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### Case Study: Intracranial Hemorrhage and Anticoagulation Reversal in the ED

#### Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.

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#### Dr. Backus:

So let me please present to you a case in order to make this theory a bit more practical for you. Let's imagine ourselves, a 50-year-old female who comes to the emergency department with acute onset of left-sided weakness. She has a history of atrial fibrillation and she is on rivaroxaban 15 milligrams per day. You have just ordered a CT scan and CDC hematoma. And my question is, what are your next step? So, let's go over them together.

First of all, sometimes we do get a call from the EMS servers saying that they're on their way with a patient who's unconscious, and who is at a risk of bleeding. So it is important to make the resuscitation of this patient a team effort. And consult your neurosurgery, radiology or even your hematologist. Consult them early in the process. As I said before, in order to prohibit hematoma expansion, it's important to lower your blood pressure under 140 millimeters mercury. If there is an indication to reverse anticoagulation, it's important to start as soon as possible and not wait until all the diagnostics have been done. Hyperosmolar therapy might help you to reduce the intracranial pressure. And then it's important to perform a CT angiogram to see if there's anything that can for example be called by your interventional radiologist.

So before we go into a little bit more detail on the reversal and repletion, I would like to take you through the clotting cascade which starts either at the intrinsic pathway or at the extrinsic pathway. In both pathways, activate factor Xa. Factor Xa on itself then turns prothrombin into thrombin which is activated factor 2. Then activated factor 2 turns fibrinogen into fibrin which then forms a stable clot. When we look at the coumarins, they block the synthesis of four clotting factors, factor 2, 7, 9 and 10. And in fact, the liver does synthesize these factors but they cannot be activated. For these patients, repletion of these inactive clotting factors into active clotting factors is the strategy we need. When we look at the DOACs, there are two different DOACs. You have the direct thrombin anti-agent, which is dabigatran so it has the T-R in its name, and we have the factor Xa inhibitors who all have an X-A in their name. And for the DOACs, we need to reverse these agents.

So, when we face a patient with a life threatening bleeding in the emergency department, we need to replete the clotting factors in patients using a coumarin. We give four factor PCC, which is a combination of the four clotting factors, and it should be given in 25 to 50 units per kilogram intravenously. And the targeted INR should be below 1.3. Also, it's important to give vitamin K 10 milligrams intravenously. It will not help you immediately, but it will help to synthesize new clotting factors in the liver and it will diminish the rebound effect a few hours later. Like I said, tranexamic acid might be indicated in some patients and for those on DOAC, we have currently two antidotes on the market. For patients using dabigatran, the correct antidote is either rituximab, which is given in five grams intravenously as a bolus. And it really quickly reduces the anticoagulative effect of dabigatran and corrects hemostasis. For those patients on a factor Xa inhibitor, andexanet alfa is the indicated antidote. And depending on the dosage of factor Xa, it should be given in either a low or a high dose. And you give it first as an initial bolus, and then as a continuous infusion over the next two hours. So in

our case, a woman with intracranial hemorrhage who is on rivaroxaban, using a factor Xa inhibitor, the indicated antidote and treatment here would be andexanet alfa.

So that brings us to a few practical steps. First of all, you must be aware whether or not andexanet alfa is available in your hospital. And if it is available, where is it? Is it at the emergency department or is it maybe at the emergency pharmacy somewhere else or on the ICU? And so you must know where to find it in an emergency situation. Also, it is important to instruct your team already before these emergency patients are coming in. So make sure that you have educational meetings, and that your team knows the right protocol, the right dosage, and how to infuse this medication. When you have andexanet alfa somewhere on the shelf, make sure that you have the necessary material also next to it. For andexanet alfa, you need a filter like is shown here on the slides. And so, beware that your team knows how to use that filter and that it's easy to grab. Then calculate the correct dosage. And well one must also be aware of the cost and know how this works in your institution.

When we look at the dosage, I've given here the two most used factor Xa inhibitors. So, if a patient is on apixaban, on a low dose, which is five milligrams per day or less, irrespective of the time since last dosage was taken a low dose of andexanet alfa is indicated. When the patient is using a higher dose of apixaban when the last dosage was taken less than eight hours ago or when it's unknown a high initial dose of andexanet alfa is indicated. When your patient is on a low dose of rivaroxaban, which is 10 milligrams per day, on any time, a low dose of andexanet alfa is indicated. In our case, our patient is using 15 milligrams of rivaroxaban. And since she's unconscious, we don't know exactly when her last dosage was taken. So a high bolus of andexanet alfa is indicated.

So let me bring this all into a flow chart. And for those who cannot read it from the backside, this flow chart can be downloaded from the EMCREG website. So in case we have a patient with life threatening bleeding, our first priority is to give supportive care. So give hemodynamic support, manage your intracranial pressure or the blood products when needed. And if you have a point of care test available, it's good to have your INR tested to measure the level of coagulation that is in the body. For those patients who are on warfarin, like I said four factor PCC is indicated with dosage of 25 to 50 international units per kilogram and also give vitamin-K 10 milligrams intravenously. For patients on dabigatran, either rituximab five grams intravenously should be given. And for patients with a factor Xa inhibitor like our patient, andexanet alfa is the indicated antidote. When you have an indication for andexanet alfa, again, we must ask ourselves, is the last dosage taken more than eight hours ago, then we should give a low initial dosage of 400 milligrams, given at a speed of 30 milligrams per minute, followed by an intravenous infusion of two hours or four milligrams per minute. When your patient is using a high dose or when the last dosage was less than eight hours, a high bolus of 800 milligrams is indicated, followed by an intravenous infusion of eight milligrams per minutes for two hours.

So, to summarize. Patients on oral anticoagulant carrier risk of severe intracranial bleeding. In case of severe bleeding, first priority is to give supportive care. Knowledge of reversal strategies is important for the emergency physician. The most important question is, which are anticoagulant when and how much. For coumarin, replete with four factor PCC and vitamin K. And for DOACs, use the specific reversal agent in the right dosage, right protocol and make use of a filter. Thank you very much for your attention.

**Announcer:**

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