

Cookbook Coagulation MPS 2019 meetng

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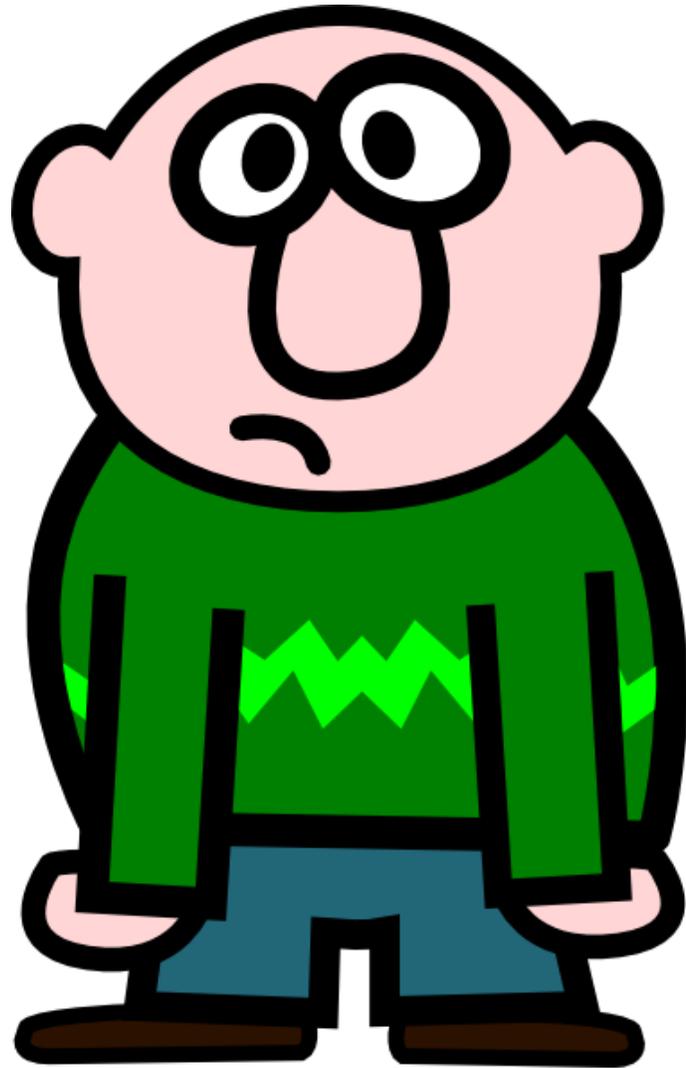
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In the Beginning...

- ▶ Give heparin bolus for initiation
- ▶ Wait for ACT to reach 300 seconds
- ▶ Start heparin at no specific protocol units/kg/hr
- ▶ Do hourly ACTs
- ▶ Titrate heparin to maintain ACTs 180-200



2011-2016 Phase I - standardized order sets

- ▶ Give heparin bolus for initiation
- ▶ Wait for ACT to reach 300 seconds
- ▶ Start heparin at no specific protocol units/kg/hr
- ▶ Do hourly ACTs
- ▶ Titrate heparin to maintain ACTs 180-200
- ▶ Send daily ATIII levels to SLU at 0200. Treat ATIII levels less than 70%.
- ▶ Send PTT or FDP/fibrinolysis panel as needed.

Corrective Action for ACT OOR



Check bag and rate dialed in on pump.



If low, consider excessive urine output or platelet infusion.



Increase heparin rate by 5-10 u/kg/hr.



Send antiXa level and fibrinogen.



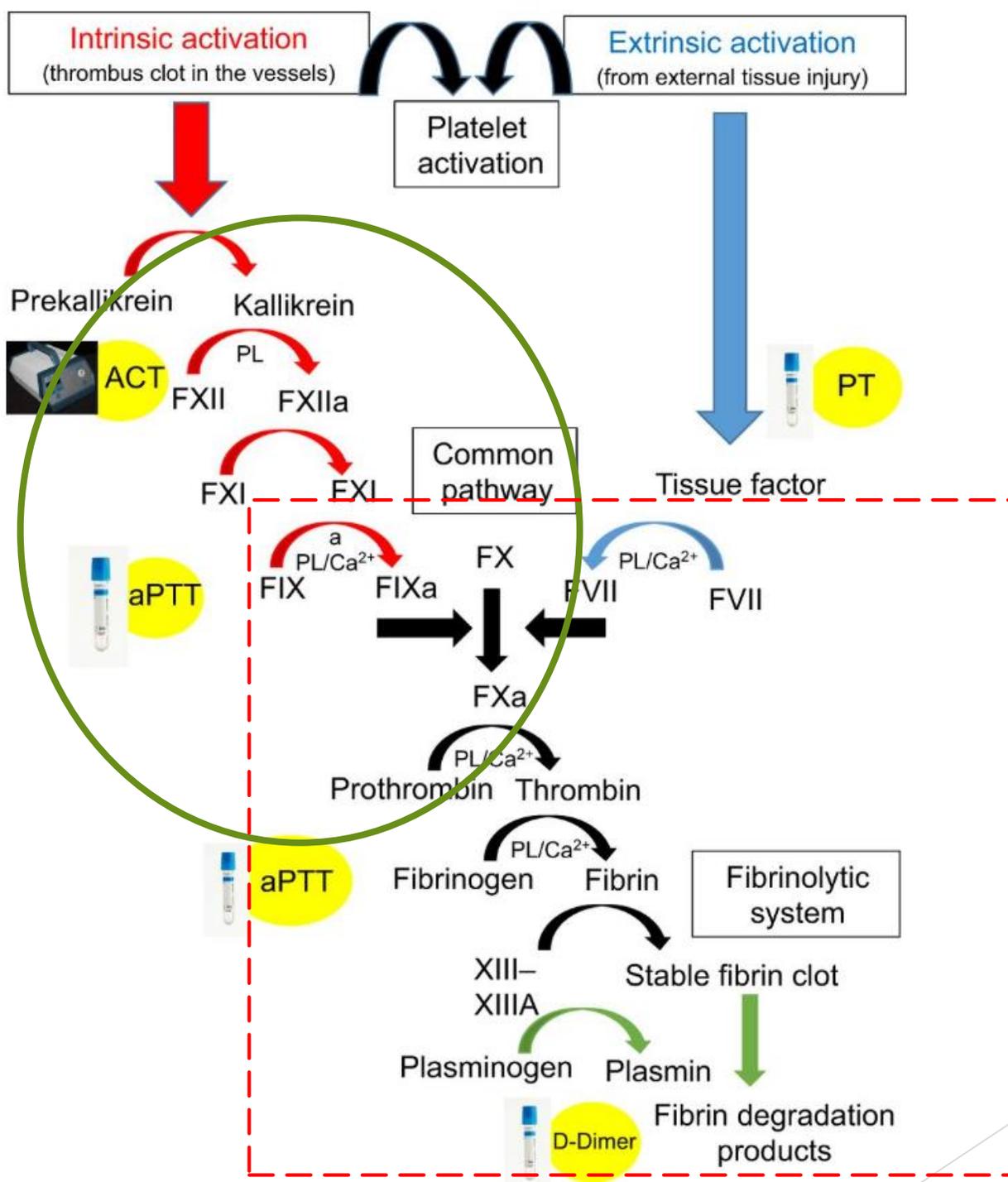
If fibrinogen level low, give FFP.



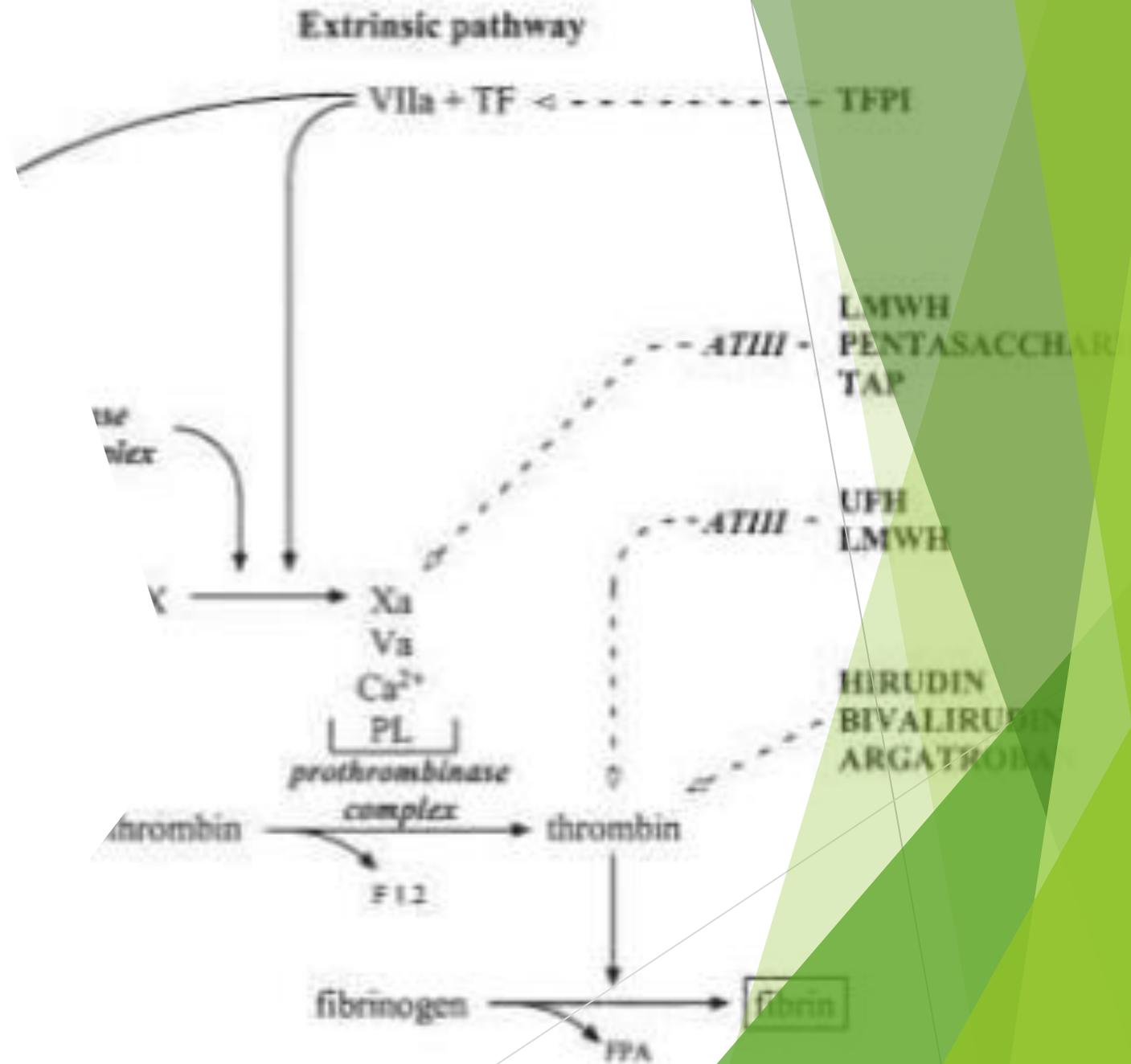
Heparin bolus if 10% increase in rate doesn't fix the problem. Bolus is half the current hourly drip rate and administered from separate source of heparin.

Functional Tests

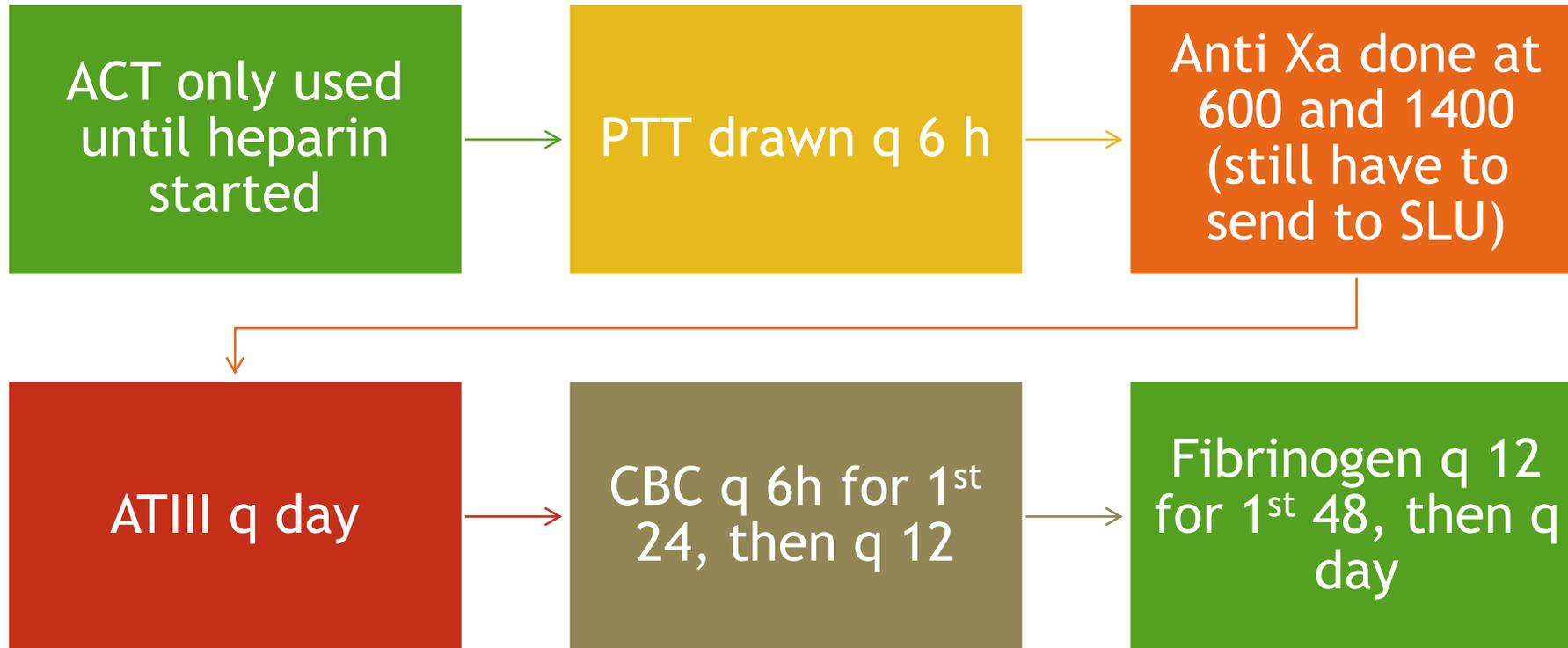
- ▶ Anti Xa measures the amount of heparin indirectly in a person's blood by measuring its inhibition and Factor Xa activity.
- ▶ It is not a functional test; the result does not tell us how heparin is working. It's simply how much Factor Xa has been inhibited.
- ▶ ATIII levels are also not functional tests. It simply tells how much antithrombin is present in the blood.
- ▶ Platelet counts are also another example of a non-functional test.
- ▶ PTT is a function test. It checks the function of the coagulation factors, but its biggest flaw is it is a diffuse test. There are many coagulation factors, and any one of them or combination of them could affect the PTT result.
- ▶ TEG/rotem also functional tests.



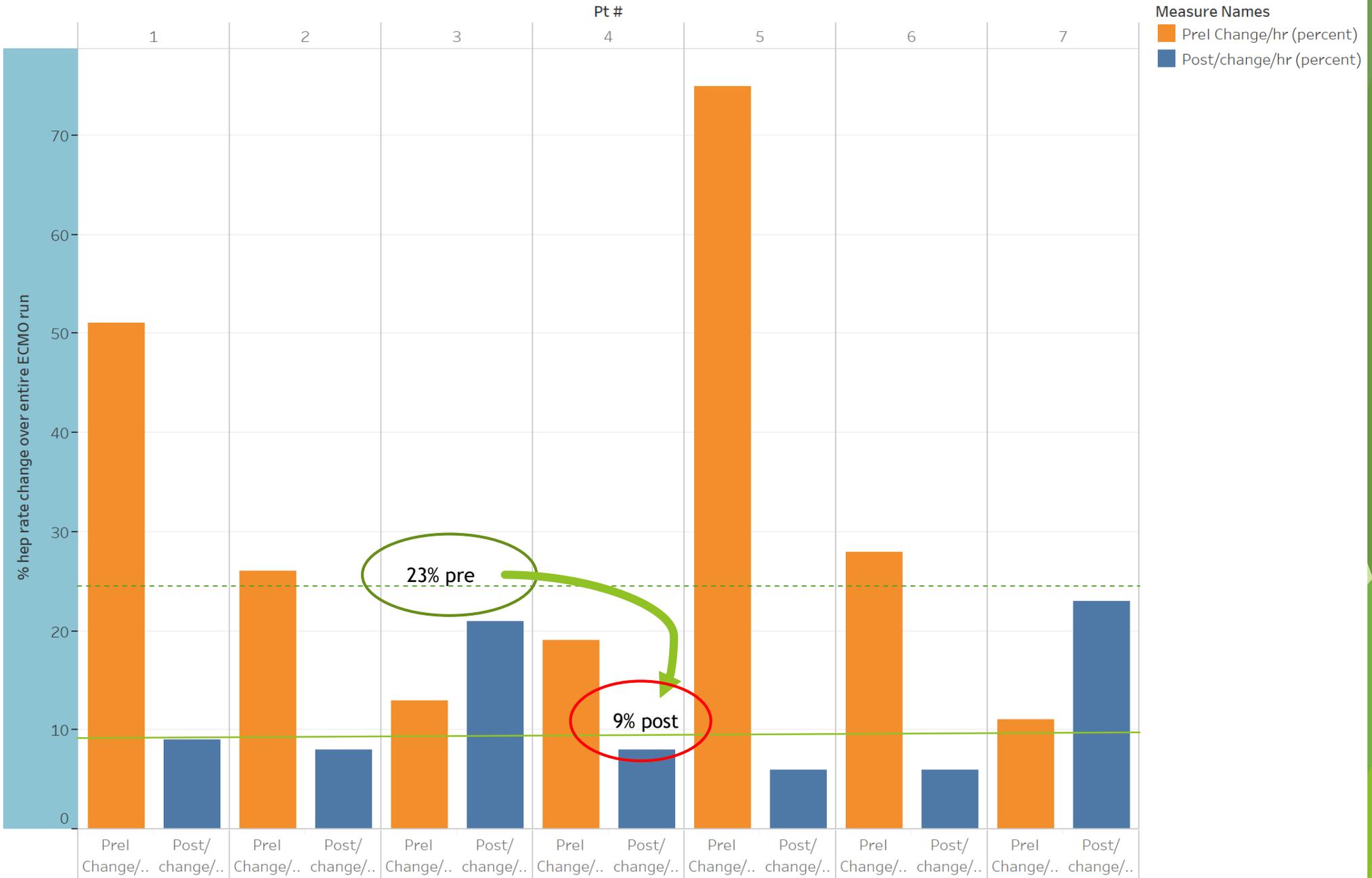
Antithrombin III (ATIII) the third leg of the triangle



Phase II - 2016

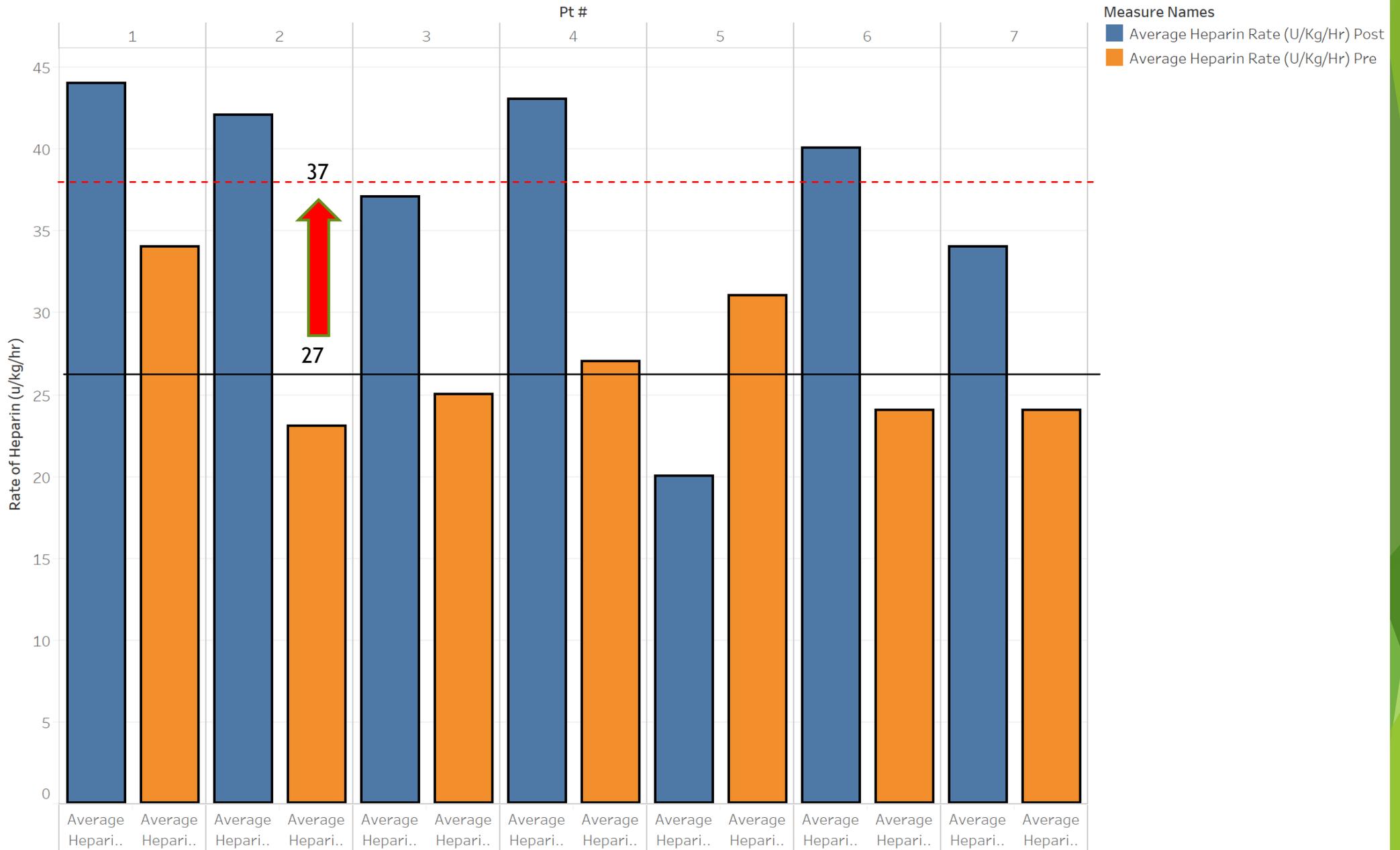


Change in Heparin Rate per Hour



Prel Change/hr (percent) and Post/change/hr (percent) for each Pt #. Color shows details about Prel Change/hr (percent) and Post/change/hr (percent).

Average Heparin Rates u/kg/hr



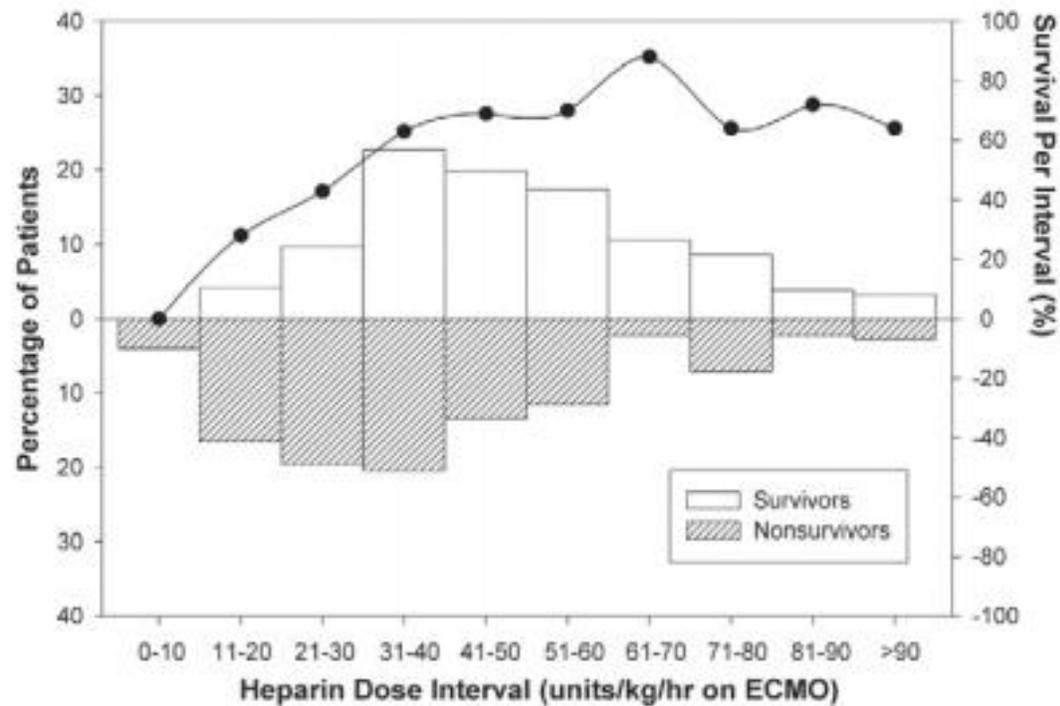
Average Heparin Rate (U/Kg/Hr) Post and Average Heparin Rate (U/Kg/Hr) Pre for each Pt #. Color shows details about Average Heparin Rate (U/Kg/Hr) Post and Average Heparin Rate (U/Kg/Hr) Pre.

Anticoagulation and Pediatric Extracorporeal Membrane Oxygenation: Impact of Activated Clotting Time and Heparin Dose on Survival

Christopher W. Baird, MD, David Zurakowski, PhD, Barbara Robinson, MD, Sanjiv Gandhi, MD, Leighann Burdis-Koch, RCP, Joseph Tamblyn, RCP, Ricardo Munoz, MD, Karol Fortich, MD, and Frank A. Pigula, MD

Children's Hospital Boston, Boston, Massachusetts; St. Louis Children's Hospital, St. Louis, Missouri; and Children's Hospital Pittsburgh, Pittsburgh, Pennsylvania

Survival Rates with Heparin Dosing



- ▶ For each interval of 10 units/kg of heparin the survival rate increases dramatically from 30 u/kg/hr to 70 u/kg/hr.
- ▶ For each increase of 10 units of heparin/kg/hr, the probability of survival was predicted to increase by 56%.
- ▶ Tight control of ACTs, PTTs or both was associated with less intracranial hemorrhage.

Bivalirudin

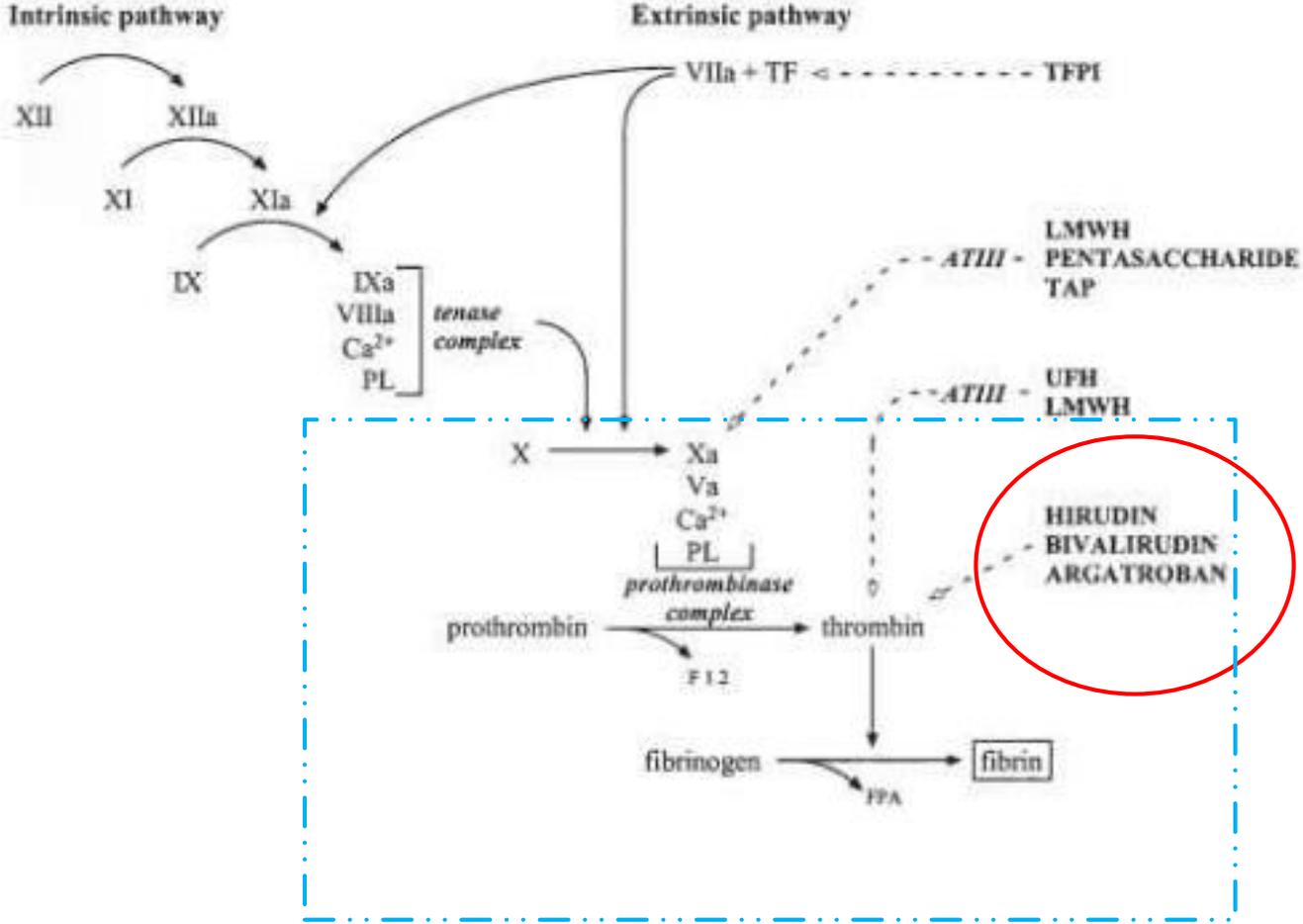
Direct Thrombin Inhibitor

Enzymatic clearance (80% enzymatic, 20% renal)

Short half-life (25 minutes)

No reversal

Bivalirudin - Direct Thrombin Inhibitor



Heparin Induced Thrombocytopenia in the Pediatric Population

Spadone D, Clark F, James E (1992) Heparin induced thrombocytopenia in the newborn. J Vasc Surg 15:306-311.

Schmugge M, Risch L, Huber AR, BennA, Fischer JE (2002) Heparin-induced thrombocytopenia-associated thrombosis in pediatric intensive care patients. Pediatrics 109:e10.

Newall F, Barnes c, Ignjatovic V, Monagle P (2003) Heparin-induced thrombocytopenia. J Pediatr Child Health 39:289-292.

REVIEW OF LITERATURE

- ▶ One prospective and two retrospective studies
- ▶ Prospective study found a rate of 1.1% in the NICU setting
- ▶ Retrospective study #1 found HIT rate of 2.3% in PICU setting
- ▶ Retrospective study #2 found HIT rate of <1% in a tertiary pediatric hospital

The Anti-Coagulation Recipe

Three Ingredients



PTT



Anti-Xa



ATIII



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Notify primary attending before any heparin boluses or infusion holds.

Heparin dose changes more frequent than every 4 hours must be discussed with attending.

aPTT	Infusion Dose Adjustment Instructions	Next Heparin Adjustment
< 40	Increase infusion by 20%	6 hours
41-50	Increase infusion by 10%	6 hours
51-70	No change	6 hours
71-80	Decrease infusion by 10%	6 hours
81-110	Decrease infusion by 20% ONLY IF ANTI-XA THERAPEUTIC OR HIGH	6 hours
>110	Hold infusion for 60 minutes, then decrease infusion by 20% ONLY IF ANTI-XA THERAPEUTIC OR HIGH	6 hours

For use only when heparin changes are based on Anti-Xa alone.

Heparin dose changes more frequent than every 4 hours must be discussed with attending.

Anti-Xa	Infusion Dose Adjustment Instructions	Next Heparin Adjustment
<0.10	Bolus 20 units/kg, then increase infusion by 25%	6 hours
0.10 – 0.19	Increase infusion by 20%	6 hours
0.20 – 0.29	Increase infusion by 10%	6 hours
0.30 – 0.70	No change	6 hours
0.70 – 0.79	Decrease infusion by 10%	6 hours
0.80 – 1.09	Decrease infusion by 20%	6 hours
1.10 – 1.40	Hold infusion for 60 minutes, then decrease infusion by 20%	6 hours
>1.40	Hold infusion for 90 minutes, then decrease infusion by 20%	6 hours

ATIII Replacement



Must meet all the requirements:

- $<70\%$
- Heparin infusion >50 u/kg/hr
- Anti-Xa below goal

What happened?



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- ▶ I followed the recipe perfectly!
- ▶ I asked for help from the experts!
- ▶ My patient is bleeding!
- ▶ My circuit is clotted!
- ▶ Are there other tests I should send?
- ▶ What factors do I need to give?
- ▶ Do I need to give a heparin bolus?



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Lessons We've Learned...So Far



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- ▶ We had a lot of head bleeds prior to 2016. We still have head bleeds but our data correlates with the Gandhi data. Our heparin rates were too low using just ACTs, and we still need to obtain tighter controls.
- ▶ We see a lot of clots early, but do few interventions.
- ▶ Our kids are sicker and on for longer and longer runs.
- ▶ Our lab sucks! Why can't we do antiXa's at our own facility?
- ▶ We do less heparin changes but we still are too slow to reach therapeutic levels from initiation.

Lessons We've Learned...So Far



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- ▶ Neonates need higher PTT ranges (60-80) because of their immature coagulation system and liver. We usually won't get a therapeutic antiXa without raising PTT limits.
- ▶ Hyperbilirubinemia causes lower antiXa values and may need to adjust accordingly.
- ▶ Bivalirudin is a bitch! Everything clots instantly. Clots even form instantly inside the heart if it isn't performing well.
- ▶ ELSO data and big data in general can hopefully drive some deep dive learning and AI to help clinicians predict or treat coagulation.



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