Hemophilia Case Study

GHEST Symposium 2019

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Objectives

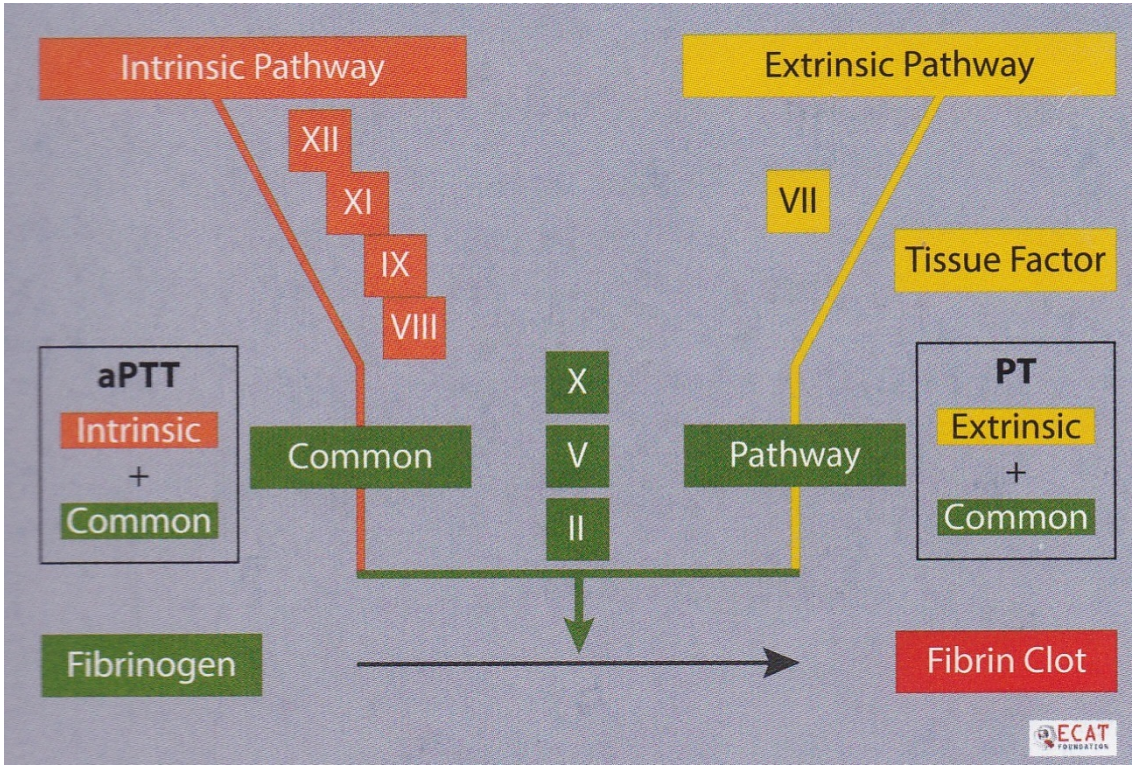
- Patient case
- Coagulation review
- Review hemophilia theory
- Treatment

Patient case:

- July 24th 96 year old male visited ER for an arm injury and significant bruising
- Laboratory test results:
  - HGB 90
  - PTT 76
  - INR normal
- what could be going on with this patient?

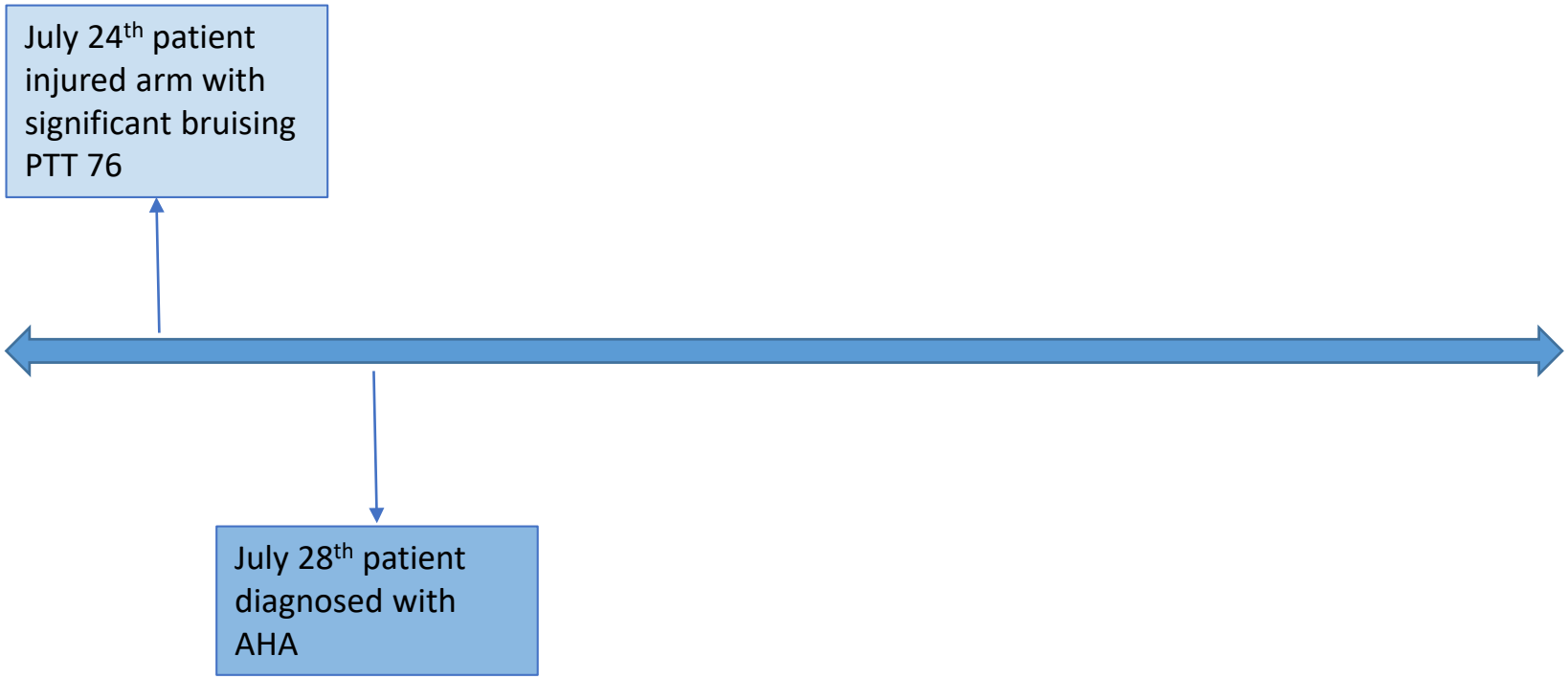
Coagulation review

- Our body maintains hemostasis through coagulation
- Laboratory tests used to monitor are prothrombin time (PT), activated partial thromboplastin time (PTT), Thrombin time (TCT)



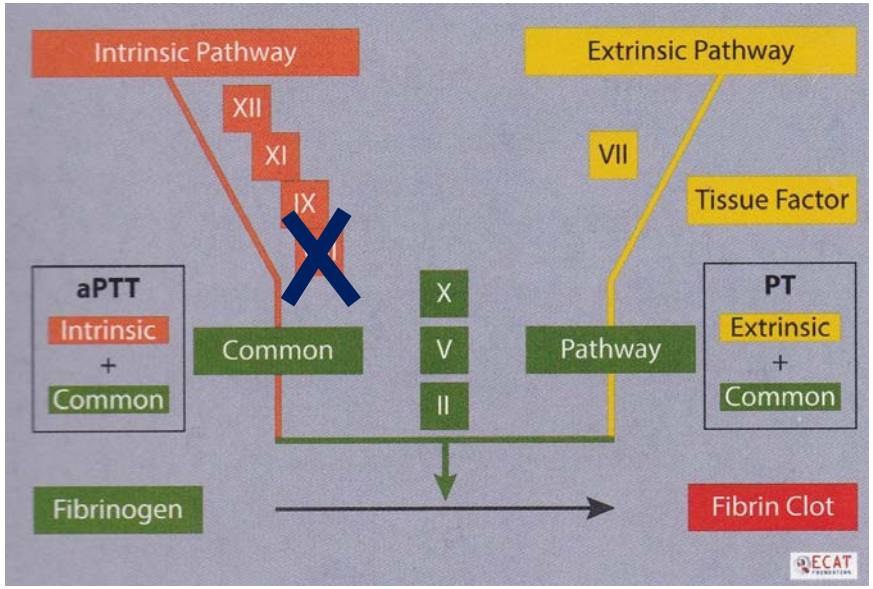
Patient Case

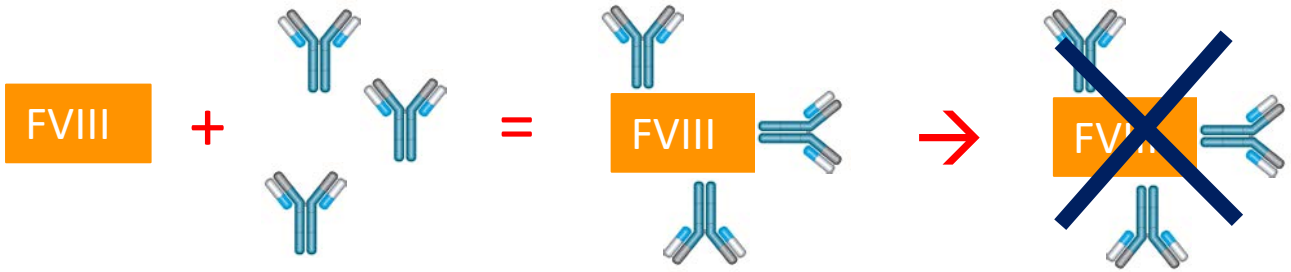
- Prior to his ER visit he had 3 months of skin bruising and visits to multiple physicians
- The elevated PTT of 76 was tested further
  - Factor VIII assay: <1% ↓
  - FVIII inhibitor: ~300 BU ↑
  - Thrombin time: 22 N
  - Fibrinogen: 3.0 g/L N
- Patient was admitted July 28th for diagnosis of Acquired Hemophilia A


July 24th patient injured arm with significant bruising PTT 76
July 28th patient diagnosed with AHA

Acquired Hemophilia A (AHA)

- AHA is a rare autoimmune disease caused by autoantibodies inhibiting the function of FVIII[1]
- Partially or completely neutralize the activation of FVIII
- Characterized by spontaneous bleeding in patients with no previous history

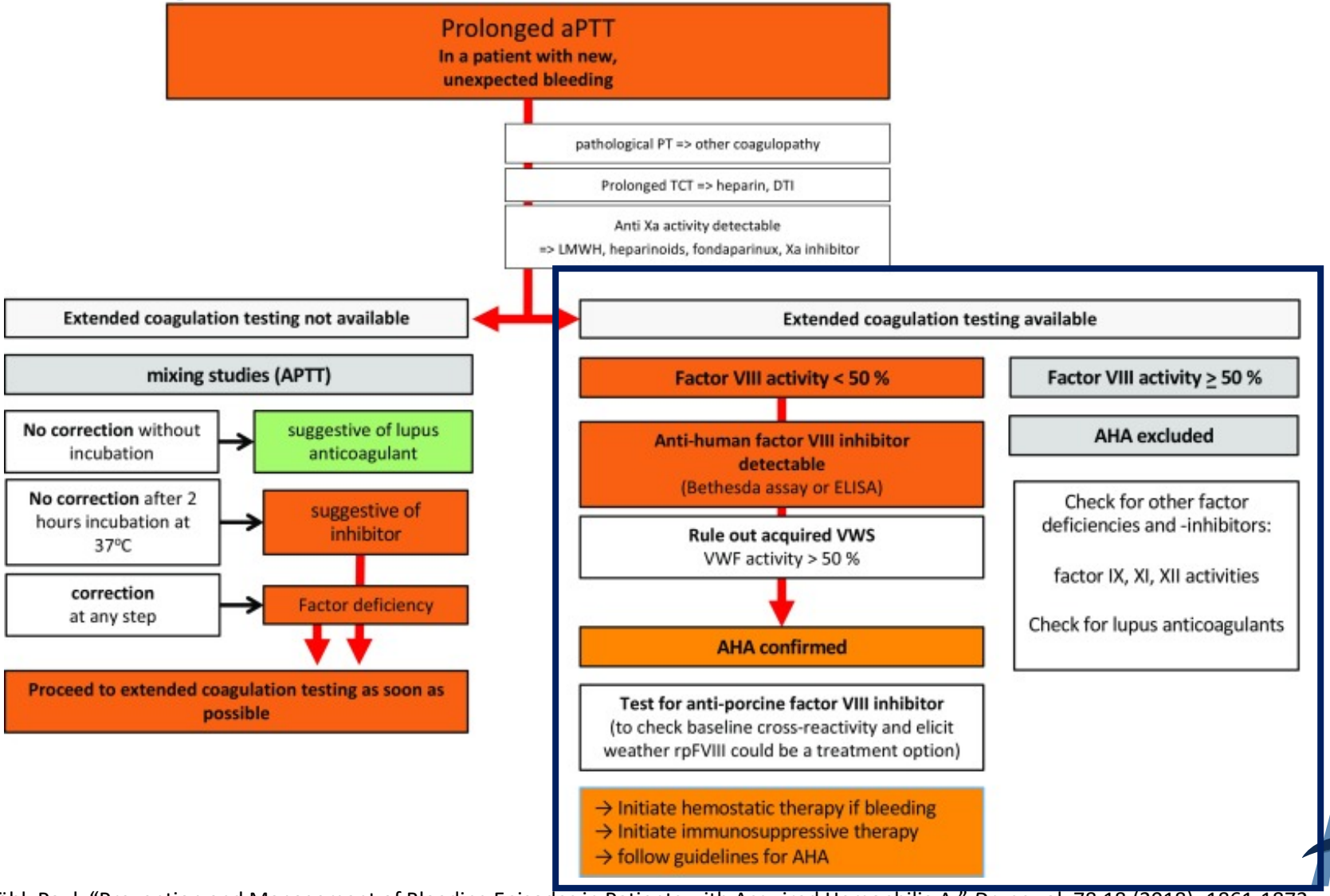




Diagnosis of AHA

"EACH2 registry showed 37% of patients were definitely diagnosed within 1 day and 26% within 1 week"[1]

Diagnosis of AHA



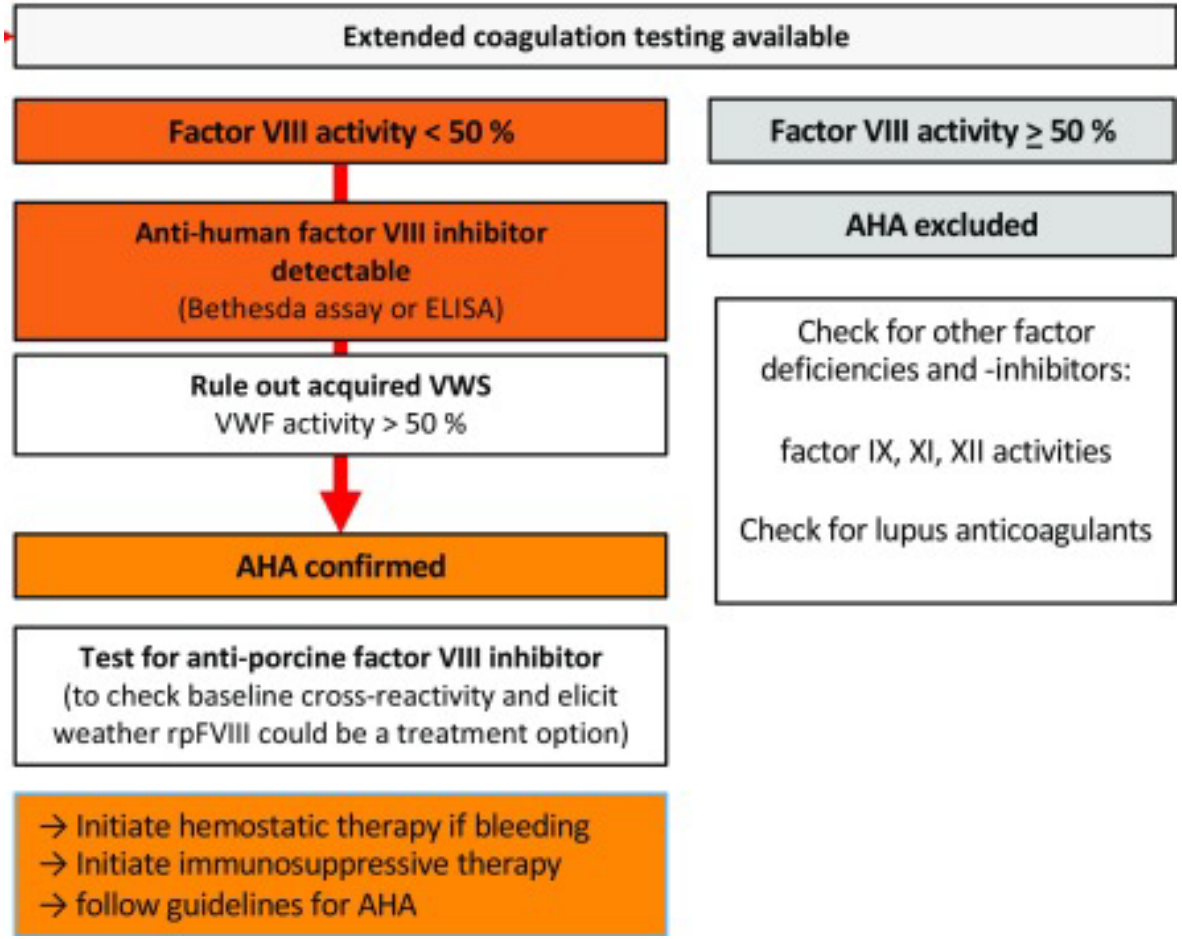
Knöbl, Paul. "Prevention and Management of Bleeding Episodes in Patients with Acquired Hemophilia A." *Drugs* vol. 78,18 (2018): 1861-1872.

Diagnosis of AHA

Recap Patient results:

Factor VIII: <1%

Factor VIII inhibitor: ~300 BU



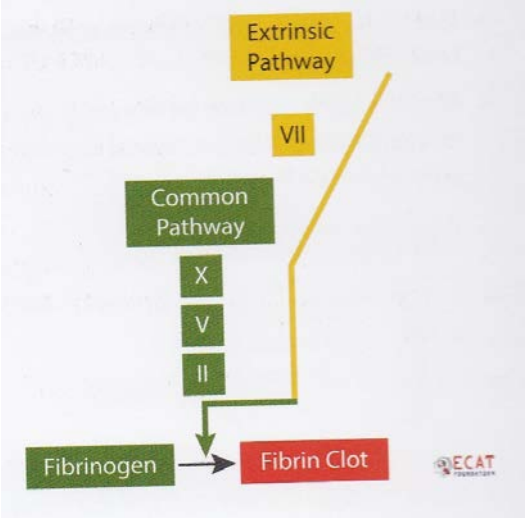
Knöbl, Paul. "Prevention and Management of Bleeding Episodes in Patients with Acquired Hemophilia A." *Drugs* vol. 78,18 (2018): 1861-1872.

Diagnosis of the patient:

- Spontaneous abnormal PTT and bruising
- Patient laboratory tests correspond with characteristics of AHA
- Patient corresponds with underlying disease and demographical pattern
  - Elder patient who was diagnosed 1 year ago with an autoimmune disease Bullous Pemphigoid

How will we treat this patient?

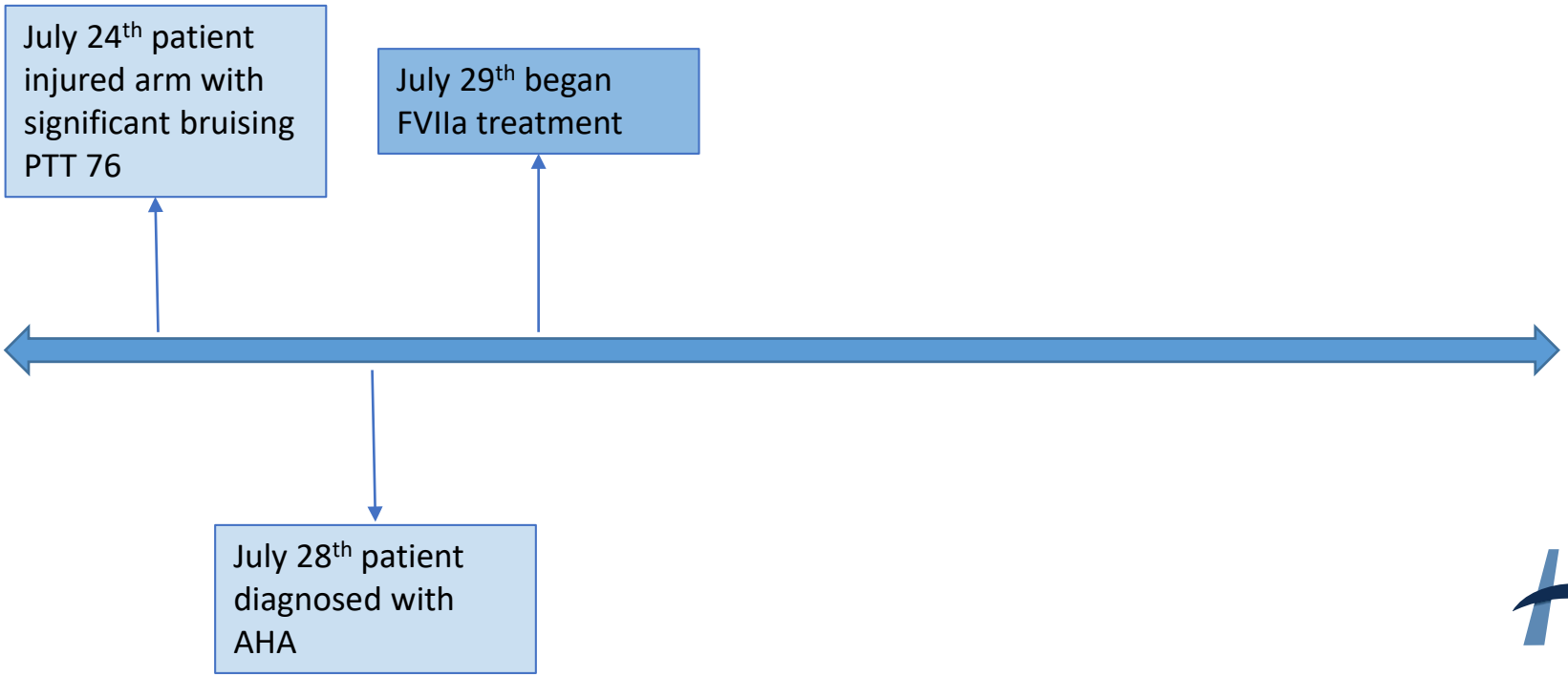
Treatment options[1]



- By passing agents
  - Recombinant human activated factor FVII
  - Activated prothrombin complex concentrates
- FVIII replacement therapy can be used in patients with low titre inhibitor levels
- Recombinant porcine FVIII concentrate

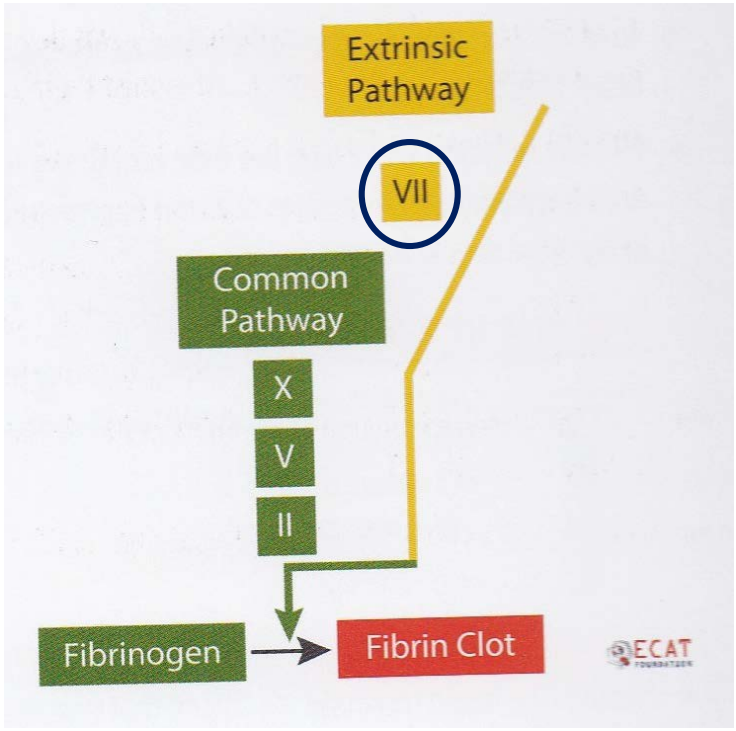
Treating AHA

- Patient began recombinant human activated FVII treatment on July 29th
  - initial dose of 5 mg
  - Continued doses of 5 mg every 3h



Factor VII

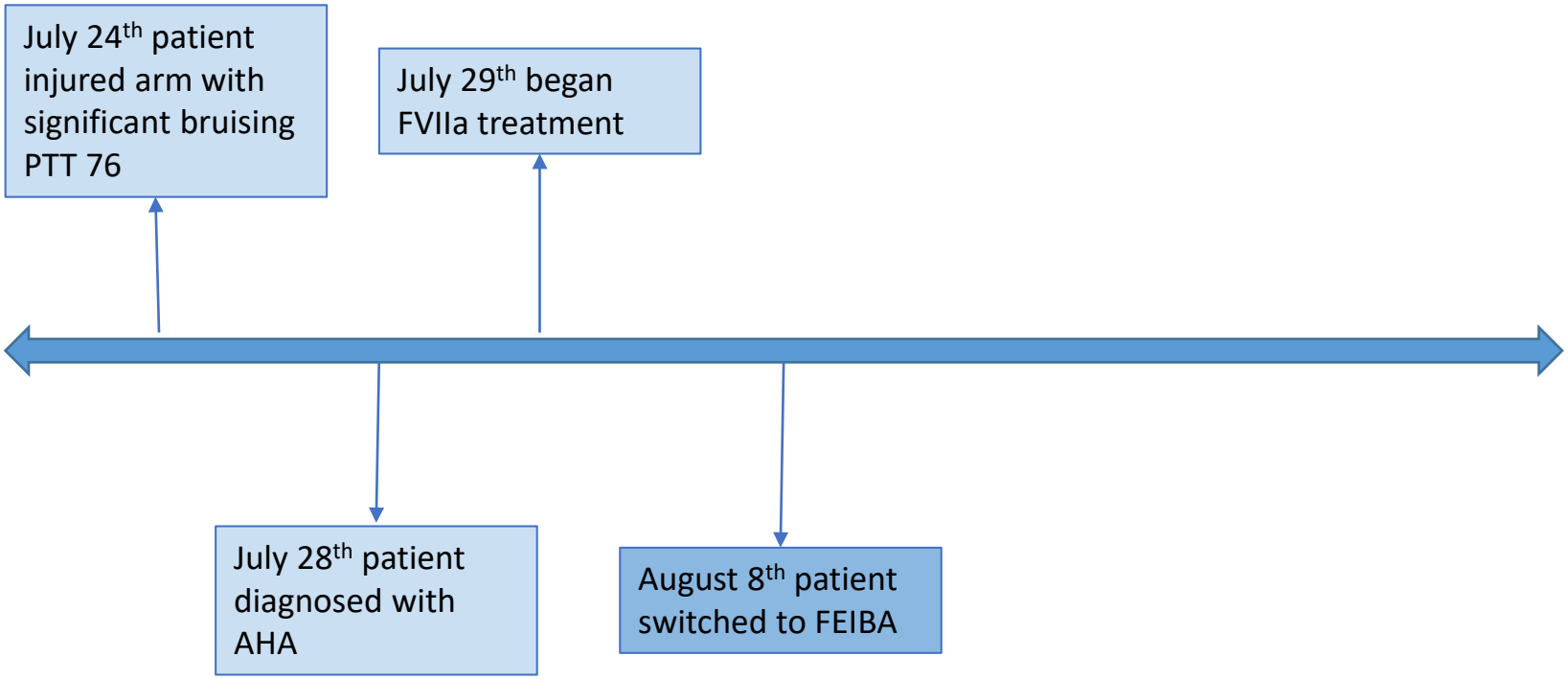
- First approach is bypassing agents
- Recombinant Human Activated FVII
  - Niastase
- Half life of FVII is short (3-6h) therefore doses are frequent
- There is no conventional laboratory tests to monitor treatment



Cost: ~ $1,246 per mg

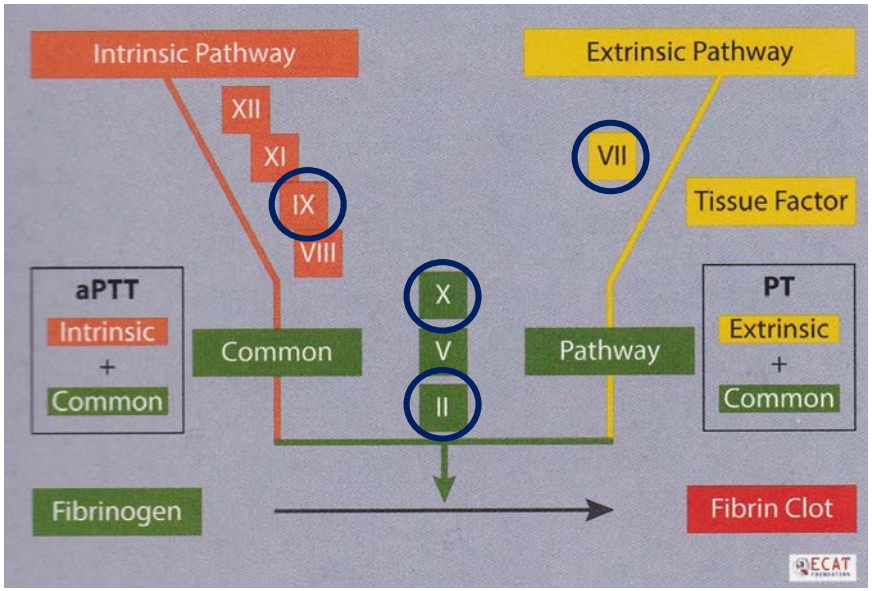
Patients total

- FVII doses of 5 mg every 3h July 29th – August 8th
  - 45 doses
- Total cost: ~ $280,350


July 24th patient injured arm with significant bruising PTT 76
July 29th began FVIIa treatment
July 28th patient diagnosed with AHA
August 8th patient switched to FEIBA

FEIBA

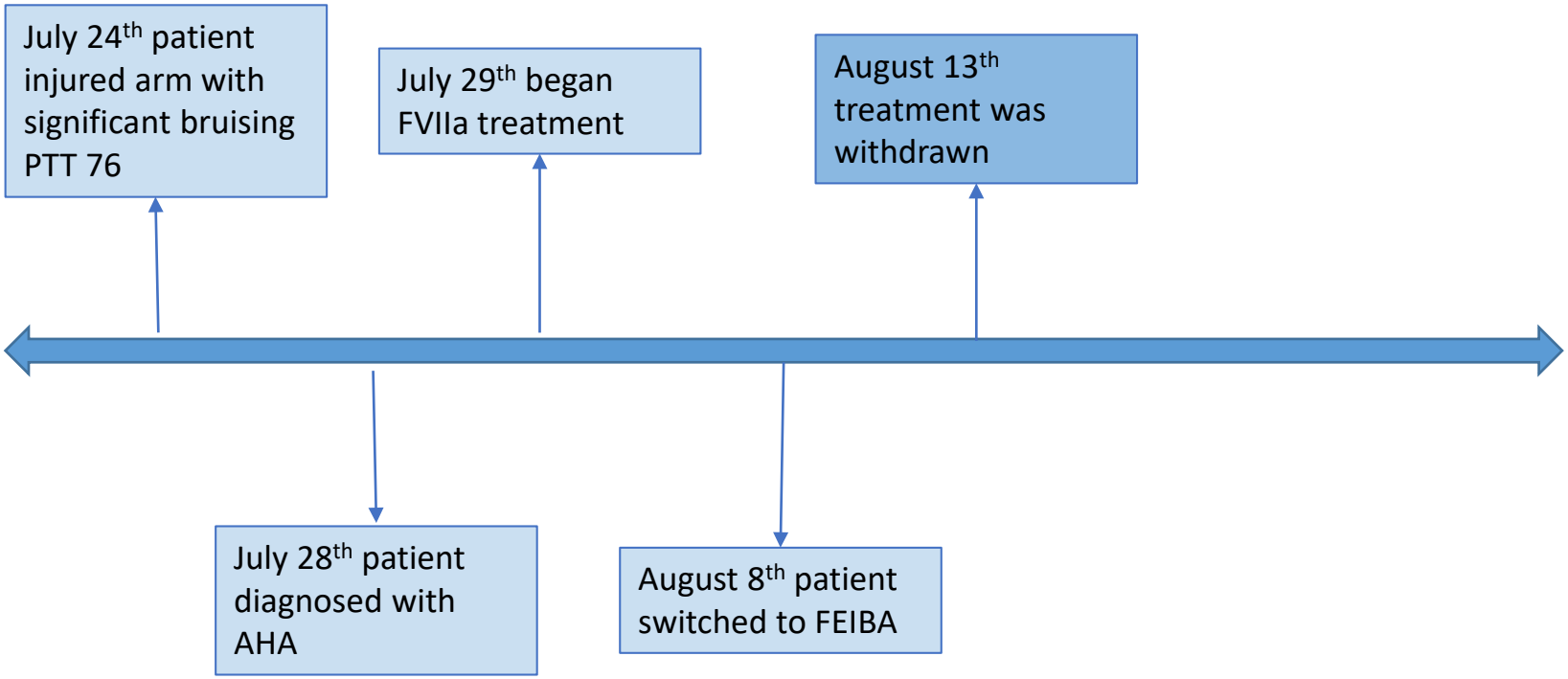
- Activated Prothrombin Complex concentrate
- Mostly contains activated FVII and activated clotting factors II, IX and non-activated X
- Similar response to Niastase (recombinant human activated FVII)
- Typical dosage is 70U/Kg every 8h
- Monitor with PPLT count, fibrinogen, d-dimer



Cost: ~ $1.95 / IU

Patients total

- FVII doses of 5 mg every 3h July 29th – August 8th
  - 45 doses
- Total cost: $280,350
- Patient was switched to FEIBA August 8th until treatment was withdrawn August 13th
- He received 3400-4500 IU every 8h
  - 14 doses
- Total costs: ~$108,640 + $280,350 = $388,990!


July 24th patient injured arm with significant bruising PTT 76
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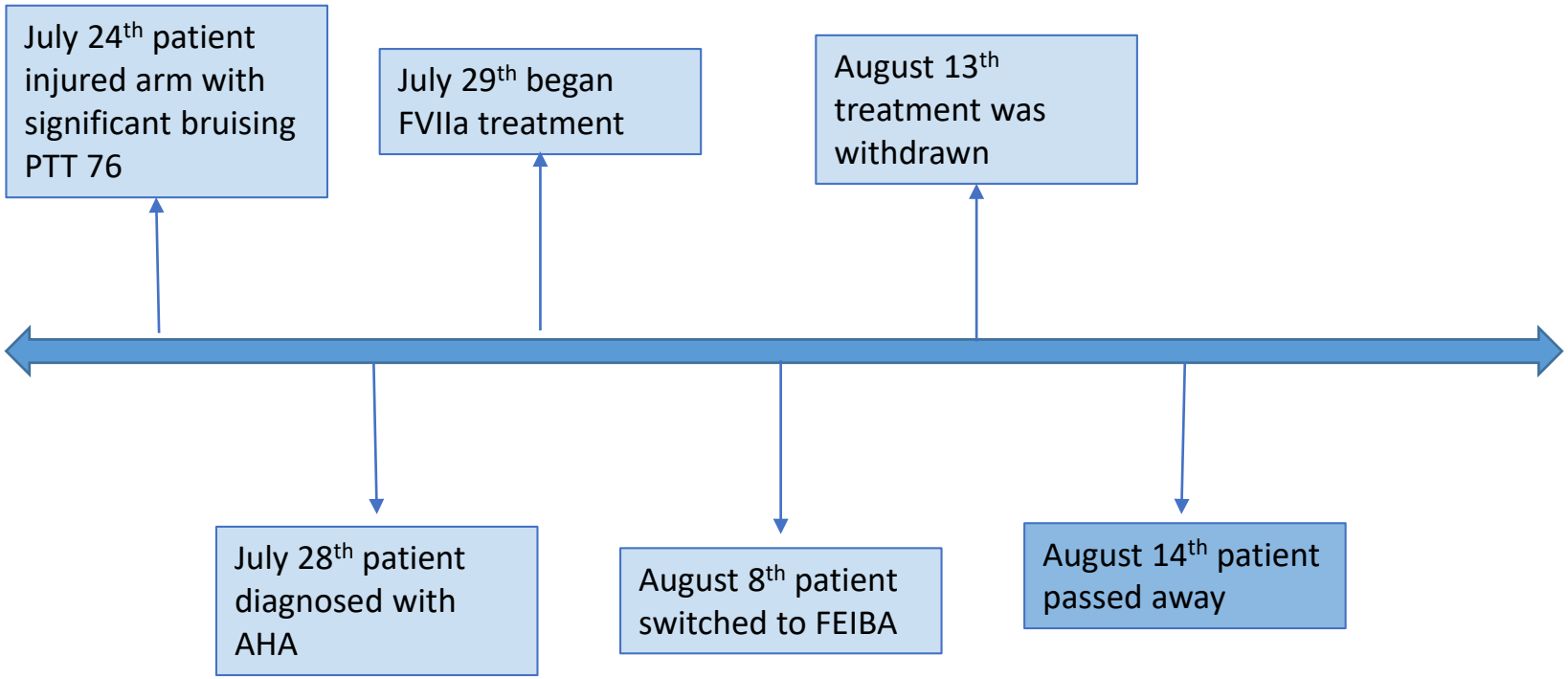
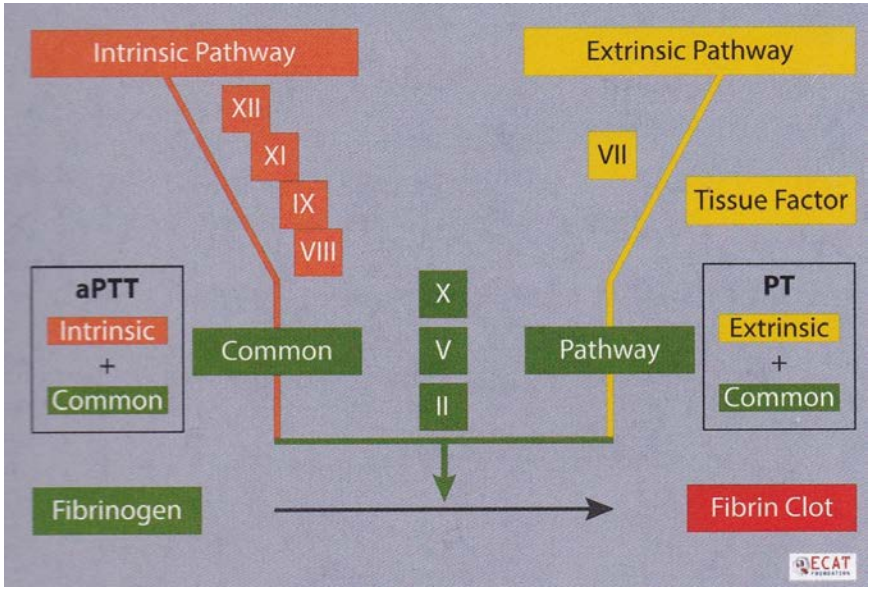
Patient Case

- Patient passed away August 14th



Looking back

- There is an interesting trend of the patients fibrinogen level and thrombin time

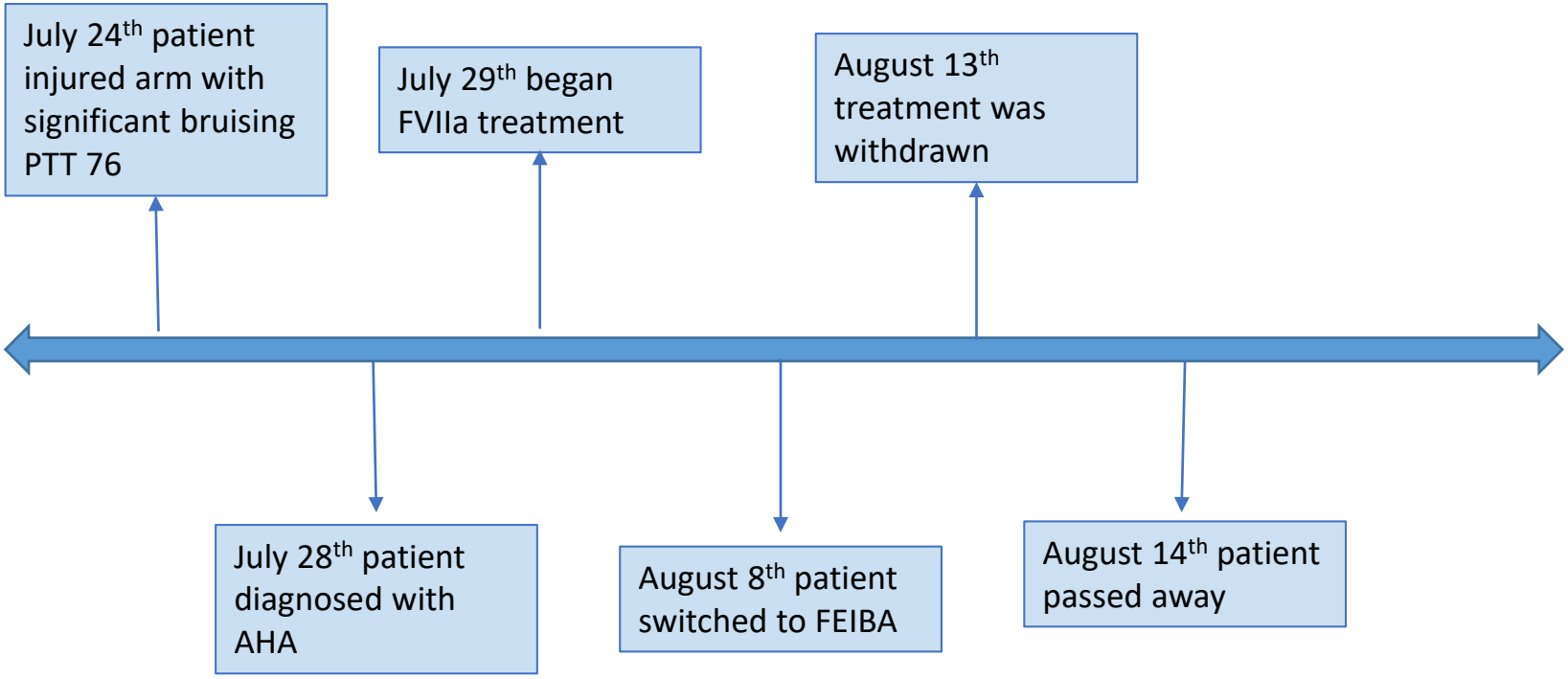


Date	Thrombin Time (sec) (20-30)	Fibrinogen (g/l) (1.6-4.2)
July 24th	22	3.0
July 28th	23	4.0
August 1st	26	---
August 5th	26	---
August 9th	30	---
August 12th	---	1.2

What was next?

- Prior to his death the next treatment option was porcine antihemophilic factor (FVIII)
- Plasma derived porcine FVIII
- Different amino acid sequence then human FVIII causing minimal cross reactivity
- Monitor FVIII levels at 30min and 3h after initial dose then 30 min after subsequent doses

Recap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August 14th patient passed away

Take home:

- AHA can develop in anyone
- There are multiple treatment options of AHA
- Transfusion medicine plays a significant role in the treatment of AHA
- Link the pieces of the puzzle

References & Appreciation

- 1. Knöbl, Paul. “Prevention and Management of Bleeding Episodes in Patients with Acquired Hemophilia A.” *Drugs* vol. 78,18 (2018): 1861-1872.

- 2. Fosbury, Emma et al. “Review of recombinant anti-haemophilic porcine sequence factor VIII in adults with acquired haemophilia A.” *Therapeutic advances in hematology* vol. 8,9 (2017): 263-272. doi:10.1177/2040620717720861

- Special Thanks to Dr. Ted Warkentin and Elysha VanderVeer for their assistance

www.hamiltonhealthsciences.ca

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