This month we will take a look at the new anticoagulants that are on the market. We have all seen the commercials on TV talking about these new meds, but what does it mean for the EMS provider.

It is estimated that approximately 33.5 million people worldwide have atrial fibrillation (AF) ¹. In 2005 in the United States there were approximately 3 million people affected by AF and it is projected to rise to about 8 million by 2050.² Only about half of the 3 million US patients with AF use anticoagulants and are largely unprotected from the high risk of life-altering strokes, even if they take aspirin.³

One of the longest used anticoagulants is Warfarin which commonly is called Coumadin® or Jantoven®. Warfarin works on the clotting cascade by blocking vitamin K which plays a key role in helping the blood clot.⁴ These meds have traditionally been prescribed for deep vein thrombosis (DVT’s), pulmonary emboli (PE) and to prevent venous thromboembolism (VTE) and stroke in people with non valvular heart disease or have mechanical heart valves.

It is recommended that patients that take Warfarin have their PT/INR (lab draw) checked every 1-4 weeks. PT stands for prothrombin time and INR is international normalized ratio. A normal PT/INR for someone not on Warfarin is about 11-13.5 seconds and an INR of 0.8 to 1.1. If you are on Warfarin, your INR is increased to anywhere between 2.0 and 3.5.

Several medications and dietary factors can inhibit or enhance the effects of this medication and it also is not dialyzed very well. Eating foods which are rich in vitamin K can affect your INR levels. Foods such as kale, spinach, brussel sprouts, parsley, collard greens, mustard greens, chard, and green tea can all affect this. This is one of the reasons why in the current TV commercials for the new medications on the market, they show people enjoying salads and drinking tea.

When people are first placed on Warfarin they may also be placed on Heparin in the hospital usually as they are monitored until they can get them to the appropriate INR levels they want. One of the other challenges with Warfarin is the ½ life of this medication. Depending on the type of Warfarin you are taking, the half life can range from 21 to as much as 89 hours. Warfarin is
mainly excreted through the urine, so having good kidney and liver function are extremely important.

The newest meds on the market are called Novel Oral Anticoagulants or (NOACs). There are 2 classes of these medications. Direct thrombin inhibitors like Pradaxa® and direct factor Xa inhibitors like Xarelto®, Eliquis® and Savaysa®. Overall indications for these meds are very similar to Warfarin. Reduce the risk of stroke and systemic embolism in nonvalvular AF, treatment of DVT and PE’s. None of these medications showed a higher risk of bleeding when they were compared to Warfarin when they were evaluated by the FDA.

**Pradaxa® (dabigatran)**

This medication was initially approved by the FDA in 2010 for DVT/PE prophylaxis following hip replacement surgery. Primarily eliminated by the kidneys and has a half-life of about 12-17 hours. When evaluating patients clotting factors with the use of this med, they typically will use the aPTT or activated partial thromboplastin time. When a patient takes 150mg BID or twice a day, their clotting time was between 40-76 seconds. A normal aPTT is 25-40 seconds in patients not taking anticoagulants. This medication can also be dialyzed.

**Xarelto® (rivaroxaban)**

Xarelto was approved by the FDA in July of 2011 to reduce the risk of DVT and PE following knee or hip replacement surgery. This medication was then also approved for the treatment of DVT’s and PE’s. It was used for non valvular atrial fibrillation to reduce the risk of strokes as well. The medication is taken 1-2 times daily and is cleared through the kidneys with some of the medication clearing through the intestines. Half life of Xarelto in elderly patients 60-76 years of age and those with renal impairment is about 11-13 hours and for those 20-45 years of age is about 5-9 hours.
Eliquis® (apixaban)
Eliquis is prescribed to patients with non valvular AF, DVT prophylaxis in patients undergoing knee replacement, and for treatment of PE. Half life of Eliquis is about 12 hours with most of the clearance coming through the intestines. Hemodialysis does not appear to have a substantial impact on the patient taking this med as well. There are agents that can be administered in the ER to bind to the Eliquis. They can consider Prothrombin Complex Concentrate or (PCC), Factor VIIa administration or activated oral charcoal which could reduce the absorption of the Eliquis.

Savaysa® (edoxaban)
This drug was most recently approved as the 4th NOAC medication. It also is a factor Xa inhibitor and prescribed for non valvular AF, treatment of DVT, PE and embolism prophylaxis. This medication is reliant on the kidney function to excrete the medication. It is noninferior to Warfarin therapy with respect to prevention of stroke or systemic embolism and significantly lower rates of bleeding and death from cardiovascular causes. The half-life of Savaysa is about 10-14 hours.

Something that all of these meds have, either in the name of the med or the actual drug name, they all have Xa in the generic name. We noted earlier in this article that they all effect the factor Xa inhibitors in the blood.

In the hospital setting there are several options that were listed above. One of which was fresh frozen plasma or FFP. Plasma we know works on the clotting factors, so giving the patient FFP will help to slow the bleeding down. Each unit of FFP is about 250ml and does contain those clotting proteins the patient needs. To get a significant change in the patients INR, the patient may actually need up to 4 units of FFP to increase the level by 10%. So they have to be very cautious on the administration to renal and heart failure patients because we just gave them all that fluid.

Kcentra®
Another med that has grown in popularity is Kcentra®. This medication contains several factors such as II, VII, IX, X, Proteins C and S. It is a blood product derivative and is classified as a hemostatic agent. It is a Vitamin K antagonist reversal in patients with acute major bleeding or need for emergent surgery or invasive procedures. This is used also for intracranial hemorrhage due to various antithrombotic agents.
**Praxbind®**
This medication is a specific reversal agent for anticoagulant effects of Prodaxa (dabigatran). It was actually accelerated through the FDA for approval in 2015 and only works on Prodaxa.

**TXA – Tranexemic Acid**
There is ongoing research happening with the use of TXA on NOAC agents. Tranexemic Acid or TXA is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect through the reversible blockade of lysine binding sites on plasminogen molecules. In other words, it would help the patient actually clot. This is why there also has been so much research with this drug in the trauma patient. If they are bleeding, there is thought that giving TXA will help with that bleeding.

The biggest caution for patients that are prescribed anticoagulants is that administering a medication to increase clotting should always be considered before administering. (i.e. life-threatening bleeding risk vs. need for non-emergent surgical intervention).

So what do we do if our patient is bleeding and is on one of these medications? First thing to do is stop the bleeding if able. Compress the bleeding area and elevate, if an extremity. The patient may need fluid replacement through IV’s. This may mean you will give your patient 200ml increments to maintain a SBP >90. This may also mean that they may need packed red blood cells, fresh frozen plasma or platelets once at the ED. The ED may even consider the use of an emergent reversal agent if that can be achieved within a reasonable time frame or concern for re-bleeding. A lot of these patients will have underlying cardiac conditions, so place them on the monitor and make sure to get a good patient history including medications to provide them with the best care. Per MWLCEMS protocol it states, Anticoagulants can increase systemic or intracranial hemorrhage; notify OLMC ASAP."
Please be extra attentive to our elderly patients on Warfarin or NOAC (novel oral anticoagulants). One example was an elderly female who had suffered a hip fx with pelvic hematoma. She was on warfarin and a beta blocker. The pt was seriously hypotensive (SBP 60s – 80s) for several hours in an ED. Pt was in ED 7 hours and the patient spent 9 days in the hospital, the majority in ICU. She was in traumatic shock when she went to ICU. She received 5u PRBC, lots of fluid, and was on 2 vasopressors. She developed anasarca (a medical condition characterized by widespread swelling of the skin due to effusion of fluid into the extracellular space) and DIC (disseminated intravascular coagulation, abnormal clumps of thickened blood (clots) form inside blood vessels. These abnormal clots use up the blood's clotting factors, which can lead to massive bleeding in other places). Family chose comfort measures only and the patient was discharged to hospice care.

We would like to thank Joe Zarek, Kari Cieslak, Mindy Lynch and Dr. Greway from Flight For Life for their contribution and work in developing this CE packet for our use.

References
10. McHenry Western Lake County EMS System Protocol page #9 Elderly SOP
McHenry Western Lake County EMS System
Paramedic, EMT-B and PHRN
Optional Continuing Education
2018 Optional #2
New Anticoagulant Therapies

Post Test

NAME: ______________________________________ DEPT: __________________________ DATE: ____________________________

(PRINT CLEARLY)

Circle one: EMT-B EMT-P PHRN

1. One of the longest used anticoagulants is ____________, or ________________.

2. The above med was traditionally prescribed for what types of problems.
   A. ______________________
   B. ______________________
   C. ______________________
   D. ______________________

3. If your patient has been placed on Warfarin, their INR may be increased to what range?
   A. 1.0-2.0
   B. 2.0-3.5
   C. 3.5-4.0
   D. 0.8-2.2

4. Eating foods which are rich in vitamin K can affect INR levels in people that take Warfarin. Name some of the food(s) and drink(s) that should be avoided.
   A. ______________________
   B. ______________________
   C. ______________________
   D. ______________________

5. What are the two classes of meds in the Novel Oral Anticoagulants referred as?
   A. ______________________
   B. ______________________

6. Name the 4 NOAC’s that were discussed in the article.
   A. ______________________
   B. ______________________
   C. ______________________
   D. ______________________
7. You respond to a residence for a male patient that cut his hand with a saw. The patient advises you he is on Pradaxa, what clinical significance does this information have on the care of this patient?

8. In referring to the above question, how would you control this patient’s bleeding?

9. Pradaxa was first approved in 2010 for the treatment of DVT and PE following what?
   ________________________________________________________________________.

10. Xarelto was approved in 2011 to reduce risk of DVT and PE, but was then approved for ______________ to reduce the risk of ________________.

11. When treating a patient on Eliquis, what two medications could be considered to help bind to the med to assist in the absorption?
   A. ______________________________________________________________________
   B. ______________________________________________________________________

12. Kcentra is a blood product derivative and is classified as a ________________.

13. Praxbind is a specific reversal agent for Savaysa?
   TRUE               FALSE

14. TXA is a synthetic derivative of the amino acid ____________ that exerts its antifibrinolytic effect through the __________________ binding sites on __________________ molecules.

15. Transexamic Acid speeds up the process of blood clotting by preventing the breakdown of ____________________________?

If you are NOT a member of the McHenry Western Lake County EMS System, Please include your address on each optional quiz turned into our office. Our mailing address is: Northwestern Medicine – McHenry Hospital EMS, 4201 Medical Center Drive, McHenry, Illinois 60050. We will forward to your home address verification of your continuing education hours.

If you ARE a member of our EMS System, your credit will be added to your Image Trend record. Please refer to Image Trend to see your current list of continuing education credits. Any questions regarding this can be addressed to Cindy Tabert at 224-654-0160. Please fax your quiz to Cindy Tabert at 224-654-0165.