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## Life-Threatening Traumatic Bleeds and Anticoagulation Reversal in the ED

### Announcer:

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### Dr. Gibling:

Finally, I want to have somebody that, just like the previous two speakers, probably doesn't need an introduction to you, because he's responsible in large part to organizing this meeting here in Berlin, and that's the Professor Dr. Martin Mockel, and he is a Medical Director of Emergency and Acute Medicine. In addition to his emergency medicine credentials, he is a cardiologist, which makes for an ideal care of a patient, obviously with chest pain, but all of the cardiologic conditions that come into the emergency department. He's at the departments of Campus Mitte and Virchow here in Berlin, Professor of Cardiovascular Process Research, he's a Vice Dean for Study and Teaching at the Charite Universitätsmedizin Hospital here in Berlin. I want to thank Martin for being here today, and we're looking for your presentation on, looking forward to it, on life-threatening traumatic bleeds and anticoagulation reversal in the ED. Dr. Mockel.

### Dr. Möckel:

Yeah, thank you, Brian, for the nice introduction. Ladies and gentlemen, your colleagues. Okay, these are my disclosures. So, I'm consulting the major companies which produce DOACs.

So, let's start with the specifics of coagulopathy of trauma. So, first, up to 40% of traumatic deaths are results of hemorrhage. So, the leading preventable cause of trauma-related deaths, and a significant number of patients arrive already in the shock room with coagulation changes. So, the event starts before the ED, and you have to keep that in mind. Depending on your specific healthcare system, you may have physicians acting in the pre-hospital space, like we do in Germany, and specifically in Berlin. And some of the steps which I describe now can be done also in the pre-hospital setting. So, many trauma patients with massive hemorrhage who die, do that despite surgical control of bleeding, and also resuscitation with crystalloid and factor-poor blood products lead to dilution of clotting factors, and may make the situation more severe. So, the lethal triad is acidosis, hypothermia, and bleeding.

So, if we come back to the scene, the initial approach is to evaluate as any other trauma patient, so the primary survey, doing ABCD, as you have heard now several times also by my colleagues, and then you start the secondary survey. And in trauma, the source control is key, so if you see it bleeding, you have to compress. You may use a tourniquet in very severe situations, and then the next step is surgery, exploratory laparotomy, if you have intraabdominal bleeding, transfixation of extremities, and maybe craniotomy for intracerebral bleeding. And one possibility is also embolization. So, the radiological approach, for example if you have a splenic hemorrhage or something like that, but in trauma, usually the direct compression, tourniquet, and the surgical approach is what primarily happens.

So, you have to assess the anticoagulation status, we are talking about patients being under anticoagulation, and if you prescribe anticoagulation, oral anticoagulation to your patients, you usually have to explain to them that one of the risks is that they get a trauma

and will bleed in a trauma situation. So, these are the two major risks for explaining to the patients. So spontaneous bleeding is mostly GI bleed, and traumatic bleed under anticoagulation. So, with respect to Vitamin K inhibitors, you have to assess PT and INR with respect to factor Xa inhibitors, PT, anti Xa levels, and also a thromboelastography. In DOACs, it's important, and you have heard that from my colleagues, that you look for the time from last dose, because this may be important for reversal. You need to look for the renal function, because we almost always see that patients, older patients who are longer on this type of medication, may accumulate also these substances, and although the intake may be 8 or 12 hours before, they may have higher levels of the agent in the system. And also, you may use specific assays for measuring concentration of the agent. And with the direct thrombin inhibitors, or the direct thrombin inhibitor, PTT and the dilute thrombin time, can be done, Ecarin clotting time, and also thromboelastography.

So, the coagulopathy of trauma has been seen differently in the last years. So, a couple of years ago, so even in the pre-hospital care, much volume was infused, and now we are a little bit on the side of low-volume resuscitation. So, when we use non-blood components, and we use crystalloid solutions, but we don't want to dilute so much, so we use it just to keep up the perfusion pressure to the minimum needed. And the next steps are packed red blood cells, or whole blood, fresh frozen plasma. And then you start in a one-to-one way with packed red blood cells and fresh frozen plasma, or in the 1:1:1 way, adding also platelets, and as you heard from Rick, usually you wait for a first platelet count, which should be available in your center within less than 30 minutes.

So, with respect to the specific situation in trauma, you have to keep in mind that you have, in anticoagulant patients, a pharmacologic anticoagulation change which is intended with anticoagulation, but you also have a trauma coagulopathy, and it could be difficult to differentiate what happened. And therefore, the strategy is a little bit different if you have a, let's say minor or compartment trauma, or a head trauma with intracranial hemorrhage, where you have not a massive loss of blood, or a massive loss of blood in amputation or polytrauma. So, important factors to consider are the last dose, as I said before, the half-life of the substance. You learned from Barbara already that we have a long half-life of the Vitamin K antagonists, and the various, but shorter half-life of the DOACs. You have to also keep in mind what the severity and location of bleed is, so, do you have direct surgical options or not? And also whether there's availability of specific reversal agents versus the off-label use of 4 Factor PCC.

So, as I said before, the main stem of resuscitation in trauma is whole blood, plasma, and platelets. And then, depending on what type of anti-coagulant the patient takes, you have the Vitamin K antagonist, where you use Vitamin K 4 Factor PCC, and maybe additional fresh frozen plasma. You have the option in factor Xa inhibitors to use andexanet alfa, or 4 Factor PCC. And then dabigatran, so the only direct thrombin inhibitor, you can use idarucizumab, and also as an alternative for 4 Factor PCC. I would like to highlight at this time that the combination of 4 Factor PCC and anti-coags is usually off-label, and you should keep in mind that the combination may place a patient also at risk for thrombotic complications depending on the situation he's in. So, it's not a reflex just to put in an anti-coag, and say okay, and then we see what type of other components we may transfuse. You should keep in mind that the combination maybe also takes some risk. Also, you have to check whether there are concomitant medications, like aspirin for example, and you may need to transfuse platelets. Also, there are may be some comorbidities, like uremia, or liver disease, or heart disease, which also may influence the coagulation situation. In addition, and this adds on the precautions which I mentioned, you should also assess a baseline risk of thromboembolism. So, the patient's on anticoagulation, they have usually an indication for that, and this indication is not away just because they have a trauma, so you need to keep in mind that after the primary resuscitation you may also need to anticipate thrombotic complication, and you have to plan, once you have saved the patient, when to restart anticoagulation.

So as a general overview, the bleeding episode may be minor, moderate to severe, or life-threatening, and we're talking here more about the life-threatening situation. So, in minor bleeding, it's only delay or hold one to two doses. You do local measures, for example, if you have nosebleed, or you have bleeding after a small fall or so in an old patient, you just stop the bleeding by local measures, and you may stop the anti-thrombotic therapy if it's more than minor, and you have supportive management, including hemodynamic support, transfusion if needed. And in life-threatening bleeding, you have to consider the reversal, which is protamine in the heparin treated patient, andexanet in the Factor Xa treated patient, idarucizumab in the patients with direct thrombin inhibitor, and as said before, 4 Factor PCCs, let's say the conventional, conservative way of treatment. And you should always aim at source control, so direct intervention in trauma, mostly surgery.

And I come back by purpose to this flow chart which have been shown already in the presentation of Barbara. So, this is just to remind you that the indication for potential reversal is life-threatening bleeding, and you have to be aware what that is. And life-threatening bleeding is always intracranial bleeding, and it is exsanguine, so it's exsanguination in a mass trauma, or in a GI bleed. So, these are other indications. And then as a reminder, you have the possibility to use andexanet in the factor Xa inhibitors. And there, it's important to know the dose, as Barbara said, and also the time of the last intake. But in doubt, you take the higher dose.

#### Announcer:

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