In my life one of the phrases that I use with my family.
There are no crisis unless there are no blood components in the blood bank. Exsanguination is my idea of an emergency.

After 41 years in high acuity nursing I find that is a true statement – but as our knowledge of diseases and the interplay of anticoagulation/thrombosis have grown- I find that I long for better switches to turn anticoagulation and clotting off and on. This presentation is a review of some of the many variables that the reasonable and prudent nurse needs to review in
the Perianesthesia arena.
I will be clear to speak to on and off label uses of medication.

No Conflict of Interest

Not a speaker’s bureau with any pharmacology industry.

Employed by the State of Alabama

FDA label versus off label uses
<table>
<thead>
<tr>
<th>Objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Outline the different types of diseases needing antplatelet and DOAC inhibitors and delineate the varying plans of care for each.</td>
</tr>
<tr>
<td>2. Compare and contrast reversibility of these pharmacological agents.</td>
</tr>
<tr>
<td>3. Analyze areas of impact of impact of antiplatelet and direct thrombin inhibitors in the perianesthesia setting.</td>
</tr>
</tbody>
</table>

Take away points for you as you walk away from this presentation.
Evidence Based Practice

And

Practice Based Evidence.
98% of the time we want the tilt of anticoagulation so that blood will flow and carry the nutrients and by products of cellular metabolism. But when there is a need for procedural intervention we need wisdom to know how to taper, stop, or continue the disruption of the coagulation cascade.
Which patients are now on direct acting inhibitors, vitamin K warfarin products and or antiplatelet medications is to be about 40% of persons over 50 years of age.

Guidelines and standards of practice for endovascular and vascular surgery advocate the use of these medications.
Like any medication genetic component of pharmacogenetics is the most powerful variable in Absorption, Distribution, Metabolism and Excretion.

FDA trials don’t have the numeracy to predict all the possible genetic variants with the person/drug interaction.

Protein C - PROC
Protein S - PROC 1 gene
Factor V Leiden - F5 on chromosome one
Autoimmune disease therapies
Antiphospholipid syndrome and Lupus create
situations that cause intrinsic cascade activation
Protonics versus Genomics.
The warnings and black boxes of these medications
Which must be pondered
When you are considering the dose and intervals of medications in an urgent / emergent case.

This can be helpful predictor of how much trouble you are in...
Anticoagulants and Antiplatelet

Antiplatelet drugs inhibit platelet aggregation. (arterial thrombus) stroke prevention

Anticoagulants disrupt the coagulation cascade. (venous thrombus) atrial fibrillation related clotting as stroke prevention

Both impact the process of coagulation

Arterial side triad that changes the forces that promote clot are trauma- platelets are typically the first responder
Intrinsic aspect

Venous side is stasis and that is force with greatest is viscosity so DOAC’s and Warfarin
Common Pathway or Extrinsic
When you are taking that home medications list these clinically relevant drug interactions.

### Drug Interactions

- Antiplatelets
- Vitamin K dependent anticoagulants
- Intrinsic Cascade Heparin
- SSRI’s
- Cinnamon, Ginger, Garlic, Ginseng
Aspirin

P2Y_{12} Adenosine Diphosphate Receptor Antagonists

Glycoprotein IIb/IIIa Receptor Antagonists

Most common medication to see on your list...
Aspirin
Each category works in a different way and has increasing potency.
Clodigrel
Turns off platelets for their 7 day life.
## Aspirin and Clopidogrel

<table>
<thead>
<tr>
<th>Aspirin</th>
<th>Clopidogrel (Plavix)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism of Action:</strong></td>
<td><strong>Mechanism of action:</strong></td>
</tr>
<tr>
<td>Blocks thromboxane A</td>
<td>Inhibits platelet activation and aggregation through the</td>
</tr>
<tr>
<td>a prostaglandin that activates platelets</td>
<td>irreversible binding of the active metabolite to the P2Y&lt;sub&gt;12&lt;/sub&gt; class of ADP receptors on platelets</td>
</tr>
<tr>
<td>Non reversible</td>
<td>Non reversible</td>
</tr>
</tbody>
</table>

Platlet transfusions
Don’t forget these pharmacogenomics issues.
Resting
Adhesion
Activation
Aggregation
Resting
Adhesion
Activation
Aggregation

Review of Platelet Plug
Review of Platelet Plug

Adhesion

Resting
Adhesion
Activation
Aggregation
Review of Platelet Plug

Resting
Adhesion
Activation
Aggregation

Secretion
Laboratory Tests

- Platelet Works

- Impedance whole blood aggregometry

- TEG versus ROTEM

Know what your laboratory go to tests for platelet function are and recognize your dialysis patients have dysfunctional platelets.
Resting
Adhesion
Activation
Aggregation
6.5 million folks have atrial fibrillation in the US
2016 numbers

<table>
<thead>
<tr>
<th>DOAC’s</th>
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</thead>
<tbody>
<tr>
<td><strong>Recommended drug classification for anticoagulation in atrial fibrillation</strong></td>
</tr>
<tr>
<td>• Dabigatran (Pradaxa) ®</td>
</tr>
<tr>
<td>• Rivaroxaban (Xarelto) ®</td>
</tr>
<tr>
<td>• Edoxaban (Savaysa) ®</td>
</tr>
<tr>
<td>• Apixaban (Eliquis) ®</td>
</tr>
</tbody>
</table>
Dabigatran is competitive, direct thrombin inhibitors. Because thrombin (serine protease) enables the conversion of fibrinogen into fibrin during the coagulation cascade, its inhibition prevents the development of a thrombus. Both free and clot-bound thrombin, and thrombin-induced platelet aggregation are inhibited.
**Dabigatran-Reversal**

**Praxbind** – idarucizumab is the reversal agent used to stop bleeding due to dabigatran and is very expensive while carrying the additional risk of allergic reaction.

**Lab Tests:**
- HEMOCLOT dilute thrombin assay
- Ecarin clotting time
- Thrombin clotting time
- Activated Clotting time assay

RAXBIND specifically binds to dabigatran and its acylglucuronide metabolites, neutralizing their anticoagulant effect immediately after administration.

Binds with higher affinity than dabigatran to thrombin.

Has no effect on other anticoagulant or antithrombotic therapies.

**Immunogenicity**

Low potential for immune reactions
- 4% of volunteers showed low concentrations of treatment-emergent antibodies that may persist.

Angioedema is always a problem with monoclonal events.
# Checklists for pondering

Consistent to help you think through

Especially helpful with elective cases
Rivaroxaban

<table>
<thead>
<tr>
<th>Mechanism of Action:</th>
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<tbody>
<tr>
<td>• Selective inhibitor of FXa</td>
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<tr>
<th>Role in the Clotting Cascade:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Inhibits free FXa and prothrombinase activity</td>
</tr>
<tr>
<td>• Indirectly inhibits platelet aggregation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lab Tests for Efficacy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Specific calibrated anti-FXa assays</td>
</tr>
<tr>
<td>• Prothrombin time obtained in seconds with sensitive reagents</td>
</tr>
</tbody>
</table>

Xarelto

**Rivaroxaban** is a selective inhibitor of FXa. It does not require a cofactor (such as Anti-thrombin III) for activity. Rivaroxaban inhibits free FXa and prothrombinase activity. Rivaroxaban has no direct effect on platelet aggregation, but indirectly inhibits platelet aggregation induced by thrombin. By inhibiting FXa, rivaroxaban decreases thrombin generation.
Apixaban (Eliquis) inhibits free and clot-bound FXa, and prothrombinase activity. Apixaban has no direct effect on platelet aggregation, but indirectly inhibits platelet aggregation induced by thrombin. By inhibiting FXa, apixaban decreases thrombin generation and thrombus development.
Edoxaban Savaysa is a Factor Xa inhibitor. This medication requires calculation of creatinine clearance for optimal outcomes and has a black box warning about renal function.

<table>
<thead>
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<th>Mechanism of action</th>
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<tr>
<td>• Direct FXa inhibitor</td>
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<table>
<thead>
<tr>
<th>Role in Clotting Cascade</th>
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</thead>
<tbody>
<tr>
<td>• Similar to Apixaban</td>
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<table>
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<tr>
<th>Special considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Requires calculation of CrCl for optimal outcomes</td>
</tr>
<tr>
<td>• Black box warning for increased risk of stroke in some patients with CrCl &gt;95 mL/min</td>
</tr>
</tbody>
</table>
## Four questions

1. Underlying disease versus procedural intervention?
2. Elective versus urgent?
3. Bridge Therapy required?
4. Impact in intraoperative and postoperative settings?

Pondering Points
### Risks versus Benefits

<table>
<thead>
<tr>
<th>CHADS2 – VASc Score</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>C</td>
<td>Congestive Heart Failure</td>
</tr>
<tr>
<td>H</td>
<td>Hypertension (&gt;140/90 mmHg)</td>
</tr>
<tr>
<td>A</td>
<td>Age &gt; 75</td>
</tr>
<tr>
<td>D</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>S₂</td>
<td>Prior TIA or stroke</td>
</tr>
<tr>
<td>V</td>
<td>Vascular disease (MI, aortic plaque etc)</td>
</tr>
<tr>
<td>A</td>
<td>Age 65-74</td>
</tr>
<tr>
<td>Sc</td>
<td>Sex category (Female = 1 pt)</td>
</tr>
</tbody>
</table>

Atrial Fibrillation stroke risk
Change them from long acting warfarin to short acting heparin

May still be relevant in mechanical heart valve and high risk series


Anesthesia Societies Recommendation

European Society of Anesthesiology and French Working Group on Perioperative Haemostasis Recommendation:

- Interruption of DOAC therapy 24 hours (2 or 3 half-lives) prior to the a procedure that carries a low bleeding risk
- Interruption of DOAC 5 days prior to an intervention with a medium or high bleeding risk

Few Randomized control trials on DOAC and Anti-Platlet discontinuation
The Clinician Should Review:

- Half life of the agent
- Renal function of the patient
- High vs low risk of procedural bleeding

Highest risk:
OB
Neurosurgery
Vascular
Cardiothraic surgery
Clinical Decisions in Elective or Urgent

Symptoms indicate:
- Severity of underlying disease
- Elective or urgent procedure
- High risk stratified procedure

RISK BENEFITS and ALTERNATIVES
Procedure Consideration

Time for Huddle
Risks and Benefits

Pacemaker versus Open Heart Surgery
How much trouble am I in?
Practice of each discipline: Nursing, Medicine
Take Away Points
Blood Management Process
Current article in Critical Care Nurse

Blood Flow

Versus

Cellular Death
Clinical Presentation: Thromboisis

ENDOTHELIAL INJURY

THROMBOSIS

ABNORMAL BLOOD FLOW

HYPERCOAGULABILITY

All about the Blood
Emergent Cases

Reversal and Initiation of Active Bleeding Protocol

Salient Questions:
1. Time and dose of last medication?
2. Half life of medication?
3. Renal Function?

Going anyway>>>>>
# Emergent Hemorrhage

**Bleeding while on Antiplatelet Medications**
- Platelet Transfusions
- DDAVP- off label use

**Acute and Operative Bleeding in Patients with Hemophilia A and von Willebrand Disease**
- Desmopressin agents
  - Give intranasal as 1 spray in a single nostril (150mcg) or 1 spray in each nostril (300mcg)
  - DDAVP injectable 0.3mcg/kg by slow infusion prior to surgery
Serious or Life-threatening Bleeding on DOAC

- **< 4 Hours**
  - Activated Charcoal
  - Coagulation Factors
  - Blood Components

- **4 – 36 Hours**
  - Coagulation Factors
  - Blood Components

- **> 36 Hours or Renal Impairment**
  - Lab Testing
  - Targeted Blood Components
Neurocritical Care Society

Recommendations in Intracranial Hemorrhage by Agent

- **Direct thrombin inhibitors (Dabigatran)**
  - Activated charcoal for accidental overingestion
  - Idarucizumab (Praxbind) for ICH within 3-5 half lives of agent
  - aPCC or 4-factor PCC if Praxbind is unavailable
  - Hemodialysis in patients with renal insufficiency or overdose when Praxbind is unavailable

Recommendations in Intracranial Hemorrhage by Agent

- **FXa inhibitors**
  - Activated charcoal for accidental overingestion
  - aPCC or 4-factor PCC for ICH within 3-5 half lives of agent
  - rFVIIa is not recommended first line due to incidence of ADE

Watchman Device

Case Study: https://youtu.be/8O2Hba-JQoQ
Perianesthesia

Takes an Interdisciplinary Team to Plan Each Patient’s Care
References


References


Questions? Comments?
We are happy to help you!

acollins-yoder@ua.edu