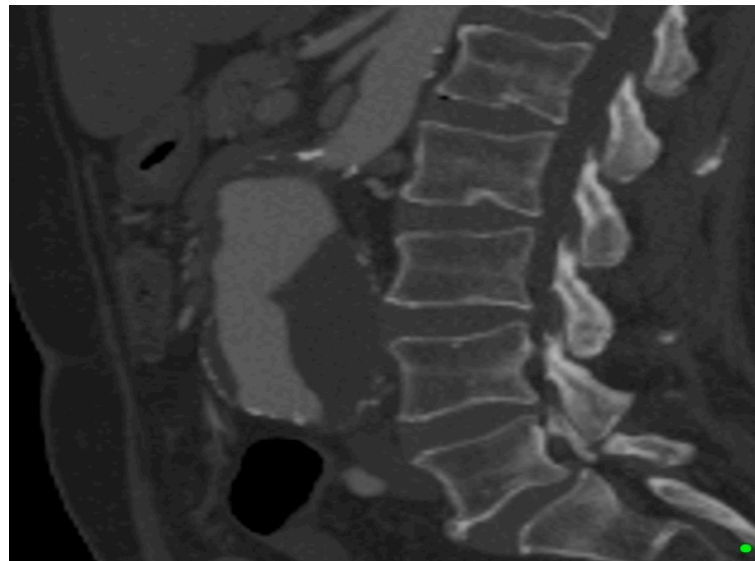
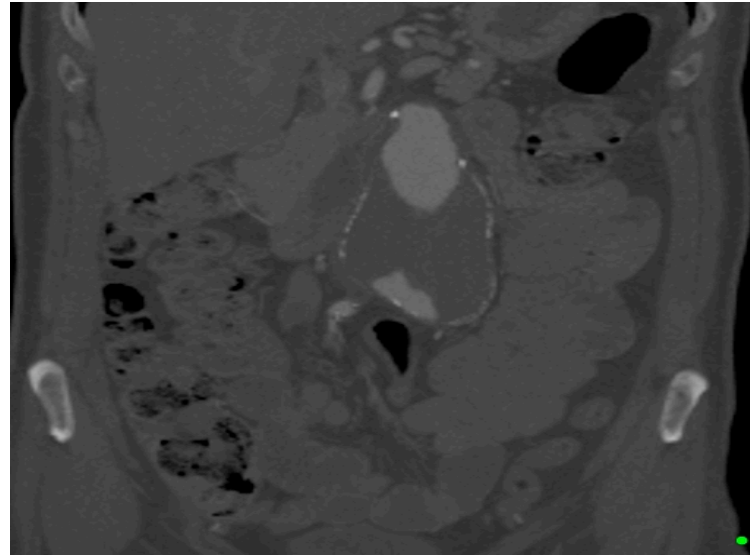
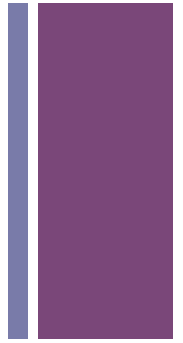
## Case report

- 70-year-old male.
- PMH: HTN, DLP, CAD and prostate carcinoma.
- Elective endovascular repair of an infrarenal abdominal aortic aneurysm.





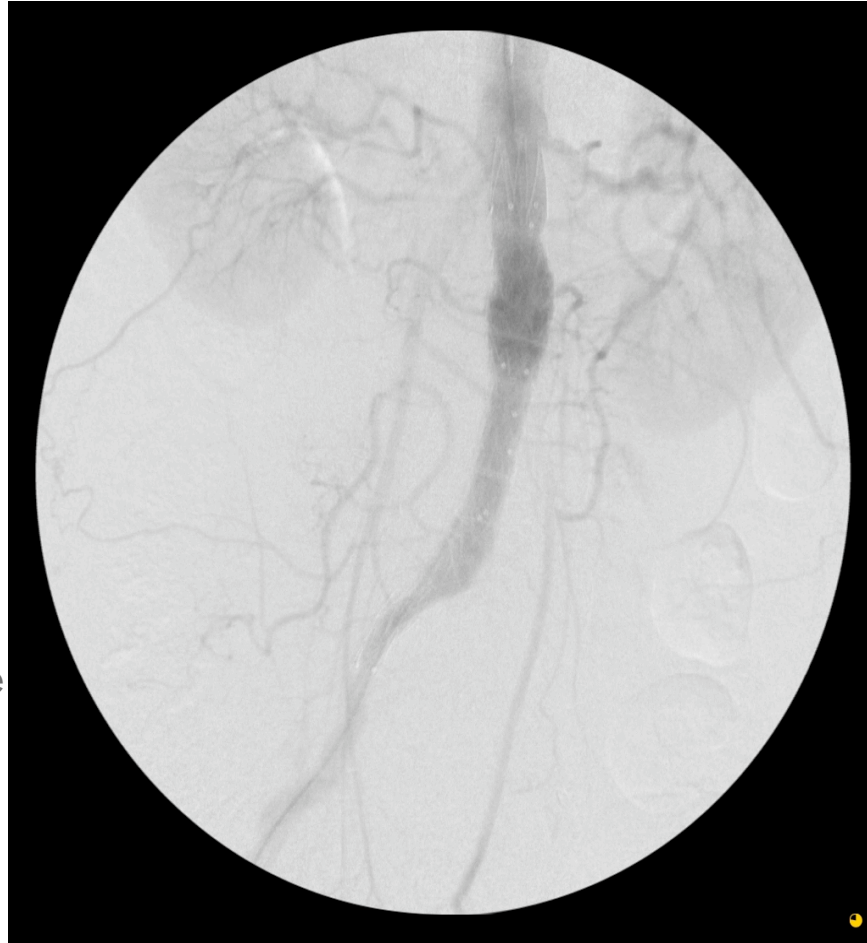
# CT angiogram images (pre-op)

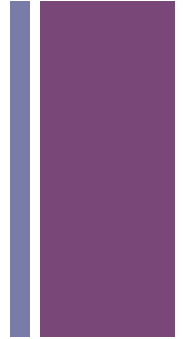




## Case report

- Endurant™, aorto-uni-iliac graft, amplatzer occluder of the left common iliac artery, and a right-to-left femoral-femoral bypass with Dacron graft.
- 5000 IUs of unfractionated heparin (UFH) was given intravenously (intraOP).
- Discharged on post-operative day 1 after an uneventful postoperative course.





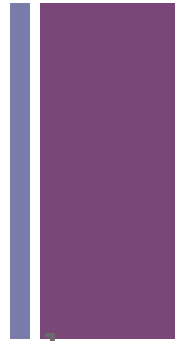
## Case report. Cont,

12 days later:

- Bloody diarrhea and general malaise.
- Abdominal exam was unremarkable; faint pulse in the femoral-femoral bypass graft and distal pedal pulses were not palpable.
- Platelet count was only 18,000.
- Duplex ultrasound: patent right to left femoral-femoral bypass with thrombus visualized throughout the graft.
- ABI: 0.48 and 0.45 for the right and left side respectively.







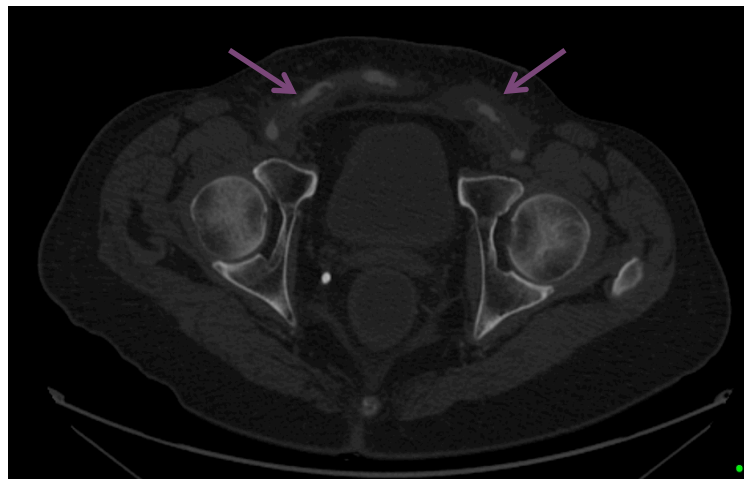
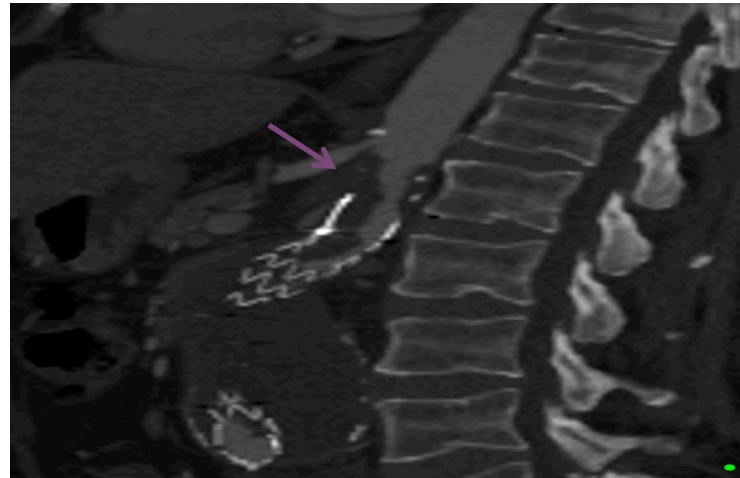
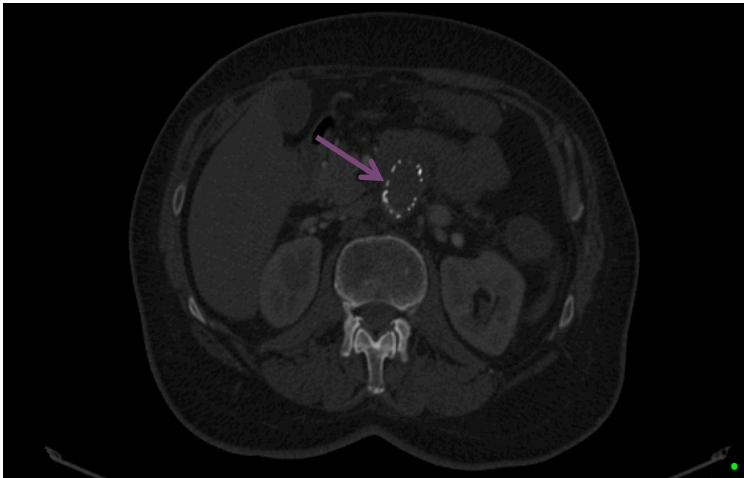
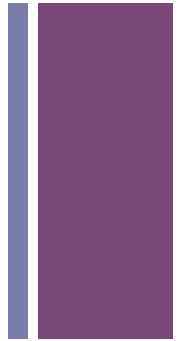
## CTA abdomen and pelvis:

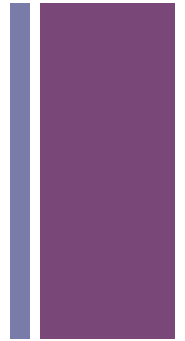
- Thrombosis of the aortic graft including the SMA and the femoral-femoral graft.
- No endoleak, the IMA was thrombosed and the IIAs were patent.
- Edema and thickening of the large bowel wall, no evidence of transmural bowel ischemia..





## CT angiogram images at presentation





- Based on the patient's clinical presentation, CT findings and drop in platelet count.

Dx:

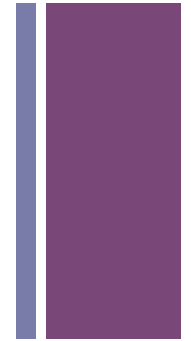
Subclinical bowel ischemia secondary to HIT  
thrombosis of the aortic stent graft and the SMA.





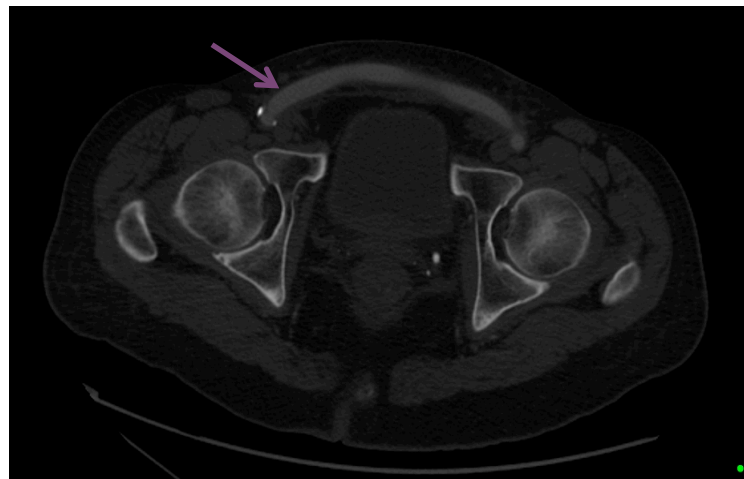
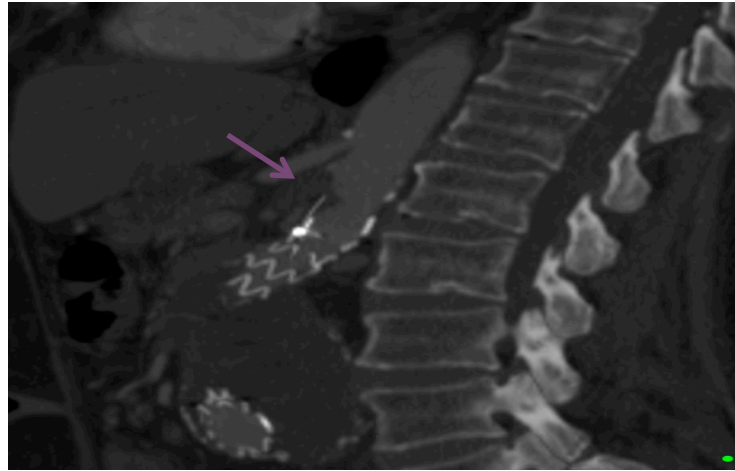
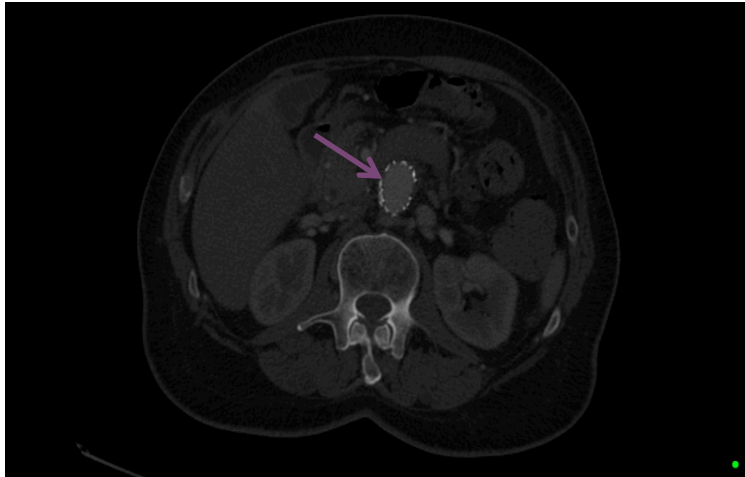
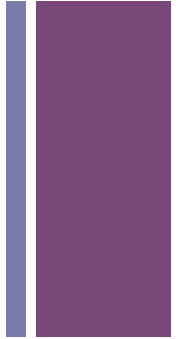
## Treatment course

- Intravenous anticoagulation (argatropan).
- Daily examination and platelet count f/u.
- Dx was confirmed by HIT immunoassay (heparin platelet factor 4).
- PLTs count (50,000 at 5 days and 80,000 at 10 days after presentation).
- Symptoms improved 10 days after presentation.
- Warfarin was started when the platelet count reached 100,000, 3 days of combined anticoagulation therapy.
- D/C home: no symptoms and normal bowel movements.





## 3 months follow up CT angiogram

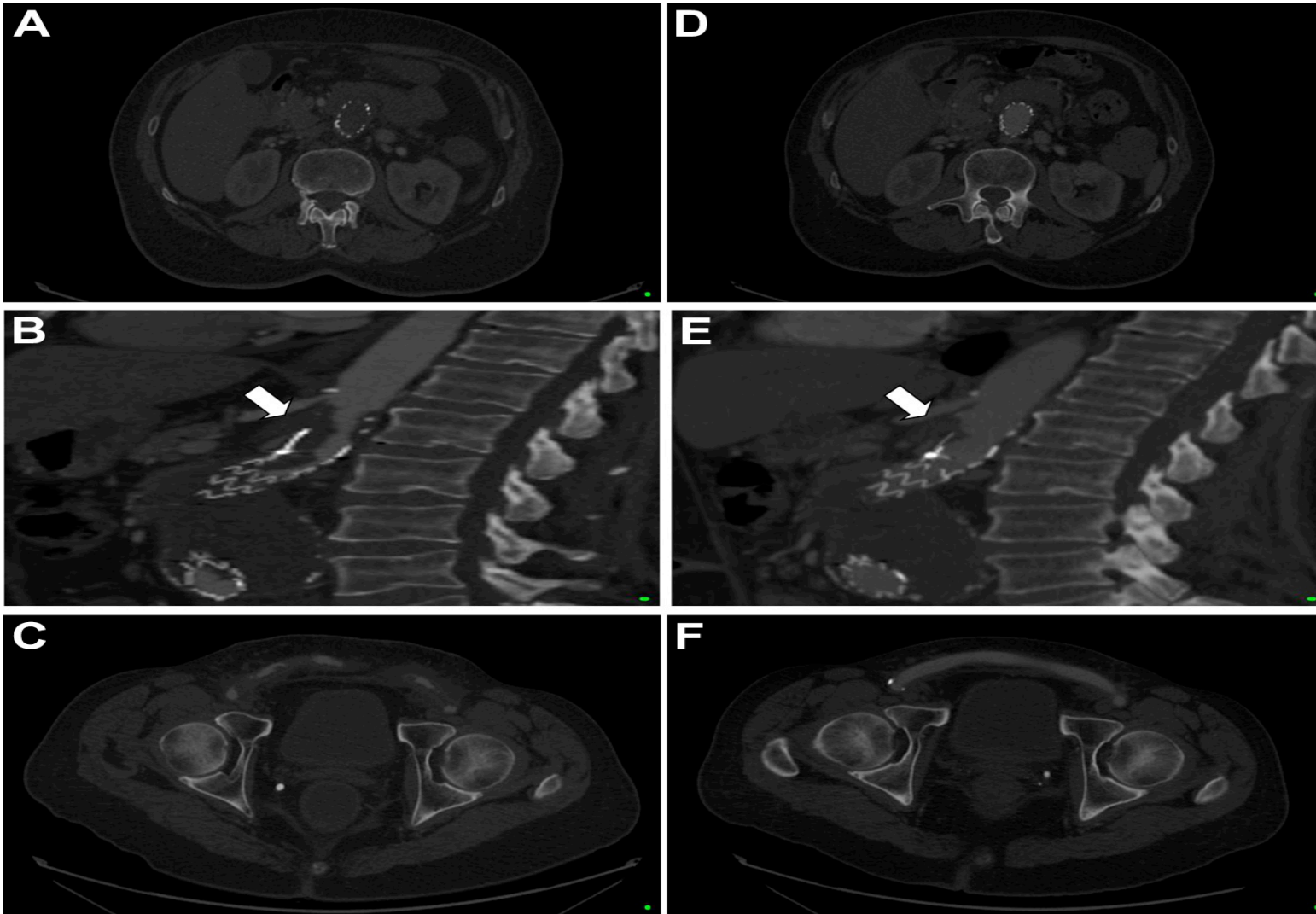
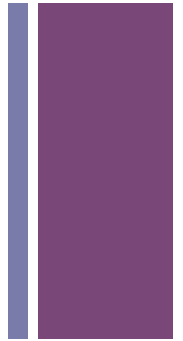


Near complete re-canalization of the endograft and femoral femoral graft and residual thrombus in the SMA origin.





**CT angiogram at presentation (left) and at 3 months F/U (right)**





# Discussion

## Heparin-induced thrombocytopenia

Known complication of heparin therapy usually occurring within the first 10 days after heparin treatment has started.

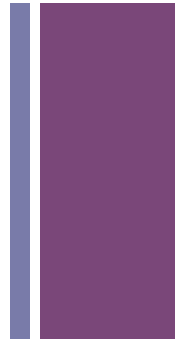
### Type one (HIT-I):

- The most common variant.
- Fall in platelet count within the first two days after initiation of heparin therapy.
- Correct itself with the discontinuation of heparin therapy. Thrombocytopenia, non-immune mechanism secondary to a direct effect of heparin on platelet activation.

### Type two (HIT-II):

- Less common and more aggressive.
- Heparin-associated thrombocytopenia and thrombosis (HITT).
- Immune-mediated disorder associated with the formation of antibodies against the heparin-platelet factor 4 complex.

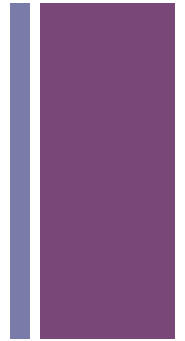




- Overall incidence of HIT-II is 2.6 %.
- 0.2 to 5.0% in patients exposed to heparin > 4 days.
- 0.2 % for those treated with UFH for < 4 days.
- Mortality rate  $\approx$  20% to 30%.
- Limb amputation in 10% to 20% of unrecognized and untreated patients.
- **UFH** rather than (LMWH), **surgical patients** and **female sex**, risk factors for HIT.



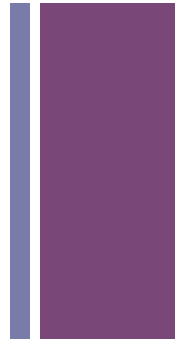




## Vascular surgery

- Not uncommon.
- Exact incidence is not clear, variation in the literature (as confirmed by HIT assay).
- Low as 1.9% and high as 21% in others.
- Postoperative thrombocytopenia could be due to platelet adherence to the graft material.
- **To date**, HIT secondary to EVAR is uncommon with unknown incidence.
- Five cases of thrombosis associated HIT-II/ three case reports.
- All of these HIT-II cases presented with either acute lower limb ischemia or lower limb deep vein thrombosis.
- Endograft thrombosis and mesenteric arterial thrombosis ischemia have not been previously reported in the literature.





## The primary finding for diagnosis

- Fall in the platelet count of more than 50%, within two weeks after using heparin therapy.

## Clinical features

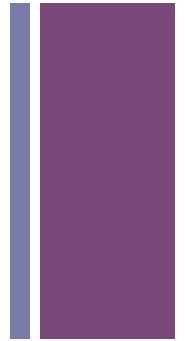
- Venous thrombosis and or embolism, including DVT/PE.
- Arterial thrombosis involving aorta and major limb arteries, resulting in limb ischemia.
- After endovascular procedures, also rarely manifest as thrombotic complication at the site of intervention.





## Laboratory tests

- Enzyme-linked immunosorbent assay
- Platelet  $^{14}\text{C}$  serotonin release assay
- Heparin-induced platelet aggregation

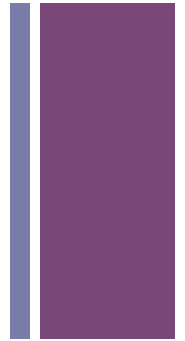




## Treatment

- Immediate cessation of any sources of heparin.
- Replacement with an anticoagulant therapy (does not cross-react with HIT antibodies).
  - Danaparoid, lepirudin, fondaparinux, and argatroban.
  - Warfarin should not be started:
    - Thrombocytopenia resolves.
    - Anticoagulation with one of the alternatives.
- LMWH **should not** be substituted for UFH after HIT develops because of frequent **cross-reactivity** with HIT antibodies.

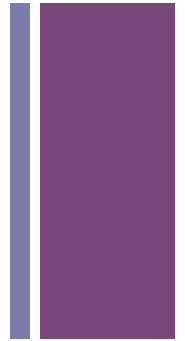




## Home Message!!

Unusual thromboembolic events and lack of response to heparin with a Hx of heparin exposure should raise suspicion of HIT; repeat platelet counts should be done along with other serologic tests.





## Conclusion

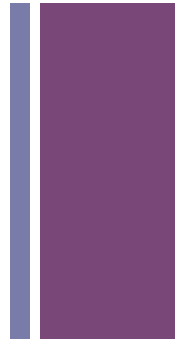
- Heparin-induced thrombocytopenia is a rare but potentially limb- and life-threatening adverse reaction seen in patients exposed to heparin.
- Patients undergoing vascular and endovascular procedures in which large dose of heparin are used are at risk.
- A high index of suspicion is required in order to diagnose it and initiate proper therapy to prevent serious thrombotic complications.





## References

- 1. Linkins LA, Dans AL, Moores LK, Bona R, Davidson BL, Schulman S, et al. Treatment and prevention of heparin-induced thrombocytopenia: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e495S-530S.
  - 2. Chuter TAM, Pak LK, Gordon RL, Reilly LM, Messina LM. Heparin-induced thrombocytopenia and graft thrombosis following endovascular aneurysm repair. *J Endovasc Ther*. 2003;10(6):1087-90.
  - 3. Kolluri R, Rocha-Singh K, Sarac T, Bartholomew JR. Heparin-induced thrombocytopenia with thrombosis after endovascular aneurysm repair. *Vascular and endovascular surgery*. 2009;43(1):89-92.
  - 4. Christiane Campolina Furquim Werneck AL, Thomas F. Lindsay. Heparin-induced thrombocytopenia and endovascular procedures: report of two cases. *Jornal Vascular Brasileiro*. 2009;8(3):4.
  - 5. Chong BH, Castaldi PA. Platelet proaggregating effect of heparin: possible mechanism for non-immune heparin-associated thrombocytopenia. *Australian and New Zealand journal of medicine*. 1986;16(5):715-6.
  - 6. Martel N, Lee J, Wells PS. Risk for heparin-induced thrombocytopenia with unfractionated and low-molecular-weight heparin thromboprophylaxis: a meta-analysis. *Blood*. 2005;106(8):2710-5.
  - 7. Warkentin TE, Sheppard JA, Sigouin CS, Kohlmann T, Eichler P, Greinacher A. Gender imbalance and risk factor interactions in heparin-induced thrombocytopenia. *Blood*. 2006;108(9):2937-41.
  - 8. Smythe MA, Koerber JM, Mattson JC. The incidence of recognized heparin-induced thrombocytopenia in a large, tertiary care teaching hospital. *Chest*. 2007;131(6):1644-9.
  - 9. Lewis BE, Wallis DE, Berkowitz SD, Matthai WH, Fareed J, Walenga JM, et al. Argatroban anticoagulant therapy in patients with heparin-induced thrombocytopenia. *Circulation*. 2001;103(14):1838-43.
  - 10. Lubenow N, Hinz P, Thomaschewski S, Lietz T, Vogler M, Ladwig A, et al. The severity of trauma determines the immune response to PF4/heparin and the frequency of heparin-induced thrombocytopenia. *Blood*. 2010;115(9):1797-803.
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- 11. Jackson MR, Gillespie DL, Chang AS, Longenecker EG, Peat RA, Alving BM. The incidence of heparin-induced antibodies in patients undergoing vascular surgery: A prospective study. *J Vasc Surg.* 1998;28(3):439-44.
- 12. Calaitges JG, Liem TK, Spadone D, Nichols K, Silver D. The role of heparin-associated antiplatelet antibodies in the outcome of arterial reconstruction. *J Vasc Surg.* 1999;29(5):779-85.
- 13. Elalamy I, Lecrubier C, Horellou MH, Conard J, Samama MM. Heparin-induced thrombocytopenia: laboratory diagnosis and management. *Ann Med.* 2000;32:60-7.
- 14. Sheridan D, Carter C, Kelton JG. A Diagnostic-Test for Heparin-Induced Thrombocytopenia. *Blood.* 1986;67(1):27-30.
- 15. Mureebe L, Silver D. Heparin-induced thrombocytopenia: pathophysiology and management. *Vascular and endovascular surgery.* 2002;36(3):163-70.
- 16. Gupta V, Tanvir R, Garg A, Gaikwad SB, Mishra NK. Heparin-induced thrombocytopenia in a case of endovascular aneurysm coiling. *AJNR American journal of neuroradiology.* 2007;28(1):155-8.
- 17. Sakai K, Oda H, Honsako A, Takahashi K, Miida T, Higuma N. Obstinate thrombosis during percutaneous coronary intervention in a case with heparin-induced thrombocytopenia with thrombosis syndrome successfully treated by argatroban anticoagulant therapy. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions.* 2003;59(3):351-4.
- 18. Warkentin TE, Greinacher A, Koster A, Lincoff AM, American College of Chest P. Treatment and prevention of heparin-induced thrombocytopenia: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest.* 2008;133(6 Suppl):340S-80S.
- 19. Hirsh J, Heddle N, Kelton JG. Treatment of heparin-induced thrombocytopenia - A critical review. *Arch Intern Med.* 2004;164(4):361-9.



*Thank You*

*Merci*

