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Acil Tıp Uzmanları Derneği



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Emergency Physicians Association of Turkey

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4

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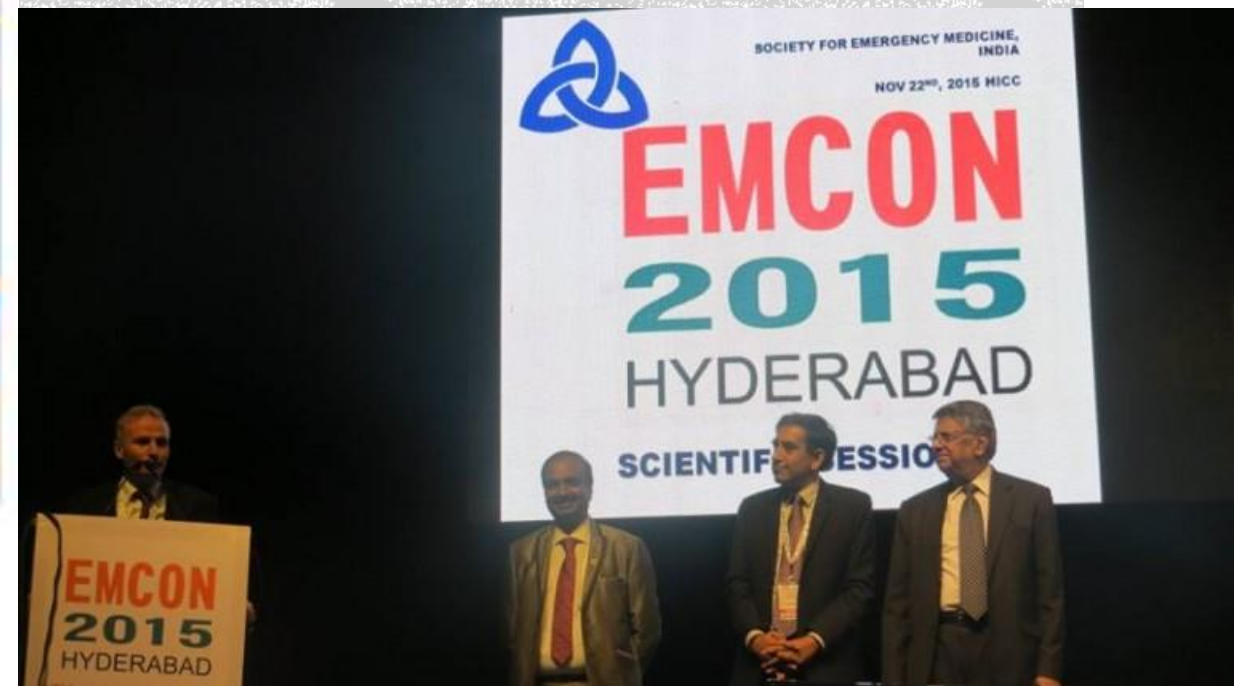



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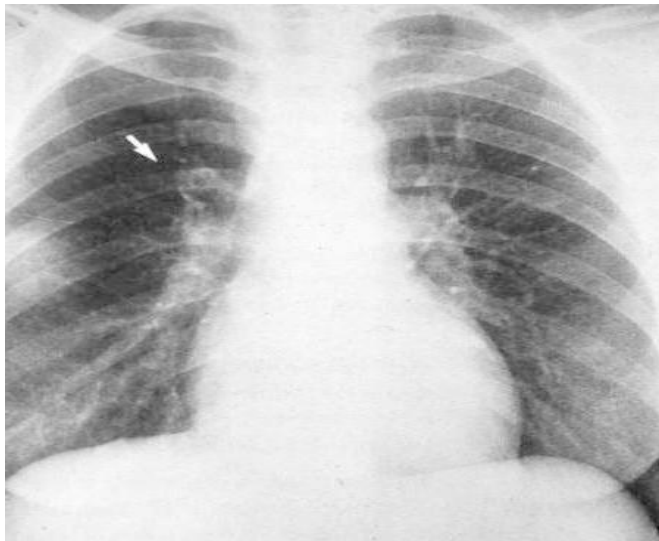
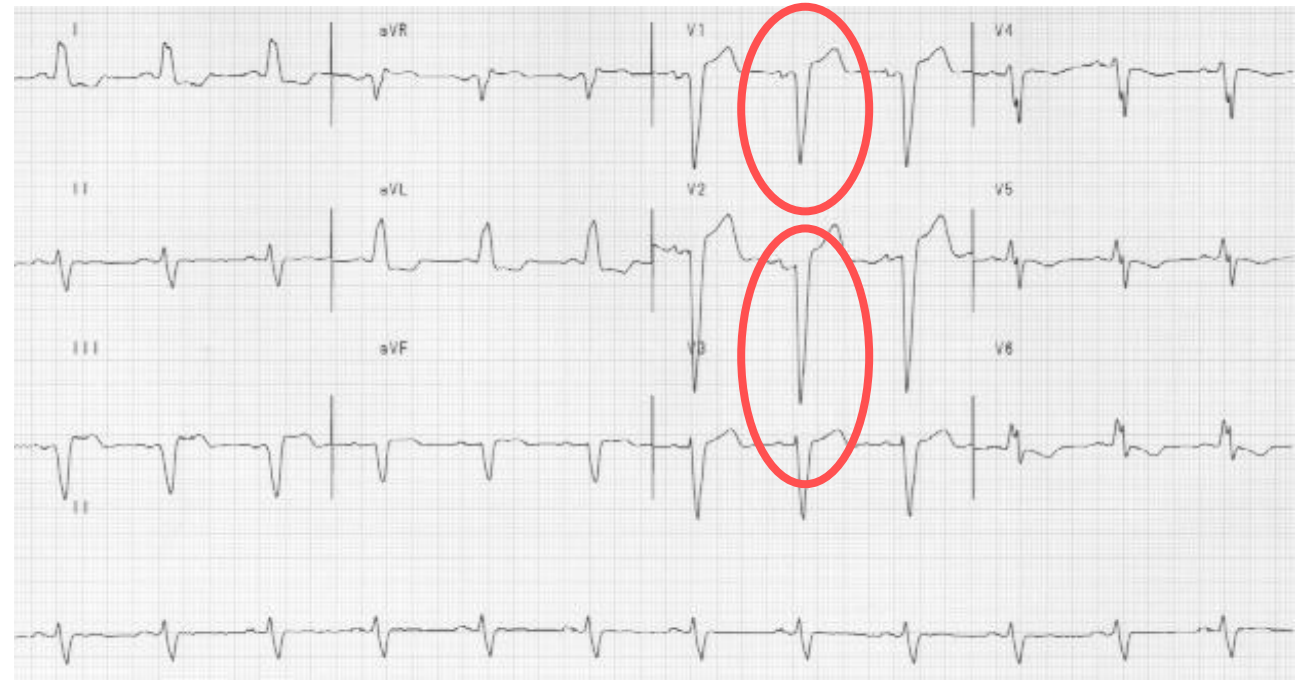
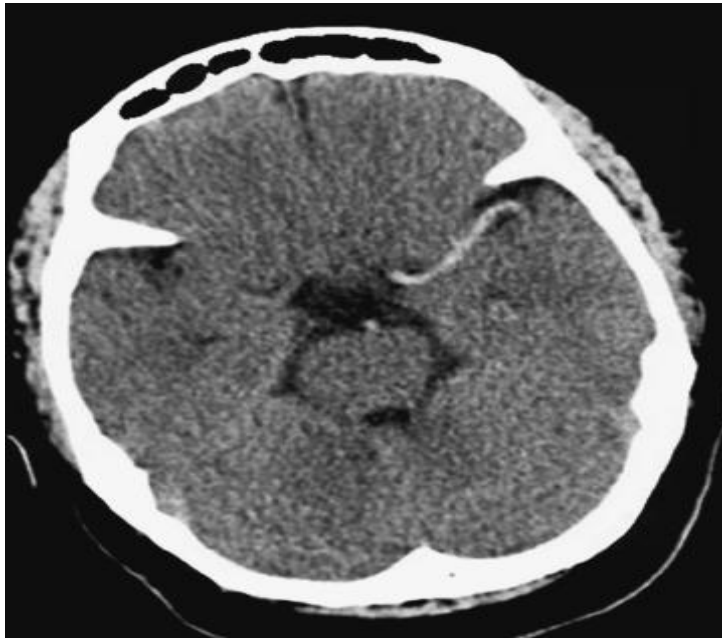


SEMI

New Generation of Anti Thrombolytics

Dr. T. S. Srinath Kumar





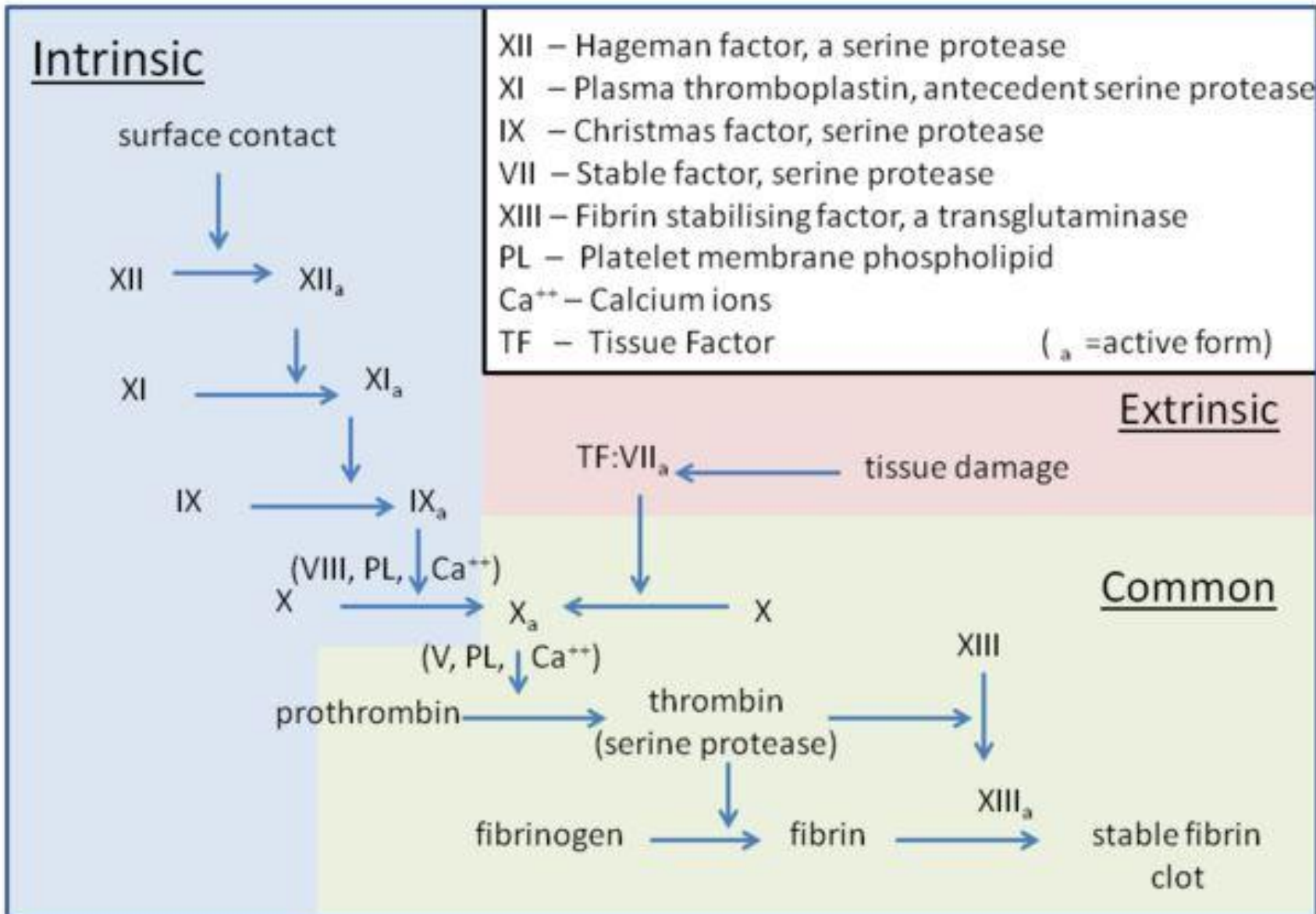


Coagulation Cascade and Site of Action of Various Anticoagulants





The three pathways that makeup the classical blood coagulation pathway





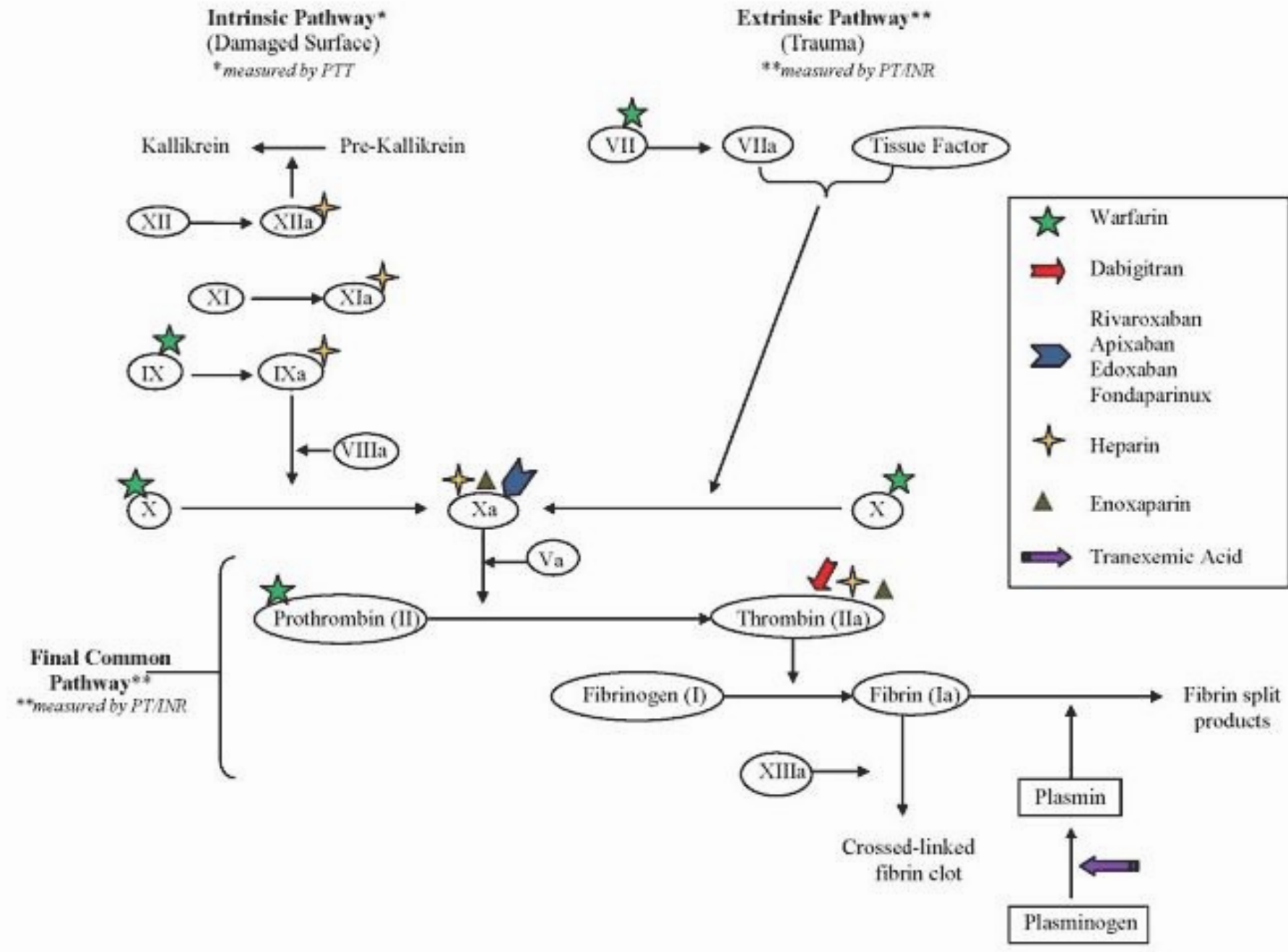
- Warfarin inhibits synthesis of factor II, VII, IX and X including protein C and S.
- Dabigatran inhibits the action of thrombin.
- Rivaroxaban, apixaban, edoxaban and fondaparinux block the effects of factor Xa.
- Enoxaparin binds to and accelerates the activity of antithrombin III, potentiating the inhibition of coagulation factors Xa and IIa.
- Enoxaparin prevents conversion of plasminogen to plasmin.

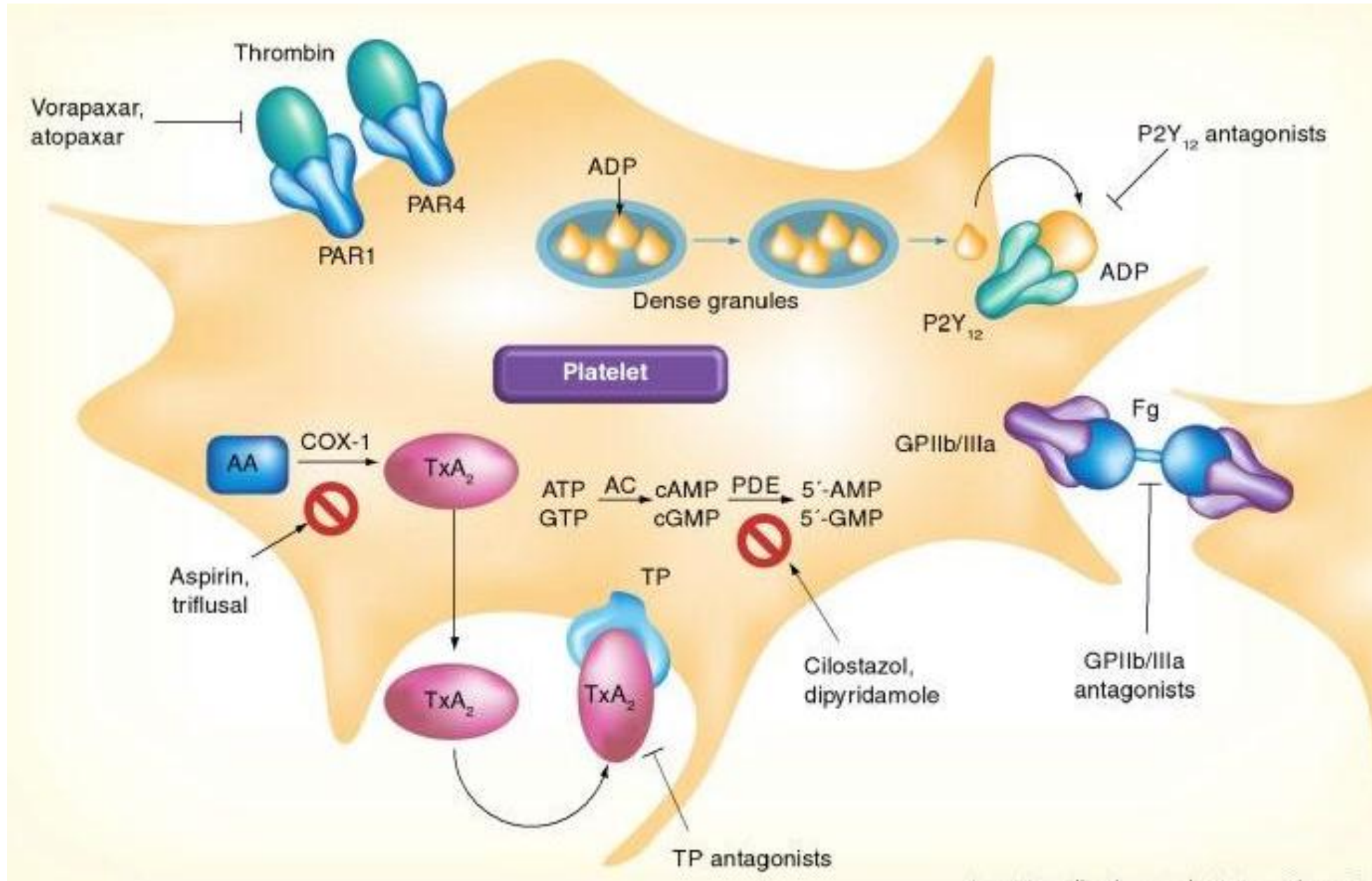




- Alteplase binds to fibrin using the fibronectin and kiringle2 domain.
- The protease portion then cleave the Arg/Val bond of plasminogen converting it to plasmin.
- Plasmin then degrades the fibrin matrix resulting in thrombolysis.









Agents for Reversal of Antithrombotics in ICH





Vit K antagonist

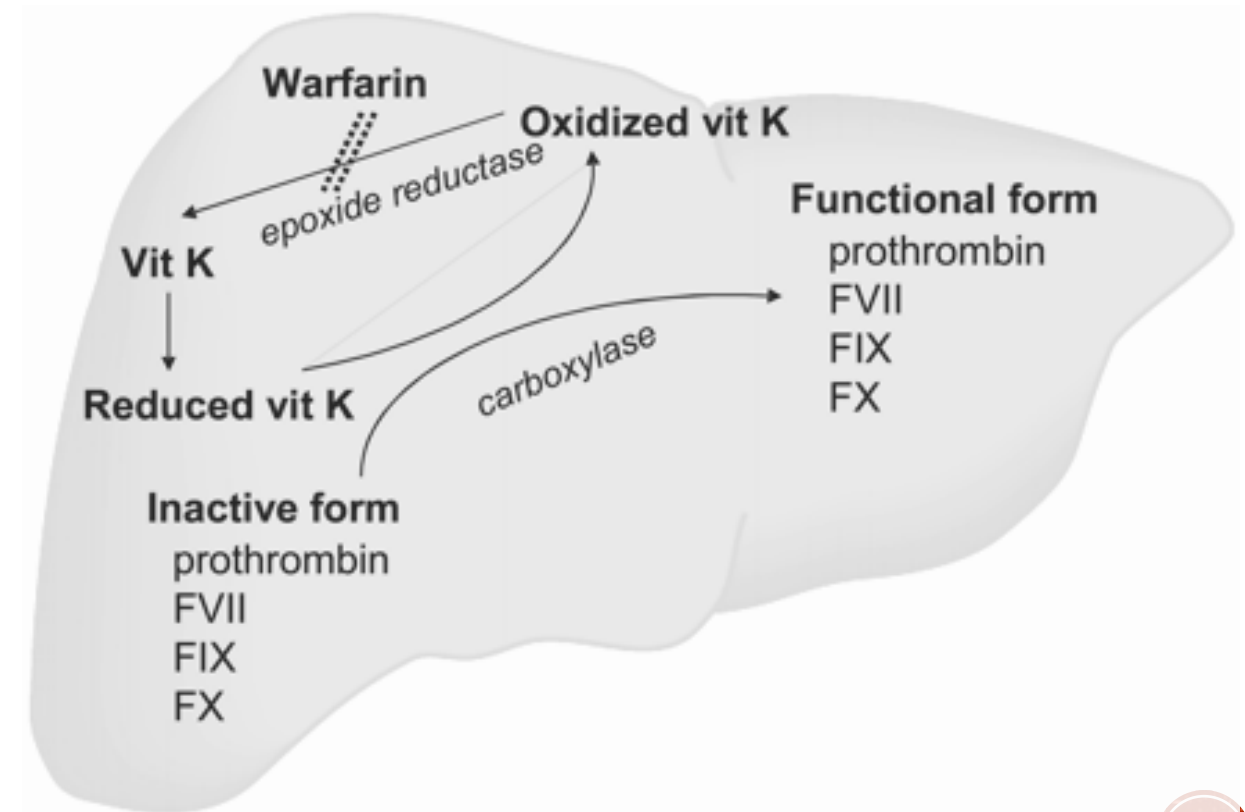
- If INR greater than or equal to 4 provide vitamin K 10mg IV and 3-4 factor Prothrombin Complex Concentrates(PCC) or fresh frozen plasma.

Direct factor Xa inhibitors

- Activated charcoal or 4 factor PCC.

Unfractionated heparin

- Protamine IV.



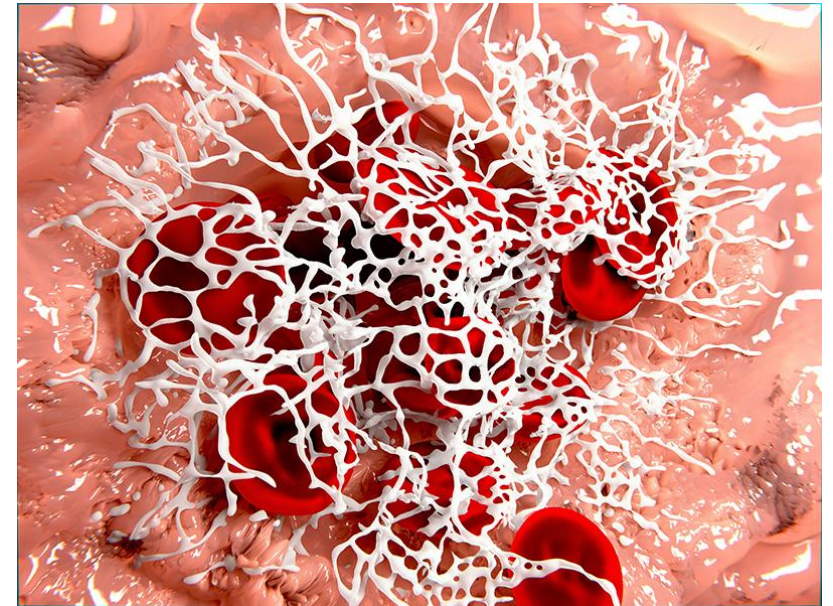


LMWH

- Enoxaparine
 - Protamine IV dose based on time of administration.
- Dalteparin/nadroparin/tinzaparin
 - Protamin IV or recombinant factor VIIa (rFVIIa)

Danaparoid

- rFVIIa





Pentasaccharides

- aPCC

Thrombolytic agents

- Cryoprecipitate 10units or antifibrinolytics.

Antiplatelet agents

- Desmopressin 0.4mcg or platelet transfusion during surgical procedures.





PCC / aPCC





- Vit K has a delayed onset of action and play no role in reversing anticoagulant effect of the newer agents.
- FFP drawbacks include time for procurement and requirements of large volumes.





- Three distinct classifications of prothrombin complex concentrates. (PCC products)
- Three factor PCC products contain three coagulation factors II, IX and X.
- Four factor PCC products containing II, VII, IX & X.
- Activated PCC products containing four coagulation factors in inactivated and activated forms.





- Factor VIII inhibitor bypassing activity (FEIBA) NF(nano filtered) and VH (vapor heated) products are aPCC products that contain mostly activated factor VIII along with mainly non activated factors II, IX and X.
- They are used to prevent bleeding with surgical intervention in hemophilia A and hemophilia B.
- These products are also used as anticoagulant reversal.





Protamine Sulfate





- A basic peptide that combines with heparin as an ion pair.
- It's effect is for about 2 hours.
- Used following cardiac surgery and other vascular procedures.
- Protamine in excess has an anticoagulant effect, by interacting with platelets, fibrinogen and other plasma proteins.
- There is a possibility for anaphylactic reactions.
- Unfortunately cannot reverse the effects of many LMWH.



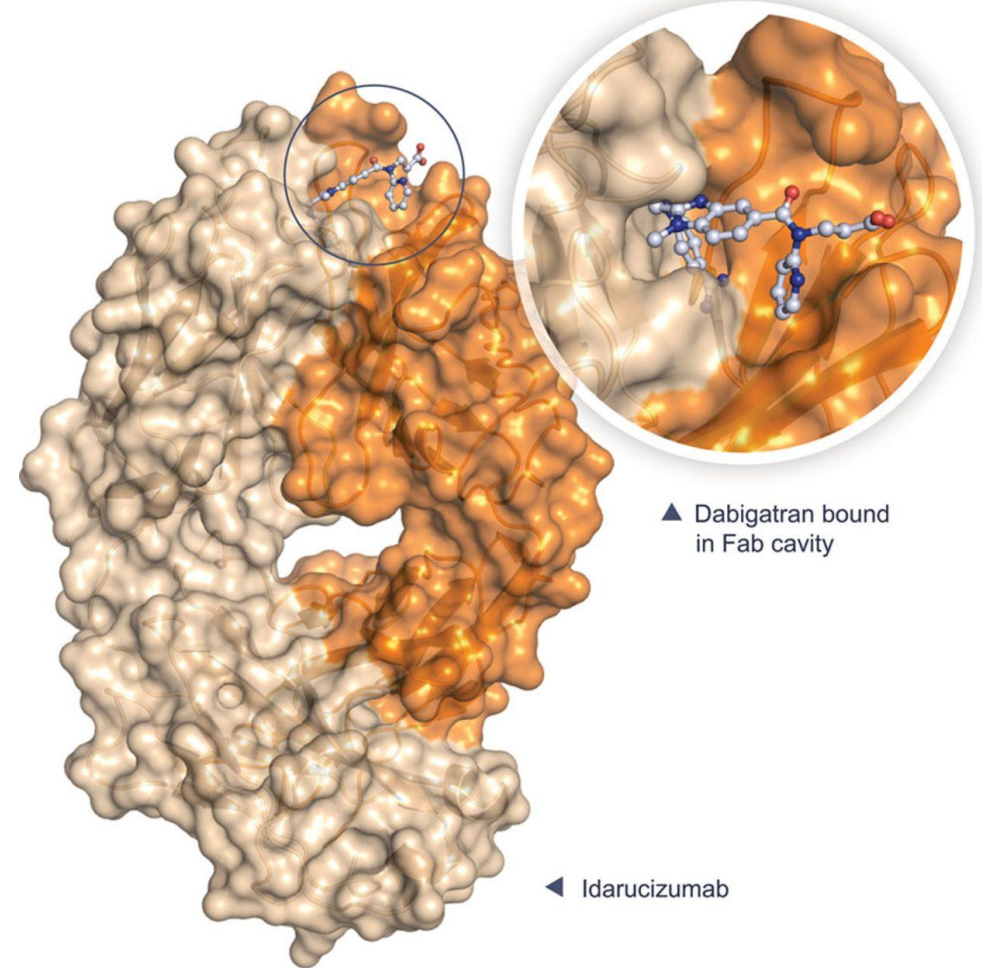


Idarucizumab





- Only works on dabigatran.
- It is a monoclonal antibody fragment.
- Binds with high affinity dabigatran.
- Rapidly reverses the coagulation effects.





Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors

Stuart J. Connolly, M.D., Truman J. Milling, Jr., M.D., John W. Eikelboom, M.D., C. Michael Gibson, M.D., John T. Curnutte, M.D., Ph.D., Alex Gold, M.D., Michele D. Bronson, Ph.D., Genmin Lu, Ph.D., Pamela B. Conley, Ph.D., Peter Verhamme, M.D., Ph.D., Jeannot Schmidt, M.D., Saskia Middeldorp, M.D., Alexander T. Cohen, M.D., Jan Beyer-Westendorf, M.D., Pierre Albaladejo, M.D., Jose Lopez-Sendon, M.D., Shelly Goodman, Ph.D., Janet Leeds, Ph.D., Brian L. Wiens, Ph.D., Deborah M. Siegal, M.D., Elena Zotova, Ph.D., Brandi Meeks, B.Eng., Juliet Nakamya, Ph.D., W. Ting Lim, M.Sc., and Mark Crowther, M.D., for the ANNEXA-4 Investigators*

N Engl J Med 2016; 375:1131-1141 [September 22, 2016](#) DOI: 10.1056/NEJMoa1607887

Andexanet Alfa





- Acts as a target decoy for oral and injectable factor Xa inhibitors.
- Targets with high specificity.
- Reverses anticoagulant effect of :-

Oral direct

Injectable indirect

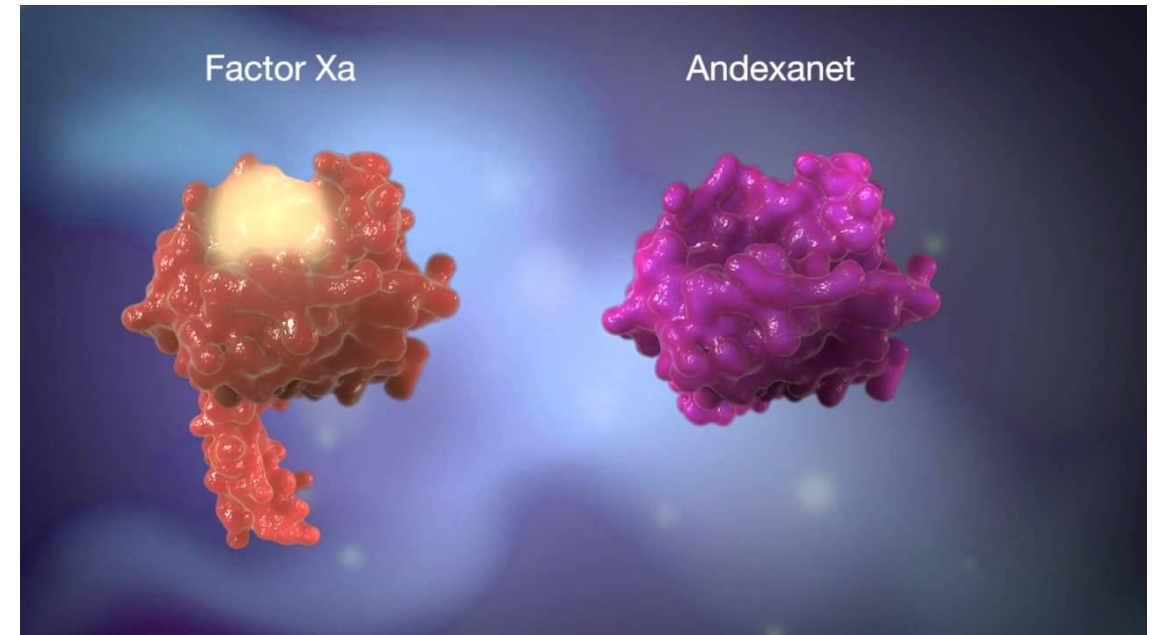
Apixaban

Enoxaparin

Edoxaban

Fondaparinox

Rivaroxaban



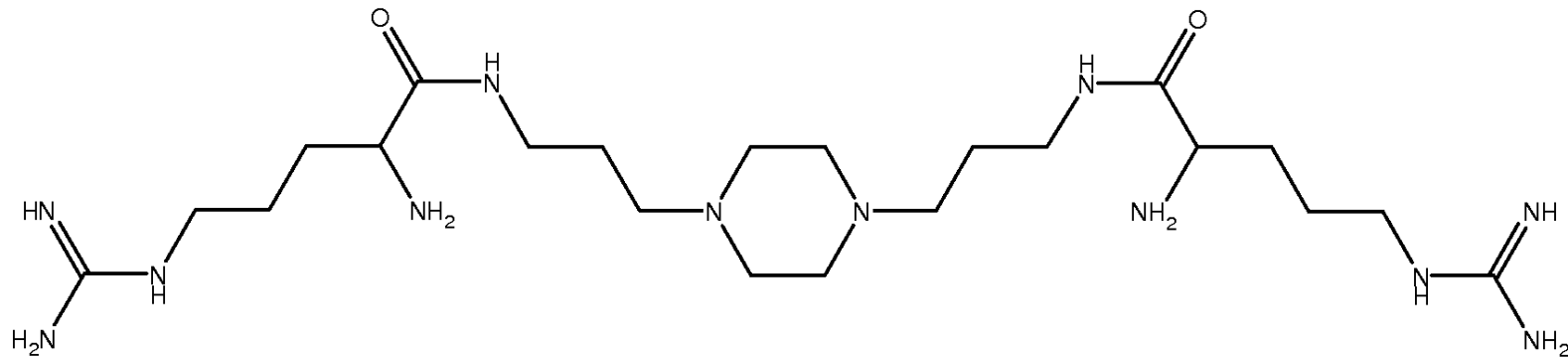


Aripazine





- It is a small synthetic molecule.
- Binds to
 - Oral factor Xa inhibitors and DTIs
 - UFH / LMWH
- Binds via non-covalent bonding and charge-charge interactions.



Reversal of oral factor Xa inhibitors by prothrombin complex concentrates: a re-appraisal. J Thromb Haemost. 2015 Jun;13 Suppl 1:S187-94. doi: 10.1111/jth.12949. PubMed PMID: 26149022.

Evidence-Based Medicine | February 2016

Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report



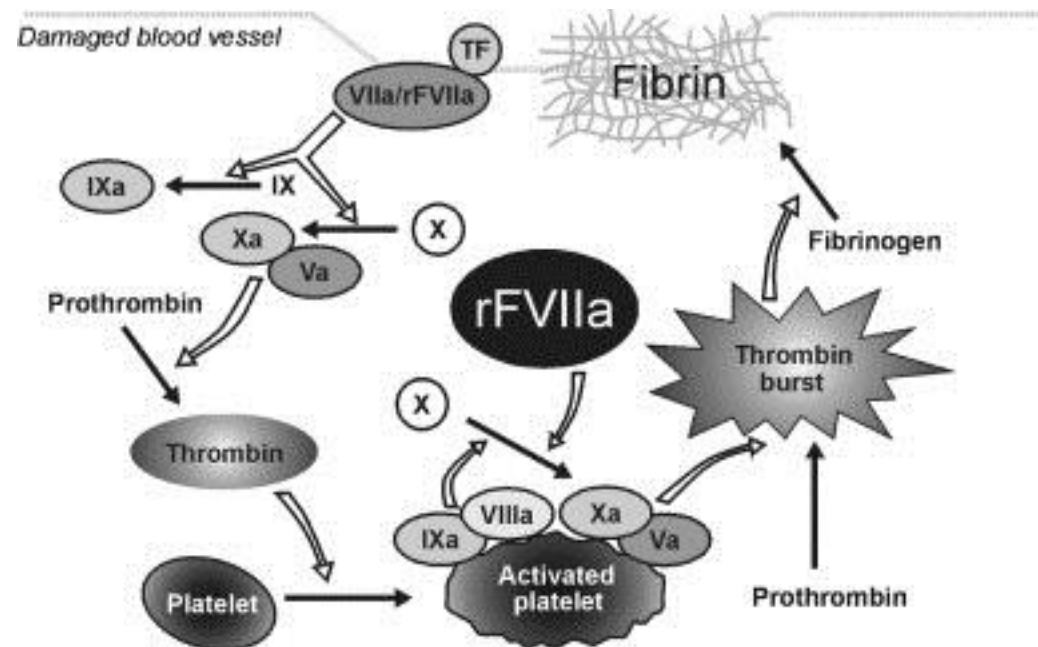


Recombinant Human factor VIIa (rFVIIa)





- Activates the coagulation cascade via the extrinsic pathway.
- The dose required for reversal far exceeds the normal dosing of rFVIIa.
- This creates the possibility of thrombotic sequelae.
- It is not recommended for the treatment of target specific oral anticoagulant (TOSC) therapy.





Desmopressin





- A Synthetic analogue of vasopressin.
- Stimulates the release of von Willebrand Factor. (vWF)
- Increases the production of factor VIII.
- Risks of desmopressin use is low.
- Used in treatment of significant bleeding when taking Direct Oral Anticoagulants (DOAC).





Oral Activated Charcoal





- Its surface adsorbent properties allows for DOAC to be held back from absorption.
- Effective if given within two hours of ingestion for edoxaban and dabigatran.
- Within 8 hours for rivaroxaban.
- Within 6 hours for apixaban.



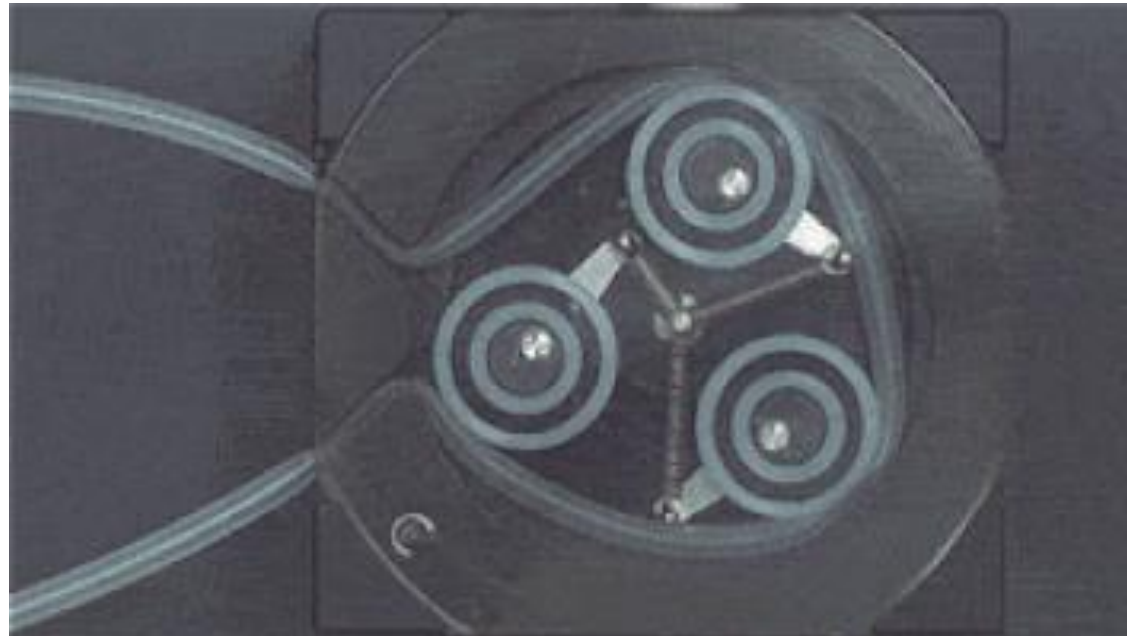


Hemodialysis





- Dabigatran is 80 – 85% excreted through kidney.
- This allows for haemodialysis to be a treatment option.
- Direct factor Xa oral inhibitors are protien bound and only 25 – 35% is excreted renally.
- Thus haemodialysis may not be a treatment option.





Cryopercipitate





- Derived from plasma supernatant.
- Rich in vWF, FVIII, fibrinogen and fibronectin.
- Raises fibrinogen level by 5mg/dL per unit.
- Each unit contains 15 mL and a typical adult dose is 10 units.
- Must be given within 6 hours of thawing or 4 hours of pooling.
- Infusion rate is 5 – 10 mL/mt.





Anti-fibrinolytic agents :-

- Tranexamic acid
- Aminocaproic acid



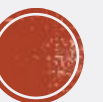


Trenexamic acid





- Tranexamic acid is a synthetic analog of the amino acid lysine, serves as an antifibrinolytic by reversibly binding four to five lysine receptor sites on plasminogen or plasmin.
- Works by inhibiting fibrinolysis.
- Achieves this by inhibiting the binding of plasma to fibrin.
- The risk of adverse reaction and thrombotic sequelae is low.
- Helps on reversal of bleeding in patients on DOACs. (Direct Oral Anti Coagulants)





Aminocaproic Acid





- Aminocaproic acid forms a plasminogen aminocaproic acid complex.
- This prevents the conversion of plasminogen to plasminogen.
- This inactive complex is also rapidly reversible.
- IV dose of 4 to 5 gms during the first hour of treatment followed by an infusion of 1g/hr.





References

- Christos S, Naples R. Anticoagulation Reversal and Treatment Strategies in Major Bleeding: Update 2016. *West J Emerg Med*. 2016;17(3):264–270. doi:10.5811/westjem.2016.3.29294.
- Awad NI, Cocchio C. DReRabMZ ^ S 2] cWP ^ MUdZM] c 2bb ^ PWMcRQ 4 ^ MUdZ ^ _ McVh. 2012;(June):696–699.
- Brockway WJ, Castellino FJ. The Mechanism of the Inhibition of Plasmin Activity by ϵ -Aminocaproic Acid. 1971. <http://www.jbc.org/content/246/14/4641.full.pdf>.
- Kim A. Guideline for reversal of antithrombotics in intracranial hemorrhage. 2017:4–7



Emergency medicine is my first choice !

Dr. T. S. Srinath Kumar

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