Reversal of Newer Anticoagulation agents in Spontaneous ICH

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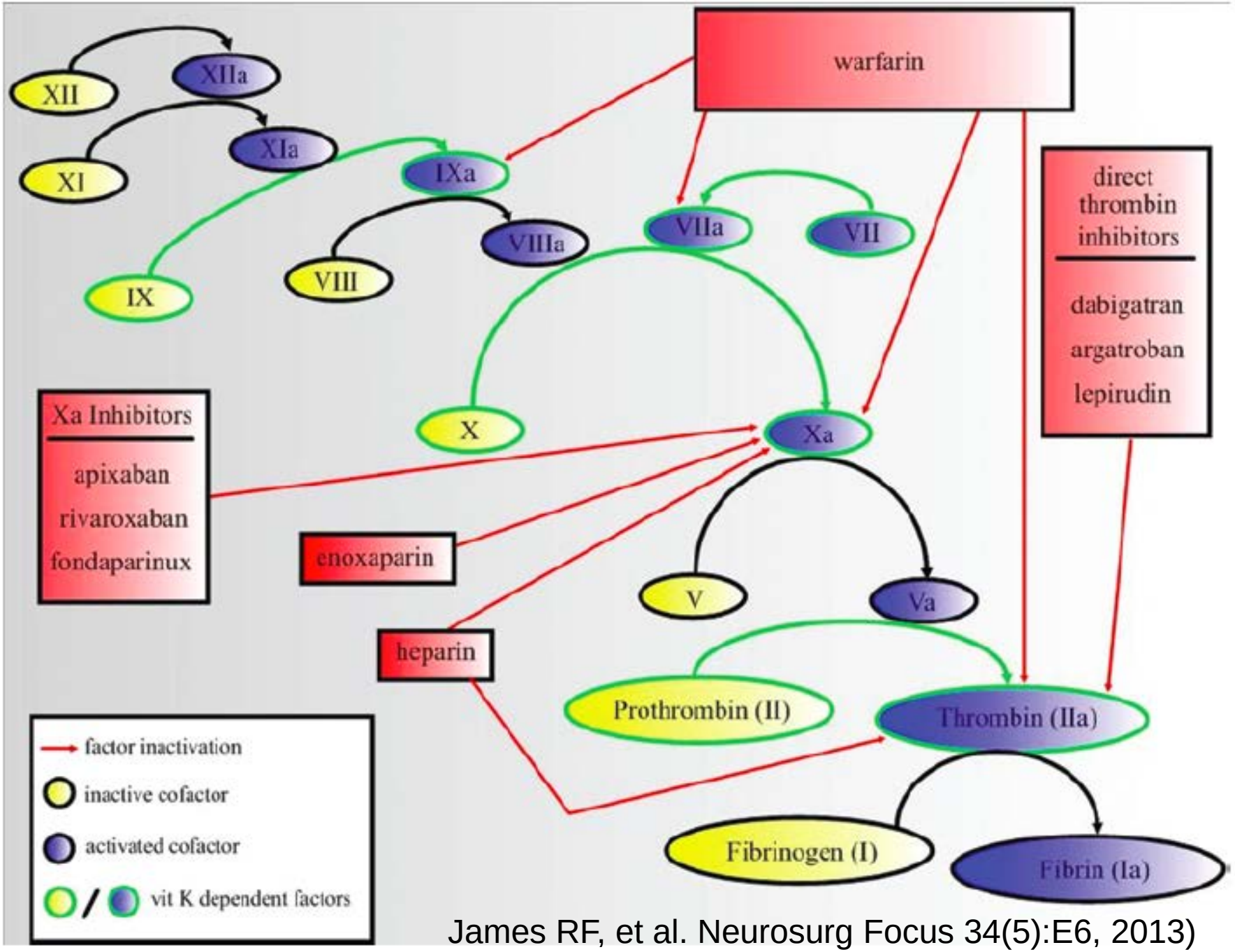
Background

- Increased risk of ICH with INR > 4.0
- Significant limitations of warfarin
- Newer agents –
  - more reliable dose-response
  - absence of need to monitor blood levels
  - Phase III trials suggest lower incidence of ICH compared with warfarin
  - Here to stay, utilization increasing

    Am Coll of Chest Physicians recommend dabigatran
  - No specific antidote



James RF, et al. Neurosurg Focus 34(5):E6, 2013)

The clotting cascade including common anticoagulant medications and their site of action. vit = vitamin.

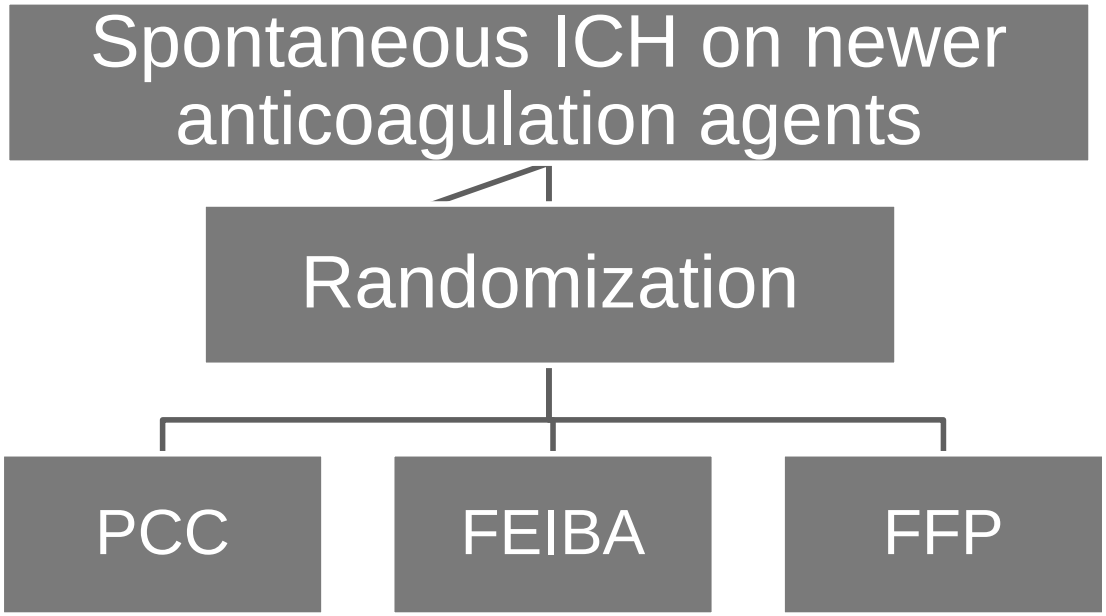
Trial Objective

- Rapid reversal of anticoagulation in non-traumatic ICH patients being treated with new anticoagulation agents (dabigatran, rivaroxaban and apixaban)

Current practice based on little evidence

- Fresh frozen plasma
- Prothrombin complex concentrate (3 factor –VII, IX and X)
- FEIBA (Factor Eight Inhibitor Bypassing Activity) – (activated factors II, VII, IX and X)

Study Design



PCC = prothrombin complex concentrate- II, VII, IX and X
FEIBA = Factor Eight Inhibitor Bypassing Activity – activated II, VII, IX and X
FFP = Fresh Frozen Plasma

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Primary Outcomes

- In-hospital
  - ICH progression-size
  - Laboratory evaluation of reversal of anticoagulation
  - Mortality / Neurologic recovery (modified Rankin scale)
  - Duration of hospitalization
  - Resource utilization – cost of therapy
  - Thrombotic complications

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Inclusion Criteria

- Inclusion
  - Low volume hemorrhage ? 30 cc
  - Minimum GCS
  - Time from last well 0-4 hours?
  - Spontaneous hemorrhage while taking dabigatran, rivaroxaban and apixaban
  - Absence of other causes of ICH, ie tumor, trauma

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Questions

- Simultaneous blood pressure management according to AHA guidelines
- Does current scientific evidence and practice justify a placebo group
- Newer agents in the pipeline. Incorporate an additional study arm to accommodate new therapy (ie Kcentra-4 factor preparation)

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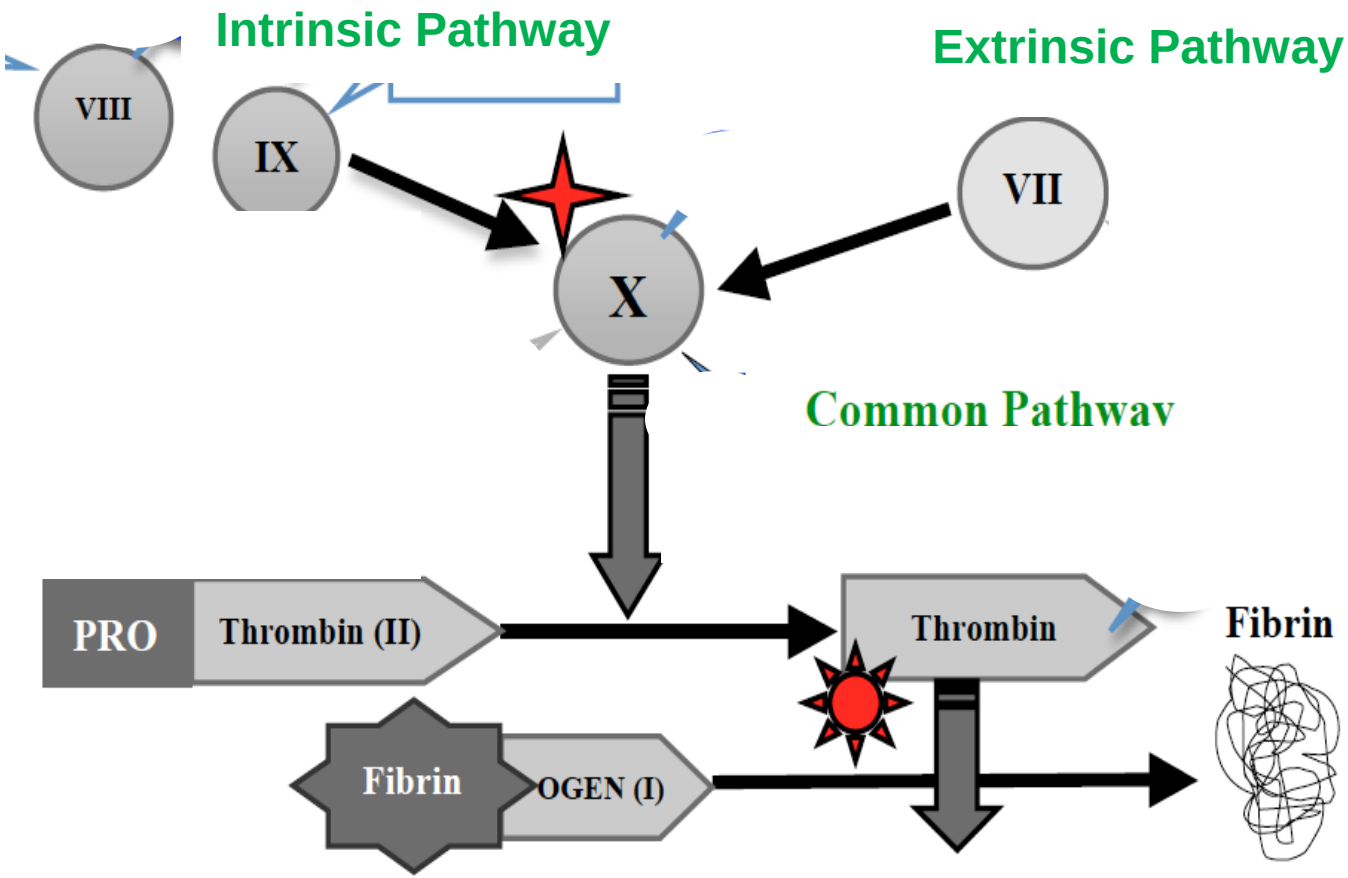

dabigatran (Pradaxa) –inhibits thrombin (factor II)
rivaroxaban (Xaralto) – inhibits Xa
apixaban (Eliquis)– inhibits Xa

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