# Peri-Operative Management of Combined Factor V and Factor VIII Deficiency

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# Medical history

- 33-year old male
- Past history of rheumatic fever
- Severe mitral stenosis
  - Status post mitral valve replacement
  - Heart failure and severe pulmonary hypertension
- Factor V and Factor VIII Deficiency
  - Factor V level 11 U/dL
  - Factor VIII level 9 U/dL

# Additional patient history

- Originally had valve replacement in India in 2008
- Required massive plasma transfusion
- Serious clinical condition at time of admission to KU

# Combined Factor V and Factor VIII Deficiency

- Prevalence of 1:1,000,000
- Middle Eastern or Indian descent
- Autosomal recessive mutation in LMAN1 or MCFD2 genes
  - Involved in intracellular transportation and secretion of Factor V and VIII
- Most patients experience only mild bleeding
- Treatment: Fresh frozen plasma (FFP), Factor VIII, desmopressin, platelets

# Goal

- Replete Factors V and VIII to hemostatic level (>30 U/dL)

# Trial of Fresh Frozen Plasma Transfusion

- Six units of FFP transfused in eight hours
- Factor V rose from 11 U/dL to 17 U/dL
- Factor VIII rose from 9 U/dL to 23 U/dL

# Trial of Fresh Frozen Plasma Transfusion

- Resulted in significant fluid overload
- Factor levels deemed inadequate for surgical hemostasis

# Trial of Therapeutic Plasma Exchange (TPE)

- 1.0 volume TPE with 15 units FFP as the replacement fluid
- Factor V rose from 11U/dL to 48 U/dL
- Adequate Factor V level and stable hemodynamics - kept euvolemic

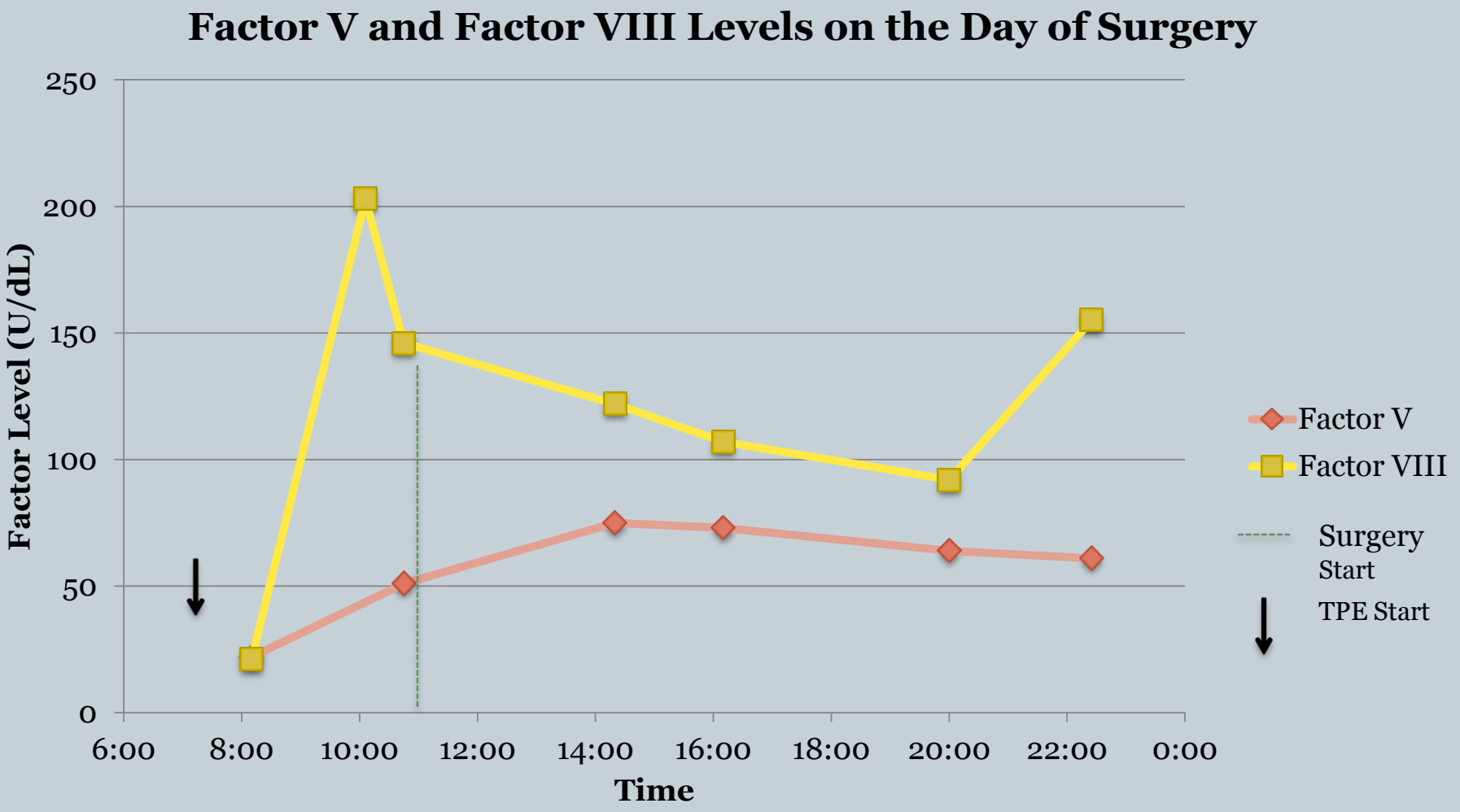
# Trials of Factor VIII Replacement

- Trial of recombinant antihemophilic factor (Helixate), 4000 units
  - Factor VIII levels rose from 9 U/dL to 20 U/dL
- Trial of human monoclonal purified antihemophilic factor (HEMOFIL-M), 4000 units
  - Factor VIII rose to 98 U/dL

# Treatment Strategy

- Daily TPE with FFP before, during, and after surgery
- Factor VIII replacement with HEMOFIL-M

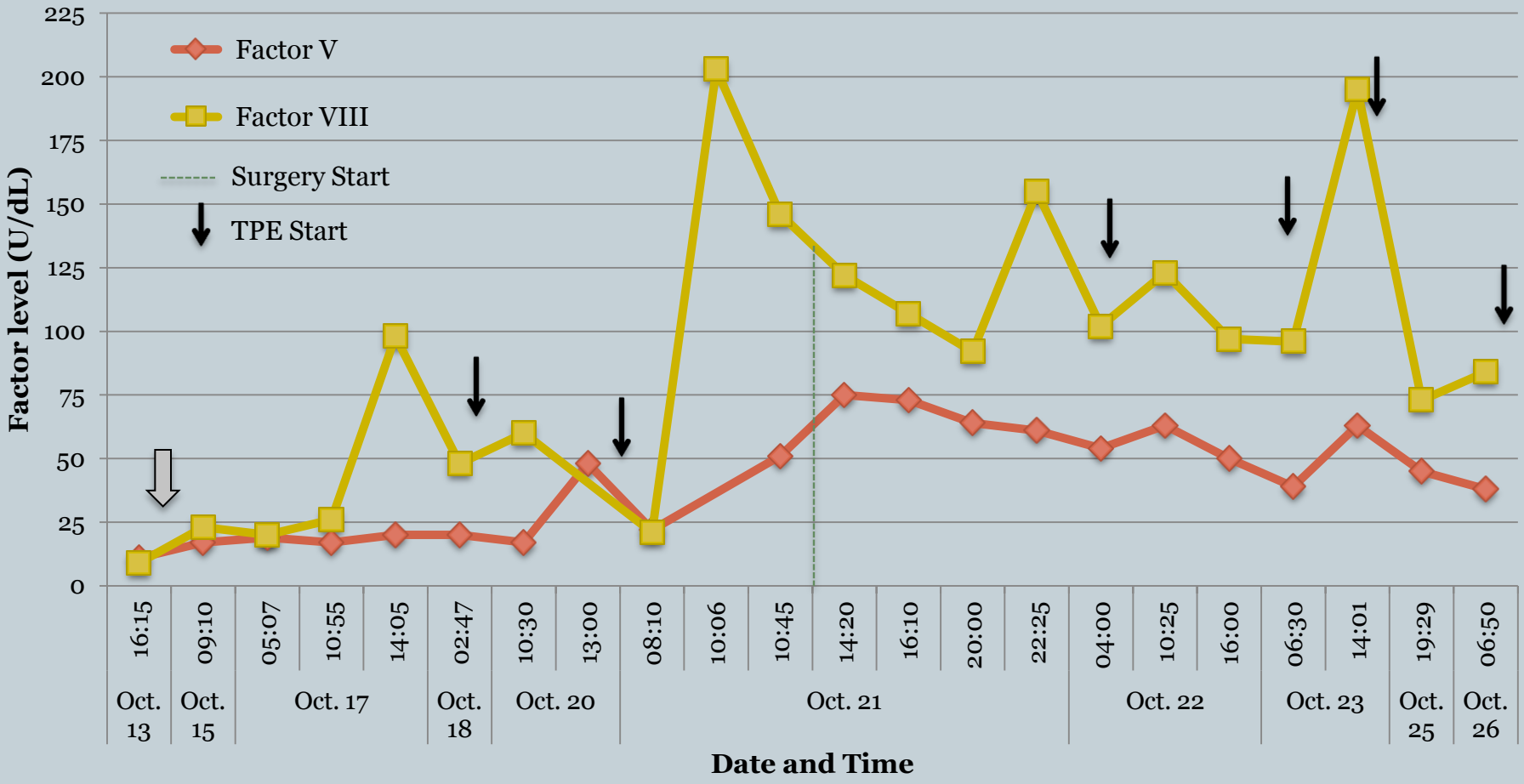
# Peri-Operative Course



# Peri-Operative Course

- No increased or unexpected bleeding during surgery
- Minimal chest tube drainage on post-operative day 1
- Patient discharged on the 7$^{th}$ post-operative day with adequate cardiac and pulmonary functions
- No hemorrhagic complications to date

# Peri-Operative Course



# Use of TPE with FFP in Similar Cases

- Patient with Factor V and Factor VIII deficiency treated with TPE with FFP
- Patient with acquired prothrombin deficiency with an inhibitor, due to antiphospholipid syndrome
- Four patients with severe Factor XI deficiency and bleeding prior to surgery
- Two patients with Factor V deficiency prior to surgery
- Patients with strong coagulation factor inhibitors

# Summary

- Peri-operative management of Factor V and Factor VIII deficiency with aggressive TPE with FFP as the replacement fluid
- The patient successfully tolerated a difficult repeat mitral valve replacement with minimal blood loss

# Conclusion

- TPE with FFP is a promising therapeutic modality for patients with coagulation factor deficiencies for which a specific factor concentrate is not available

# References


- Spreafico M, Peyvandi F. Combined FV and FVIII deficiency. *Haemophilia* 2008;**14**:1201–8. doi:10.1111/j.1365-2516.2008.01845.x
- Zheng C, Liu H-H, Yuan S, *et al.* Molecular basis of LMAN1 in coordinating LMAN1-MCFD2 cargo receptor formation and ER-to-Golgi transport of FV/FVIII. *Blood* 2010;**116**:5698–706. doi:10.1182/blood-2010-04-278325
- Scott E, Puca K, Heraly J, *et al.* Evaluation and comparison of coagulation factor activity in fresh-frozen plasma and 24-hour plasma at thaw and after 120 hours of 1 to 6°C storage. *Transfusion* 2009;**49**:1584–91. doi:10.1111/j.1537-2995.2009.02198.x
- Wang A, Liu X, Wu J, *et al.* Combined FV and FVIII deficiency (F5F8D) in a Chinese family with a novel missense mutation in MCFD2 gene. *Haemophilia* 2014;**20**:e436–8. doi:10.1111/hae.12549
- Kolde H. *Haemostasis*. 2nd ed. Basel, Switzerland: Pentapharm Ltd 2004.
- Sallah AS, Angchaisuksiri P, Roberts HR. Use of plasma exchange in hereditary deficiency of factor V and factor VIII. *Am J Hematol* 1996;**52**:229–30. doi:10.1002/(SICI)1096-8652(199607)52:3<229::AID-AJH19>3.0.CO;2-A
- Alsammak MS, Ashrani AA, Winters JL, *et al.* Therapeutic Plasma Exchange (TPE) for Perioperative Management of Congenital Factor XI Deficiency Patients. *J Clin Apher* 2015;**30**:61–133. doi:10.1002/jca
- Baron BW, Mittendorf R, Baron JM. Presurgical plasma exchange for severe factor V deficiency. *J Clin Apher* 2001;**16**:29–30.
- Rech J, Hueber AJ, Leipe J, *et al.* A case report of plasma exchange, steroids, mycophenolate mofetil and cyclophosphamide in acquired factor VIII inhibitors. *Ther Apher Dial* 2008;**12**:406–8. doi:10.1111/j.1744-9987.2008.00618.x
- Valentino LA, Cooper DL, Goldstein B. Surgical experience with rFVIIa (NovoSeven) in congenital haemophilia A and B patients with inhibitors to factors VIII or IX. *Haemophilia* 2011;**17**:579–89. doi:10.1111/j.1365-2516.2010.02460.x

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