If not heparin for bypass then what?

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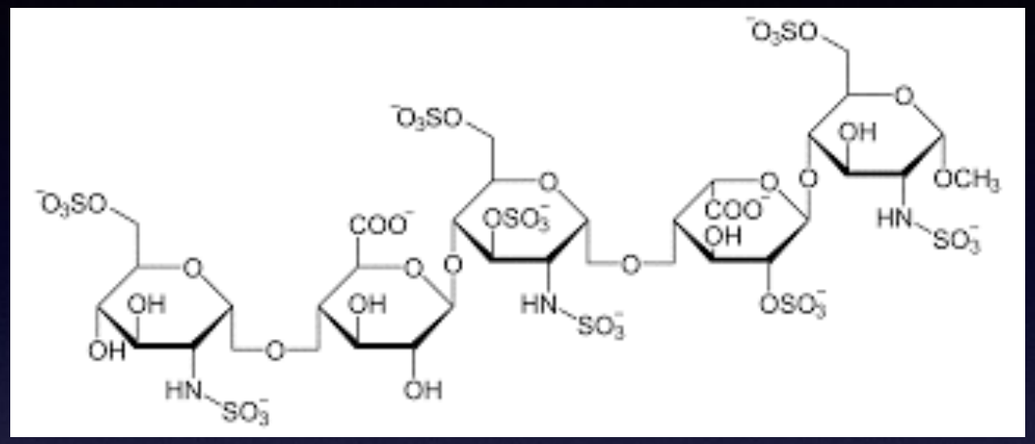
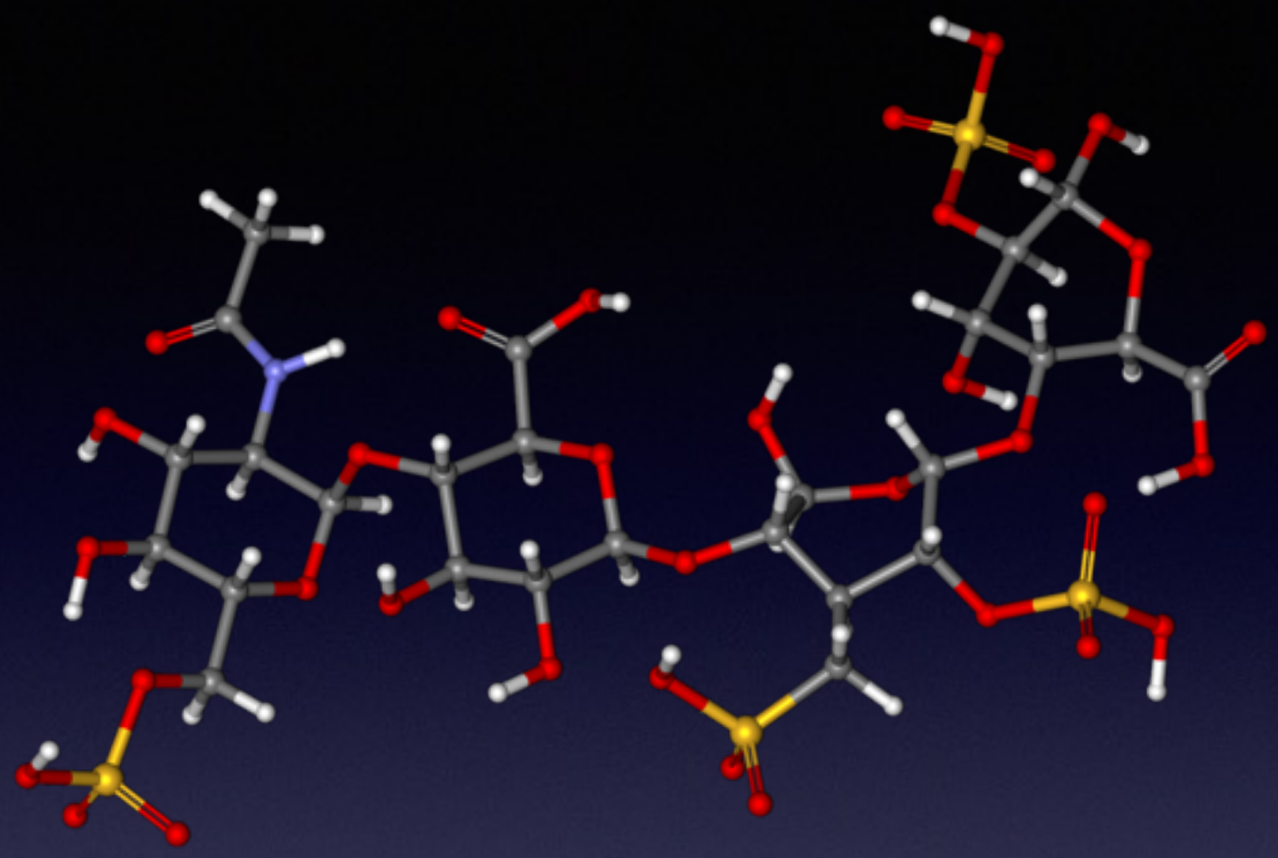


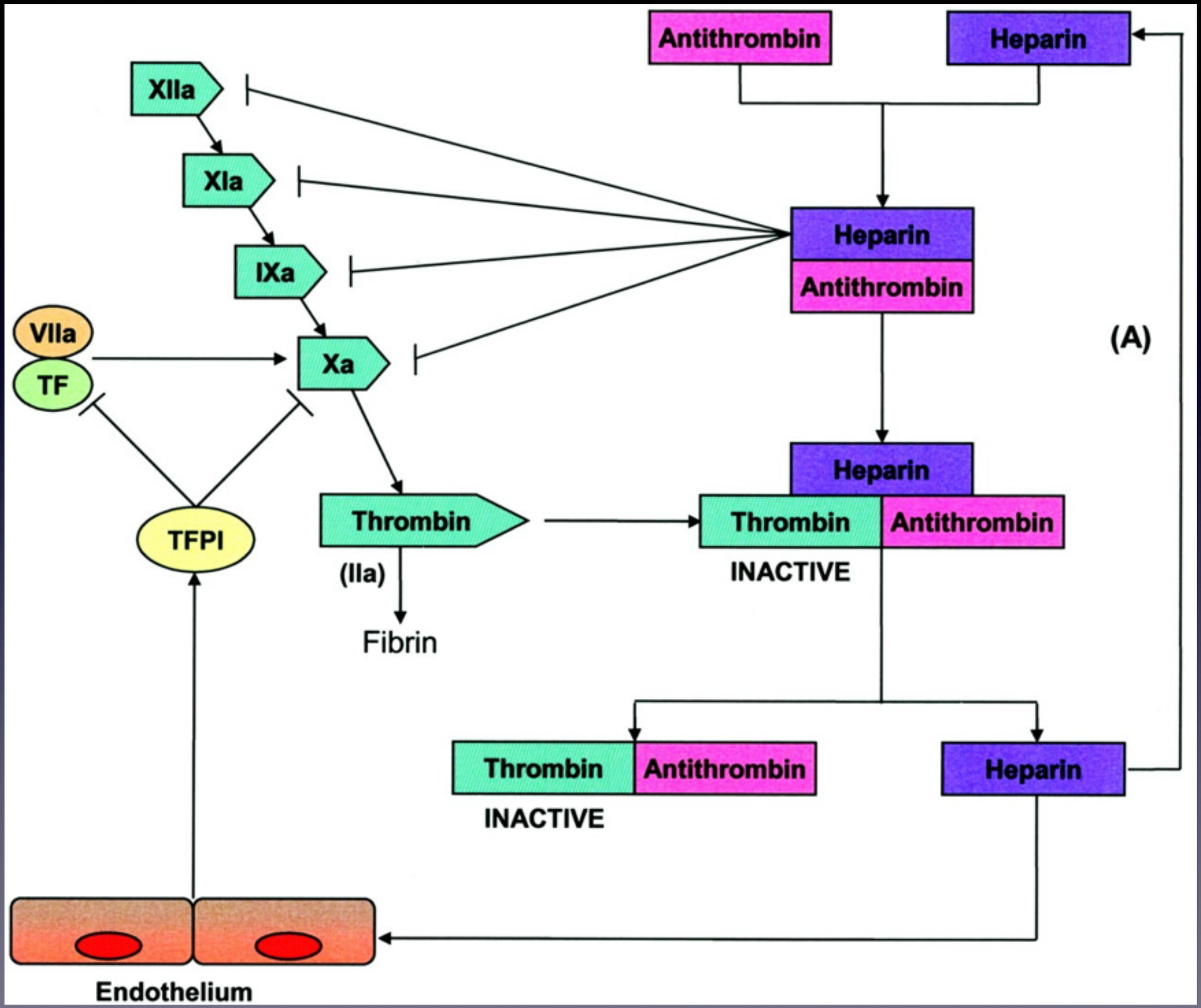


Heparin

Discovered 1916, commercial available 1935

Heparin

- Is there an alternative , not really
- Many many years of experience
- Easily titratable
- Easily measurable effect
- Easily reversed
- Very very few side effects


Antithrombin
Heparin
XIIa
XIa
IXa
VIIa
TF
Xa
TFPI
Thrombin
(IIa)
Fibrin
Heparin
Antithrombin
(A)
Heparin
Thrombin
Antithrombin
INACTIVE
Thrombin
Antithrombin
INACTIVE
Heparin
Endothelium

Why would we not use heparin?

- Heparin Allergy, extremely rare
- Heparin induced thrombocytopenia. 1-4%
- Heparin ‘resistance’.
- Antithrombin inactivity

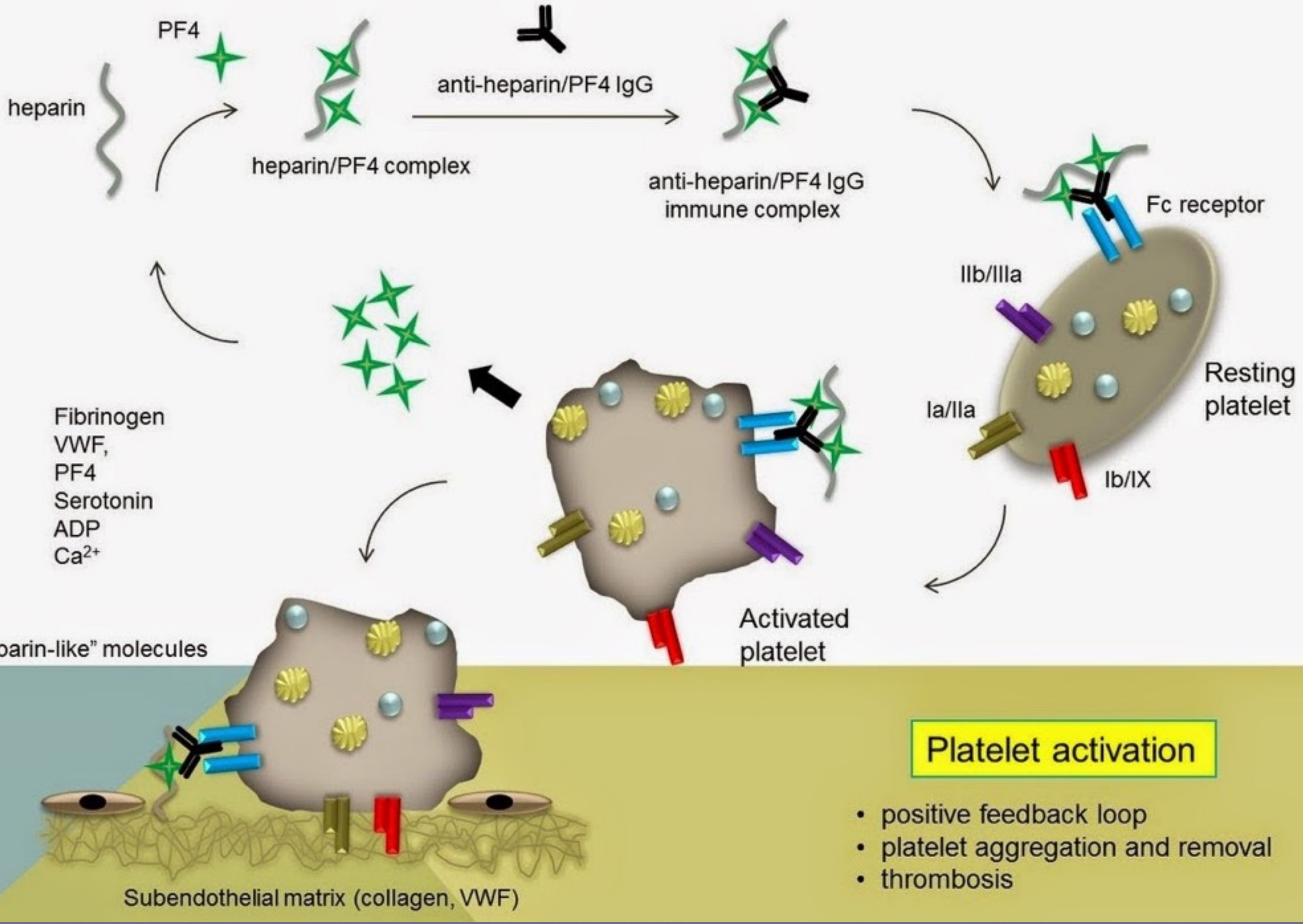
ATIII activity

- Low in neonates
- Low on CPB
- Can be measured by factor Xa assays.
- ACT may not recognise low ATIII levels.

Heparin induced thrombocytopenia (HIT)

- incidence of1-4%…why don't we see it more?
- Heparin and PF4 from an hapten,
- this stimulates IgG activation
- This activates platelets to clot
- Resulting in thrombocytopenia and thromboses.
- High percentage of patients produce PF4-haparin complexes but few of these develop HIT

Heparin-induced thrombocytopenia (HIT)



Platelet activation

- positive feedback loop
- platelet aggregation and removal
- thrombosis

Heparin induced thrombocytopenia

- The platelet count fall is not enough to produce bleeding and commonly occurs 5-14 days AFTER heparin administration

- Unless recent administration of heparin when fall in numbers will happen within a day

Heparin induced thrombocytopenia

- Previous exposure to heparin may result in circulating IgG Antibodies to heparin, however these only last 3 months

HIT

- Diagnosis
- 1) a falling platelet count on a patient receiving heparin
- 2) 4 Ts score
  - Thrombocytopenia
  - Timing
  - Thrombosis
  - Think of another cause

HIT

- Thrombocytopenia
- Fall in platelet count >50 % 2 points
- or count 20-100 x 10^9 2 points
- Fall in count 30-50% or lowest count 10-20 1 point
- fall in count<30% or count less than 10. 0 points

HIT

- Timing
- 5-10 days after treatment 2 points
- after day 10 1 point (except previous exposure and early fall 2 points)
- No fall. no previous exposure 0 points

- Thrombosis
  - Proven thrombosis, skin necrosis, systemic reaction 2 points
  - progressive thrombosis, silent thrombosis, red skin lesions 1 point
  - no symptoms 0 points

HIT

- Think of another cause
- none 2 points
- possible 1 point
- found 0 points

HIT

- Score 6-8 Highly likely
- 4-5 possible
- <4 not possible
- Positive score has Negative prediction value 0.98
- Intermediate score value 0.64

HIT

- Investigation
- 1. ELISA test for heparin-PF4 antibodies
- 2, If positive-functional assay…. rare and delayed
- 3. Doppler sonography of leg veins

HIT

- Treatment
- a) stop Heparin
- b) Start secondary anticoagulation
- c) Warfarin is contraindicated
- d) Danaparoid, Argatroban, Fondaparinux, Bivalirudin

HIT

- If you don't start a separate anticoagulant, the risk of clinical thrombosis is 56%

CPB

- If patient has history of HIT
- Redo surgery
- ECLS
- Check HIT antibodies. (PF4 solid phase immunoassay)
- If > 100 days probably safe to use heparin
- do not use LMWH (long half life/Not totally reversible)
- ? Bivalirudin when not on bypass.

CPB

- Antibody positive.
- ? still use heparin (check the effect off heparin on platelets with a functional assay)
- Urgent surgery-bivalirudin
- Urgent surgery - heparin and plasma exchange

Alternative drugs

- Argatroban
- Bivalirudin
- Danaparoid
- Fondaparinux
- Others.

Current practice

- Oschman A. Survey results: characterization of direct thrombin inhibitor use in pediatric patients. J Pediatr Pharmacol Ther 2014;19:10–5.
- Argatroban 80% hospitals
- Bivalirudin 41% hospitals
- 2-4 times a year

Current practice

- Moffett BS, Teruya J. Trends in parenteral direct thrombin inhibitor use in pediatric patients: analysis of a large administrative database. Arch Pathol Lab Med 2014;138:1229–32.

- Bivalirudin use doubled over the periods 2004-7 and 2007-11

- Significantly less bleeding with bivalirudin

Argatroban

- Direct thrombin inhibitor, does not need ATIII as cofactor
- without bolus, steady state in 1-3 hours. peak effect 2 hours
- Half life 45 minutes
- Metabolised in liver, not dependent on renal function
- Monitored by ACT/ APTT, what ACT is correct?
- (300 <450)
- NO reversal agent

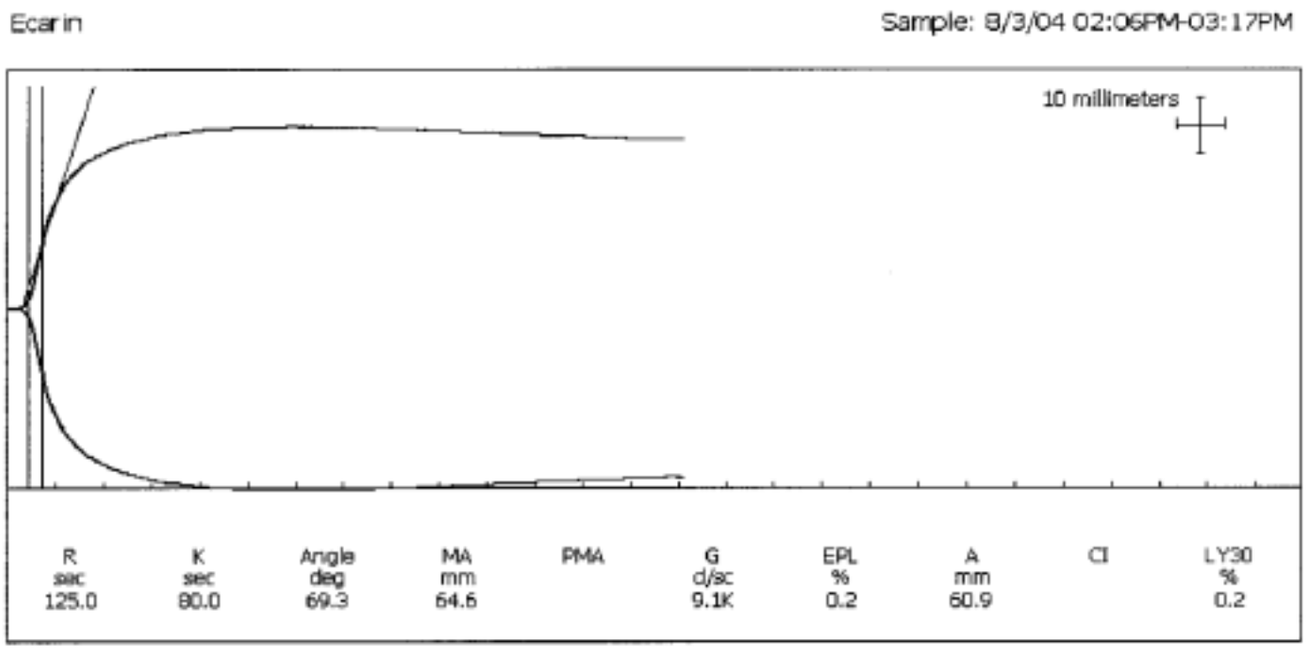
Argatroban

- 100-350mcg/kg bolus, 25mcg/kg/min infusion
- ACT check 5-10 minutes later, therapeutic after 15 minutes
- if ACT <300, give 150mcg/kg/min bolus and increase infusion rate
- still clots even with ACT > 450 seconds …
- No blood cardioplegia
- No heparin bonded lines
- Decrease dose in hepatic impairment

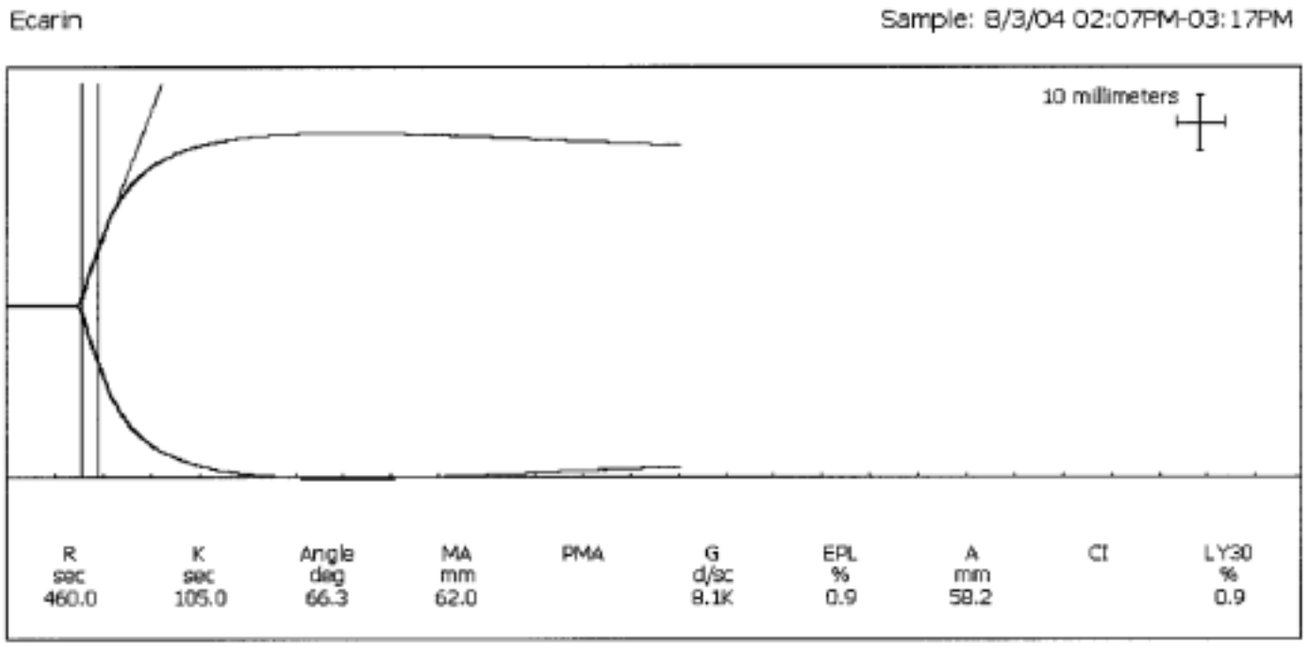
Bivalirudin

- Direct thrombin inactivator
- No antidote
- Shorter half life than Argotraban (25<50 minutes)
- 80% metabolised by proteolysis, 20% Renally excreted
- 0.5-1mg/kg bolus, 1.5-2.5mg/kg/hr infusion
- Cam be haemofiltered out of circuit.
- Monitor by ACT/APTT/TEG
- can monitor anti IIa activity but very rare

A. Before Bivalirudin Treatment



B. After Bivalirudin Treatment.



Thombelastograph® ecarin clotting time traces before (A) and after (B) bivalirudin treatment.