BBGuy Essentials 086CE:
Scary Stories from the Transfusion Service with Mark Fung and Jay Hudgins
Released October 30, 2020

Mark: Hi, this is Mark Fung from the University of Vermont.

Jay: And I'm Jay Hudgins from the University of Southern California, and this is the Blood Bank Guy Essentials Podcast.

Joe: Are you scared? Well, maybe you should be! Hmmm… Welcome to episode 086CE of Blood Bank Guy Essentials, the podcast where I'm really just trying to do one thing: Help you learn the essentials of Transfusion Medicine. My name is Joe Chaffin, and I'm your host! OK, maybe today, on this special Halloween 2020 episode, I have one other goal. I want to share some SCARY stories from the transfusion service, with my friends Mark Fung and Jay Hudgins.

But first, you should know that this *is* in fact a continuing education episode. The free continuing education credit is provided by TransfusionNews.com, and Transfusion News is brought to you by Bio-Rad, who has no editorial input into the podcast. This podcast offers a continuing education activity where you can earn several different types of credit, including: One *AMA PRA Category 1 Credit™*, one contact hour of ASCLS P.A.C.E.® program credit, or one American Board of Pathology Self-Assessment Module (or "SAM") for Continuing Certification (that is, as long as the American Board of Pathology requires those). To receive credit for this activity, to review the accreditation information and related disclosures, please visit www.wileyhealthlearning.com/transfusionnews.

I've got a "treat" for you today (ok, no tricks!). A couple of weeks ago, my friend Dr. Mark Fung emailed me, and Mark said something to the effect of, "Joe, you've been a lazy bum all summer. You haven't put out podcast episodes in forever, so how about if we get together and talk about scary stuff in the transfusion service to release right around Halloween?" So, I have to give him credit; it was a great idea, and this podcast episode came together fairly quickly after that. So Mark, and Dr. Jay Hudgins from USC, and I are going to discuss some of the most intimidating things we've come across in our collected years in blood banking. We are going to hit eight different situations, and try to help you understand how to approach some of those tough situations that at first seem impossible. And I have to say, some of these cases actually come from an appeal that I out out on Twitter last week, to try and get people to talk about some scary situations. We were overwhelmed with your responses, and couldn't include even a fraction of them! But we are so grateful for the cases you sent in.

But you should be really clear on this: What we are about to share are opinions! You must not think of this episode as being proscriptive and this is the only option, these are the only things you can do. You need to check with local medical and regulatory authorities, because where you practice may be different, and opinions may be different than what we are giving here, ok?

So, before we start, let me tell you a little about my guests. **Dr. Mark Fung** is professor of pathology and laboratory medicine at the University of Vermont. Mark

has served in various leadership capacities within the AABB and related organizations. He has been the chair of both the AABB Hemovigilance Committee and the AABB Clinical Transfusion Medicine Committee. He plays a significant role in leadership positions in the BEST research collaborative, and he was the editor-in-chief for the 18th and 19th editions of my favorite blood banking textbook, the *AABB Technical Manual.* He is currently also on the editorial board for the journal *Transfusion*.

Dr. Jay Hudgins is the medical director of the tissue and transfusion medicine service at Los Angeles County Medical Center at USC Jay is also an assistant professor of clinical pathology at Keck School of Medicine. Jay graduated from Philadelphia College of Osteopathic Medicine, and went on to complete his training in clinical Pathology at Rutgers-Robert Wood Johnson Medical Center, followed by a transfusion medicine fellowship at The Cleveland Clinic. Jay joined the faculty at USC in 2015 and has served in his current post since 2018.

I really love this episode! I'm so excited to share it with you. I hope that you will love it, too! Try to keep your courage up as we discuss, "Scary Stories from the Transfusion Service."

****

Joe: Mark, welcome back to the Blood Bank Guy Essentials Podcast, man.

Mark: Thank you. It's great to be back here and joining you with Jay.

Joe: It's awesome to have you! And Jay, my man. Good to see you. How are you?

Jay: Hey, I'm great. I'm really excited to be on here. I've been listening to this podcast for a while.

Joe: Well, thank you so much for that. I'm so excited to have both of you here. You guys both bring so much to the table and there's so much that we have to talk about today. I don't want to waste a whole lot of time. We've got to jump in and talk about these cases today. We're going to hit eight cases of scary stories from the transfusion service. You guys ready to go? Mark? You ready?

Mark: I am.

Joe: All right. So here's your case one, Mark: You have an, you have an 18 year old, very anemic who's who comes in with a hemoglobin of 5.0 with a positive DAC and warm auto antibodies. Everything that was tested in your blood bank for this patient or cross-matched was incompatible and the patient was tachycardic and tachypneic. What do you do?

Mark: Oh, happy Halloween to all of us. The first question out of my mouth is, you know, "what's the transfusion history and what's the gender?" If it turns out it's a guy and, you know, a young guy, then I'm not concerned at all, because there's really no risk for sensitization. On the other hand, if it's a woman, you might then hesitate because there's a concern, a greater

concern for some sensitization. And I want to point out that even with women or guys, they often will say, "We have no history of transfusion." Well, that's because they were unconscious when they had blood given to them when they were in the OR, or unconscious when they were being revived. But certainly with a guy that makes it easier. You know, then the next question is, you know, with a hemoglobin of five, that's pretty low. And we were seeing that this patient's tachypneic and tachycardic.

And so the question is, you know, what to do? And it reminds me of what I used to say when I started my job at the University of Vermont many years ago, my usual statement was, "Oh, let's keep working on this. And, you know, if the patient becomes unstable, we'll just go ahead and use the otherwise ABO compatible blood." But, you know, I heard at an annual meeting, national meeting many years ago from Paul Ness (who I think taught many of us in the audience), to remind us that actually, if you wait until a patient is unstable with their vital signs, you're actually waiting too long. I think the term he used was "mechanical-electrical dissociation," sort of like the pre-event before a patient goes into some kind of cardiac arrest.

And so if anything, he says, focus on whether or not there's mental status changes, because if there are mental status changes, that patient's brain is starving. It's time, it's time to give blood. Even if you haven't finished working everything up, they need blood.

Now, the other question of course, invariably, is, you know, can you wait for the adsorption studies to sort of "clear out" the autoantibodies. And I think, you know, at where this patient is at, I think it's...Of course, go ahead and send it out or start the process. But the reality is, you'll probably going to give blood beforehand. You won't be able to wait.

The other question that I know a lot of people think about is, you know, because it's cross-match positive, should I look for "least incompatible" blood? I think, you know, it makes many of us feel better that, you know, we've chosen the least incompatible blood, but the patient's own blood was incompatible, right? So I think you're just going to have to use it as needed.

The other thing is some...there are a few hospitals have this thing, they call the "In-vivo crossmatch," which I basically term, instead of using a tube to do the crossmatch, the PATIENT is the tube. So you're trying maybe a trial dose of a little bit of red cells to see if you can elicit hemolysis. And if there's no intravascular hemolysis, then it's supposedly safe to do that. We actually, in our hospital for many years, did the in-vivo crossmatch and, and thank goodness, and we know in the literature, the likelihood of intravascular hemolysis is uncommon. And so we stopped doing the in-vivo crossmatch because, you know, if the patient is going to have intravascular hemolysis, you'll see it when they start having signs and symptoms.

Joe: Mark, for people that are unfamiliar with that term (and we don't have a ton of time for this), but what exactly are people looking for when they do an in-vivo crossmatch? So you're saying they give a little bit of this blood and they check to see if it's incompatible. How do they do that?

Mark: Correct. What you do is you have a, you usually have a pre sample. So you know that they have no hemolysis. Then you, you give them, you know, 30 to 50 mL over half an hour, see if anything happens, the line stays open. They send down the specimen after that. Sort of a test dose, make sure everything's okay. But the reality is if you monitor that patient, if they have no signs and symptoms, you're probably good to go, and you can probably monitor Foley if you had to.

I think, you know, the other question which we do is sometimes is try to quickly phenotype the patient a bit, you know, molecular will take forever so that won't come back in time, but, you know, get like, at least your DCE and Kell. If you can't do that, that's fine too. The idea is just, you know, try to minimize or anticipate some alloantibody, but you know, if it's a guy, I'm not worried.

If it's a really young patient, like a pediatric patient, I know for patients who drop down into that sort of extreme anemia, they have expanded plasma volume. I know some of our Peds team members are very cautious with giving transfusions in that setting, to go actually double slow or give half of a dose over the usual time to avoid circulatory overload. It's weird, it seems to be only in the Peds patients that I hear that phenomena and that request and not on the adult side.

Joe: Jay, any thoughts on this that struck you as you were hearing Mark talk about this?

Jay: I started in pediatrics before I went into pathology. In general, like even an 18 year old that's presenting this way usually has a lot more reserve than what you would typically see in a more advanced adult. And if you're starting off with someone who's already like severely tachycardic and tachypnic, my threshold for transfusion is a little bit lower in those particular cases for those pediatric group patients. And that does sort of extend to say like a 17 or 18 year old, which is more akin to what you would find in an adult. But if they're already, if they're already sort of dipping into the reserve, my threshold for transfusion is a lot lower.

Joe: Mark, you mentioned the "least incompatible" thing. I am well on record, and I recently said on this podcast that I think that's the dumbest phrase that we use in transfusion medicine. And I stand by that! It has no clinical meaning. It makes us feel better and doesn't really do squat for the safety of the patient, but that's my opinion. The second thing is something that I heard, Jill Storry actually quoted this in a recent episode, and I heard Ed Snyder say this a long time ago, which is, people get really nervous about transfusing incompatible blood. And you said this Mark, it's all going to be incompatible. You get to the point where you have to make the best

possible choice for the patient, and "finding perfectly compatible blood for a corpse is not a therapeutic triumph." I think that's what Ed said a long time ago, and I 100% agree with that.

So, great case. I think that gives us a lot to think about. And I think we're ready to move on to the next one, Mark, unless you have anything else to add for that one?

Mark: No. Sounds good.

Joe: All right. Good deal, Jay, your first case, are you ready? My friend?

Jay: Absolutely.

Joe: All right, here we go. So Jay, you've got a 69 year old male with a ruptured abdominal aortic aneurysm who's taken to the OR for an emergency laparotomy. The transfusion service calls you to alert you to the fact that the patient has a known anti-c and anti-E, and the surgeon is screaming for fully compatible blood right away. What do you do, Jay?

Jay: This is a more common occurrence than I would like to say at the hospital. The first thing that I usually do is I try and get the stakeholders all like on the phone at the same time, in order to be able to sort of explain the current situation. Generally speaking, for someone like this, if it is an emergent situation such as such as this, you can take certain steps in order to be able to try and provide something to them. My first instinct is to get anyone in the blood bank to review the inventory at that moment in time for those specific antigens and then try and do my best in order to pull through the inventory to get partial antigen typing for whatever I am able to identify. I also simultaneously do know, at least in part, some of the the overall blood utilization for large volume sort of situations; ruptured AAA, Bentall procedure, things of that nature, in order to give myself an idea of what I would be looking at for that particular subset of surgeries. And then I lay out what is currently available.

Now, typically I also do simultaneously have someone in the lab or my resident reach out to one of the blood centers in order to see what is currently available in the depots, because unlike some of the other hospitals in other locations and cities, such as LAC currently is, we are a lot farther away from our donor centers than I would typically like. And so the acquiring of those particular products can be more difficult. Transporting products between locations in Southern California can take a significant amount of time.

Once I have an idea of what my current inventory is, I lay out with the surgeon and the anesthesiologist with what I can provide them immediately, and then what they're going to have to probably use in the context of the surgery. Sometimes that goes well, sometimes it doesn't.

And so, you know, what I find is that I've been very fortunate to be able to work with some great trauma surgeons who are remarkably

accommodating and understand that we're working together tin order to best facilitate the survivability of any sort of injury that the patients are having in the hospital. I think that there is some limitation in the way that other subspecialties learn about transfusion medicine, and they come from a slightly more limited knowledge space than what we would provide them in those short situations, because it's such high pressure, but we do our best in order to provide those things.

Now, one of the other things that you could do in this, in this particular case is mass screening. And if you have the ability to do so, then that will be another avenue to be able to provide at least some antigen-negative units. The likelihood is that if you're transfusing a significant amount, which likely to be the case in this particular setting, you may not be able to do that in a more timely fashion. Because I'm also the one of the individuals who reviews the SOPs and quality assurance for periautologous, and cell salvage in surgery, I always recommend that upfront as well as an adjunct to the allogeneic red cells in the blood bank.

Joe: Before I go to Mark, I do want to ask one last thing, though. What if worst comes to worse? What if you've done all that? You're doing everything you've done. You call your blood center, which one of the ones you call, would it be mine actually! So you call your blood center, but we can't get it to you in time. Patient's bleeding like crazy, they're doing all that stuff. And, you know you've got to give something that's either c or E positive, or both. What do you do?

Jay: I give it and I explain to them that that's...that they don't really have an option at this particular point in time. I also try and reassure them that generally for these Rh antibodies, E and c, that they're not really going to see acute hemolytic transfusion reactions. They can, but, you know, it's unlikely, and that we can manage delayed hemolysis more aptly in those particular individuals. From the standpoint of giving these particular antigen-positive products, we might start earlier than later and save the ones that we're able to identify that are antigen-negative and crossmatch-compatible for later on in the post-operative course.

Joe: That's a great tip. Mark, anything to add?

Mark: No, Jay hit all, I think, the key points, which is, you know, cell saver, if you can, for any type of intraoperative blood use for massive blood loss, if you need compatible blood, recycle patient's own blood. I think it's always really important when it comes to antibodies against the Rh system, whether what is D, C,, or E that because of the nature of how the Rh molecule's anchored in the red cell membrane, it makes it very hard for it to activate complement. So that the likelihood of intravascular hemolysis is low. And so your ability to give incompatible blood is relatively safe over a 24 hour time period, you'll just have rapid destruction. And then the last piece that Jay mentioned, which is, we call it the "sandwich procedure" where I trained in fellowship, which is, you know, you start with your partially compatible units, and then you just end the case and top the

patient off with the compatible units, and use random, otherwise ABO compatible units in the in between.

Joe: That certainly requires a lot of communication. And that's, that's the one thing I wanted to mention as, as an emphasis in this and Jay, you talked about this beautifully. One of the things that I have said for years to learners is that sometimes in blood banking, you have to have challenging conversations. And I truly believe with all my heart that those challenging conversations are only possible when you have lots of EASIER conversations beforehand. In other words, the surgeons that you're talking about, Jay, when they know you, when you have already established your credibility with them, that you're on their side, that you're trying to help. Then when the moments come when you have to talk to them about something like this, where they're surely going to be uncomfortable, giving quote, unquote, incompatible blood, you already have the credibility established that they know you know what you're talking about and you're there for their patients and for them. So I think that's huge.

Jay: Right. I think, yeah, that's, that is definitely the most key. And it has been the most evident change over the time that I've been the medical director at LAC. When I first started, people were like, "Who are you? Where's Ira?"

Joe: Yep. Totally understand.

Mark: Yeah, Joe, you're absolutely correct. What I do and I still do is whenever a new chair of surgery or a new chair of anesthesia arrives, I make a point of introducing myself to them because I figure that's my best time to meet them and talk to them instead of over a bleeding patient in the OR.

Joe: Jay, great job. Let's move on to, Mark, your case number two. So Mark, you have a young man of about 150 Kg coming in with ITP, a platelet count of 3000 and intracranial bleeding; bad combo. There's a lot of concern in your region right now for kind of a "skinny" platelet inventory. And the patient's already taken two doses of apheresis platelets and his platelet count has not budged. What do you do?

Mark: Check to see if I'm really on schedule? Am I on call? Oh gosh. I think the question that comes up is, what are you going to do? Options that come to mind is, you know, I think a number of folks around the country, you got a patient who's got an intracranial bleed. You know, I think some go-tos for folks would be consider the use of recombinant Factor VIIa, or the prothrombin complex concentrates would be something that some people would consider, to sort of "supercharge" the coag system in the absence of being able to raise the platelet. Right?

So the problem here is, this patient is double size. So they need a double dose. Oh, the ITP! They have an autoantibody against the platelets. So anything you give in them, it's not going to stick around. You know, some

people will try to do a double-dose and it becomes futile after a certain point, if you're not making headway with the bleeding.

And I should point out before I go on, you know, thinking about, you know, using the supercharged factors, that the data isn't good there. There's select anecdotal data that says maybe it might work. It's what they call the "Hail Mary maneuver" when you do that, because you're about to burn through all of your platelets and you won't have anything left.

You know, certainly what we try to do sometimes when we get these terrible cases like this is, I would try the double-dose real quick and see if it makes a difference. You know, hopefully they're in the OR and they can give me immediate feedback as to what they're doing if they're in there, if they have to evacuate, unfortunately. Otherwise, you know, if they're just sitting in the ICU, I probably would push back eventually and say, "We need to go to some kind of continuous drip, if you want platelets."

And for us a continuous drip, what that means is I'm giving half a dose over four hours and then another half a dose over the next four hours. So it's a continuous transfusion of three doses over a 24 hour time period. You know, no good evidence for that. There's no evidence. I mean, I always say, "So what's the evidence for it?" Well, I know that if I keep bolusing this patient, it's not helping, because their platelet count's not improving. And so I know that won't work. So the idea is really that, you know, I'm giving a bag that's hanging on the patient, and there's something dripping in at any given time. So in the absence of them being able to have what I call a prophylactic reserve, right? We would have wanted this patient to have a platelet count of, ideally 50,000 or higher, but that's not happening.

So the idea is that if I have a bag, that's a prophylactic reserve, it is dribbling in any given moment. And I certainly have colleagues, esteemed colleagues in the Northeast who would say, you know, "Really? Do you think that that little bit of dribbling will make a difference?" And I would say, "I don't know, but I know the other way of bolusing, it definitely won't."

So, the other things I do consider, you know, I always ask about, "So where's the patient's coag status? Can we sort of tweak them up and fix them for other things that we can fix? "You know, if their fibrinogen's even a hair on the lower end of normal, I'll raise it with CRYO. If their coag factors are starting to get a little "punky" for whatever the reasons, you know, I ask the question, can we give them a dose of vitamin K to start fixing that? I.

I will raise the hematocrit. We know from works from Bob Valery in the past that, and those of us who have done bleeding times in the past, we know that if you have a low hematocrit, your bleeding time increases or worsens. And so I raise the hematocrit. In this case, I definitely would push for the hematocrit to be raised to 30%.

Joe: The hematocrit thing is something that learners struggle with a little bit. Can you thumbnail why raising the hematocrit might help platelets work better?

Mark: Sure. It's a good question. You know, I think the traditional teaching is that when you raise the hematocrit, you can almost imagine that if you were to draw a circle, it's like the cross section of a blood vessel, that when you raise the hematocrit, that center is all of your blood red cells and the platelets are on the periphery. And so that somehow raising the hematocrit pushes the platelets into the outer edges of that circle. So there's more platelets in contact with the endothelium. We do know also from in-vitro studies with rabbit vessel models, that when you do that, when you raise the hematocrit, you do increase the ability for the platelets to have contact with the endothelium, which is where they need to go. It's also possible that the viscosity is a factor. We also know that red cells themselves, inherently the membrane might have a little bit of stuff like a coag factor surface, it is a phospholipid surface as well. But I think most folks would attribute it to pushing the platelets closer to the periphery of where the endothelium is. And so you have greater contact.

You know, the other thing is certainly in terms of additional adjuncts in the absence of good platelets, you know, I talked about the drip, you know, the other thing is I ask myself, "Would there be value to giving them cryoprecipitate?" We know, for instance, in patients with uremic bleeding, where you know, end stage renal disease or acute renal disease, where the high BUN "poisons" the platelets, we will compensate with using cryoprecipitate. And you know, how that works, I'm not completely sure. It's, probably a combination of elevating the fibrinogen elevating the Von Willebrand's factor, both of these you know, coag factors interact with platelets, making the best of those platelets. And then probably the other thing I would consider, it's a tough one, cause this patient is acutely ill is, you know, whether or not IV form of anti-D would make sense. We know with some of our folks normally with ITP, some folks will intentionally, if the patient's Rh-positive, give them anti-D so that the spleen becomes "busy" removing red cells instead of removing platelets. And we've seen improvement in platelet counts that way. And so those are the things that come to mind immediately.

Joe: Jay, any thoughts on this one?

Jay: I think he hit literally everything that I was going to say about this. I do agree with pretty much everything that Dr. Fung said. You know, I do also attempt to try and give them additional cryoprecipitate in order to try and give ourselves the best possible options. Generally speaking, I do also recommend giving the transfusion of platelets over an extended period of time. And they also usually try and give IVIG in conjunction with that in order to try and be able to give random platelets to the individual, if you're able to control the ITP. Generally speaking, the RhIG is not something that I will give to them in that situation, only because I don't have to. If you're in

a different location and you're having issues getting IVIG then giving RhIG is an alternative.

Joe: This is one of those unsatisfying situations where nobody's really happy with almost any choice. I have used the drip in the past myself as well. I question whether it does a whole heck of a lot, either. And I agree with both of you in that using the intravenous form of Rh immune globulin, if this patient is Rh positive, I would kind of consider that last resort. I do think it's important what you said, Jay, to remember that even though we're dealing with this urgent situation, there's still the treatment of ITP, which is IV immune globulin, as you mentioned, or steroids, et cetera, and there are lots of further treatments. And the clinicians, obviously, shouldn't forget about that while we're trying to treat this urgent issue with the intracranial bleed,

Mark: It's a tough case. You know, some people will, you know, certainly there are those TPO agonists that can be used as well. But I think that the bigger issue...

Jay: Oh, I forgot about that...

Mark: ...the bigger issue is you know, what are you going to do about this patient? And then what's going to happen to everybody else who needs platelets when you're on the shortage. That's always a problem.

Joe: And we will come to that. We will come back to that. All right, so Jay, let's do your second case as we roll on here with our scary situations in blood banking. Jay, you've got one that I think makes us makes us all feel really awful. You have a 24 year old O negative female who started hemorrhaging due to uterine rupture, following an apparently uncomplicated vaginal delivery. And before I go on, can we just all agree that OB hemorrhages scare people more than just about anything in the hospital? Is that fair to say for both of you guys?

Jay: Oh yeah.

Joe: It is for me. I'll tell you that.

Mark: Yes, yes.

Joe: Terrifying. So she has this uterine rupture. She's 24, she's O negative. They activate the massive OB hemorrhage protocol. Your transfusion service, Jay calls you and says, "Oh my goodness, we've only got four units of O negative red cells on the shelf. We've called our local blood supplier. They've only got four units that they can send, and it's going to take a couple hours or an hour or two before those four units arrive." So you've got a bleeding, O negative young female, not a lot of supply. What are you going to do?

Jay: Okay. So first I'll cry in the corner for about two minutes. Then I will put on my brave face and walk out of the door. So, unfortunately for us, this is not an uncommon situation. Our general, our population, unlike the rest of the

United States is about 60% O. And I have more Rh negative females coming in than I've ever thought possible.

So our inventory is a little bit better than most places for O negative, but it's still not extensive. The likelihood is that we'd be able to support somebody like this for maybe one round of one or two rounds of an MTP. In this particular situation where I only have four O negative units on the board, you have two options in my estimation. So one is to have the frank conversation with the OB, and the anesthesiologist as well, in order to give them the lay of what we're sort of dealing with. How much bleeding are we actually looking at? Can we adjust any of her coagulation issues upfront and then try and replete slowly with red blood cells in this inference. If there is massive bleeding, then you can either try and type some cells in your blood bank to see whether or not they're A1 or A2, and have that as a reserve population of cells that you could give, knowing that there is a risk that she might have a more acute hemolytic transfusion reaction, less likely, but still possible. Or give O positive units if you're really dealing with a massive, massive transfusion, similar to what you would see in an ultra-massive transfusion situation, which is what often happens in these OB exsanguination or hemorrhage cases.

I think Jay Herman and Ayache [NOTE: Ayache S and Herman JH. Prevention of D sensitization after mismatched transfusion of blood components: Toward optimal use of RhIG. Transfusion 2008;48:1990-1999] did a review of prevention of anti-D in the setting of incompatible transfusions to the D antigen. And they did come down on the idea that you can give fairly large doses of Rh immune globulin in the post-transfusion timeframe in order to get people through this. Now, what I would suggest in that particular situation and in this situation in particular, because there is the potential for so much transfusion, is that if you go the route of giving Rh positive units, you do that for the transfusion, get the bleeding under control. If you can stabilize the patient enough that you can apherese them and do a red cell exchange, once you've been able to build up some Rh negative inventory, do that, and THEN give Rh Immune globulin. That's what you could do in order to approach it. I would be very reticent to use the A2 units even if I had them.

Joe: And Jay, just for, again, for the learners, why is A2 potentially better than A1 in that setting?

Jay: All right. So A1 units have a higher density of A antigen overall. About 80% of people are A1, about 20% of people are A subtypes, the most common of which is A2. The amount of A antigen on the surface is significantly less than what you would find in an A1 unit. That is also supported by the fact that we often will give A2 organs to O individuals, and they're able to maintain them, but it is still a very scary situation.

Joe: Is it your position that you would choose to switch the Rh before you go out of ABO group like that?

Jay: I would. I would switch the Rh. I would manage the transfusion throughout this particular situation, try and convince people to do a red cell exchange and then give give RhIG because the amount of Rh Immune Globulin that you'd be giving in this particular situation would be so massive that I would be afraid that it would cause an acute hemolytic transfusion reaction.

Joe: Yeah...agreed. So, Mark your thoughts on this one?

Mark: I think the question is not IF, it's WHEN do you switch over to Rh positive, O pos blood. You know, I think I'm of two opinions: I suspect many in the community might just upfront switch immediately to O pos. Because the units that you transfuse will be lost anyway. I think the others, there might be some in the community that might say, "Well, we don't fully know how bad that uterine rupture will be. Let's give them a chance, at least with the first four units of red cells as O neg, and then the rest switch over to O pos." So I think there's some gradations there. Some people will say, "Well, uterine rupture, let's not kid ourselves! This is a massive OB MTP. We're switching immediately and conserving the O neg blood for everyone else in the community that might come in later on."

I think the other thing is to remind the team, it's not that the team doesn't know this...I'd like to believe that our physicians in the blood bank can sometimes help nudge a well-meaning but stressed out of their mind colleagues in the OR to ask the question, you know, "Have you considered balloon tampanade in the meantime?" So balloon tampanade is a known sort of adjunct to sort of slow the bleeding down, just literally physically pressing on the ruptured uterus to slow the bleeding down in time. So if the patient's stable enough to then go to interventional radiology and then they can attempt to coil or, you know, shoot in some coils to sort of clot off some of the uterine arteries, and cut off the blood supply. And then the final thing is to go into hysterectomy to take it out. And so with those steps, you know, some people would say, "I'm just going to go straight to O pos from the beginning and just see where this patient lands. If this patient survives still with a uterus, then we can consider, you know, doing a red cell exchange that Jay had mentioned and followed up with an IV, intravenous anti-D, but that's only if they still have a uterus." So, you know, so those are the things I think go through my mind for that.

Jay: I remember in medical school that one of the worst bleeds I've ever seen was a uterine rupture case. That sort of sticks with me all throughout my entire, throughout the entirety of my life. So I take these situations very seriously, and I assume that their approach is to salvage the uterus as much as possible. If she's G1, then I feel like they're going to try their best to maintain her ability to reproduce in the future. If it's, you know, G5 or something like that, the likelihood is that they're going to push for the hysterectomy.

Joe: The RhIG question is one that I get a lot, you know, whether or not it's appropriate to hit someone with massive amounts of RhIG. I've always been pretty scared of that. The red cell exchange to me is a better option if

that's possible as opposed to giving someone gargantuan amounts of Rh immune globulin, which I don't really care for that particular idea.

Let us move on. Mark, your case number three. So this kind of builds a little bit on your last case, where we talked about kind of conserving platelets a little bit, but this is a little bit of a different situation. So, your resident, your blood bank resident calls you Mark and says, "We're coming to the end of the day. And the hospital only has four doses of platelets left in inventory. And the local blood supplier is also down to only four doses, and we've got a pretty massive regional platelet inventory shortage. And there's no real hope of us getting anything anytime soon." So what are the steps that you think of in that scenario and how do you handle those cases?

Mark: Well, just a tip to all the learners out there, important tip: Do check the inventory, not at the end of the day, but in the middle of the day, so that you're not surprised because certainly is easier to triage who needs blood w.hen you have more to triage with. Can't do anything now that it's down to just a couple of doses locally and in the region, you know, so to speak. So I would say, you know, if there's anything you can take away from this podcast, do check in with your staff more frequently than just once a day. Unfortunately, this pops up for all of us around the country periodically.

You know, I think what I always tell folks is, you know, when that happens, it's a "full stop" in the blood bank. No one's getting platelets unless they're bleeding. That's the first thing, until we get better understanding of when will we get more doses, you know, if it's that bad, you might have to just give a heads-up. We do have a communications plan in our hospital when we hit a certain trigger to be able to communicate and say, "this is what we're going to do. If you're not bleeding, you're not getting anything. If you're not meeting a certain platelet threshold, you're not getting it even for prophylactic transfusions." So that's the first thing. So that means calling OR internal control, the front desk in the OR, calling the ED, giving them the heads up.

You know, the other question is then if there are any procedures that are coming in for the next day, depending on how long this shortage will be, you know, we're going to have to have the conversation with some of the providers to say, "Here's the situation. You might not want to cut into a patient for a massive bleeding case because we might not be prepared to support you."

The other thing that I think a number of us do around the country for the learners to be aware of is the use of splitting a standard dose into two. So it's not magic. It's not like you somehow split it, you have two doses. But it turns out that the FDA requirement for a minimum dose is 3 x 10(11) platelets per bag. So what happens, and I know both Jay and you Joe know this, that, you know, when we get a dose of platelets that's collected at the blood center, if it looks like it is more than double that minimum amount, there's an attempt to split it, even at the blood center level, so

there are more doses available. But because of the math, you won't get a...if a dose comes in at like a 6, they're not going to split it into 3 and 3 x 10(11) because it's too close to that cut. And so it's not uncommon to have doses, if you get a chance to look at the bags in your inventory, that have 4 or 5 x 10(11) platelets. And so what that means is actually when you split it in half, you're probably going to have at least two-thirds of the minimum dose. So that means you've basically doubled your inventory temporarily. So we'll do that. And basically everybody who needs a dose whose bleeding are getting split doses. And certainly for the patients who just need that little top off, like our Heme-Onc patients who are right at 8 or 9,000, they want them at 10,000, they're getting a third of a bag amongst a bunch of them to really just sort of cover them for that day.

You know, the other question is, you know, who else in the region has platelets if they're available? The other question that we sometimes will ask is who has doses, depending on what time you're at and how long this shortage goes. Some of the hospitals only hold their platelets until day five, because they don't use additional testing to assess for bacterial contamination. We certainly do in our hospital where there's a test that we use that's a point of care, so to speak, test, to look for evidence of bacterial antigens. We'll do that, and we can extend our products out to seven days. And so there might be a way of getting products from other hospitals who won't go beyond five days, if it's eligible to be extended if you do the testing in house for the bacterial contamination to give it the seven days.

The other thing mentioned in some of the other cases is just tune up the patients. You know, if they have other patients, if they have coag issues, now's the time. You would think we do this all the time, but vitamin K, vitamin K for everyone! Tune them up. So yeah, those are things I think of immediately.

Joe: Vitamin K for everyone. That's Mark's new motto: "Vitamin K for everyone! You get vitamin K! You get vitamin K!" I love it. Jay, do you have anything to add?

Jay: Unfortunately (or fortunately; depends on how you look at it), my hospital systems do not use supplemental point of care testing for our platelets. So we are limited to five days for them. So there's definitely a need and a use to splitting products in that particular setting. I do also take the responsibility in conjunction with the chief medical officer, as well as my direct superior, which is Dr. Shulman, the clinical laboratory director, in order to allow for me to communicate with the physicians within the hospital. The limitation of elective surgeries is going to be something that is going to be done fairly quickly after having this information. Limitation of transfusions to non-emergent situations or patients with potential for spontaneous intracranial hemorrhage will likely be utilized too. And, because LAC is a trauma center, you do have to divert the traumas that are coming to the hospital as a result of that, because you're just not

gonna be able to support them, from the standpoint of the massive transfusion protocols that typically follow those patients when they come into the hospital.

Joe: As a blood center chief medical officer, I feel these cases. I'm the one that gets the calls and the texts from people like you guys that, "Hey Joe when are we getting more platelets, big guy?" That's the polite version of it. I have to say, Jay though, you are always polite. I will give you credit for that, my friend. I will tell you this, and most learners don't have a lot of experience with how this feels from the blood center side. I can just tell you having been both a hospital blood banker and a blood center blood banker, I can tell you, it feels just as awful from the blood center side, when we're sitting there knowing that patients are suffering because of a lack of inventory. And, I promise you, we are working as hard as we possibly can to make those shortages go away. It's an awful situation for everybody involved.

But I appreciate the tips. I think both of you guys have made some great points, but we need to move on. So Jay, your case, number three, are you ready? This is one that I know you have experienced. So you've got a 51 year old guy. He's brought to the ER, he's got multiple injuries and massive blood loss because he's been driving in LA and had a motor vehicle accident. They activate the MTP, but once you get the sample and once you actually get an identification on this patient, your blood bank says, "Oh, hang on a second. We've had this patient five years ago after a gunshot wound. He's A neg, and he has an anti-D!" Uh-Oh! So what do you do, Jay?

Jay: This happens, literally, every week, I think. So, not specifically for this particular antibody, but like somebody with an antibody in the history. And, so, at least by the time that this comes up, the person's probably already received somewhere between 6 to 12 units, either in the emergency room from our satellite refrigerator or in the OR, from our satellite refrigerator. So, the decision is sort of already made. They likely will be getting Rh positive throughout the timeframe that they're gonna be running through the anti-D. We do insist that they monitor the patients consistently after they've completed all of the bleeding. And I will try and transition them to Rh negative in the post-operative period, because a lot of these people tend to continue to bleed for significant time afterwards. And so we're continually sort of replacing the cells that have already been transfused during the, during the procedure.

The other thing that I tend to do is I often tend to monitor their hemolysis and icterus and indices just an adjunct to see whether or not we're seeing increasing hemolysis. And if we are, then I tend to reach out to the teams at that point and talk to them about the possibility, depending on how many units were actually transfused throughout the MTP about red cell exchange in certain situations. But most of the time it's, low-level

hemolysis that we're seeing with these individuals, and we manage them supportively throughout the time that they are in the hospital.

Joe: Mark, what are your thoughts on this?

Mark: You know, the patient's an A neg. This happens, right? So the question is whether to burn through the O neg inventory is the other option. Certainly I'm sure that the blood bank has already thought about that. Thank you to the many folks who responded to your Twitter request for cases, Joe, you know. We saw consistently people talking about incompatible blood transfusions.

You know, the other thing is, you know, addition to, you know giving, you know, some IVIG if you're in this situation, it is off label use as well, I'm going to talk about is, you know, there has been increasing experience with the use of the compliment inhibitor that was not designed for this purpose is "eculizumab," but some folks have begun using that if there is significant concern for you know, complement activating incompatibility. But again, that's where we're, I think there's still data to be gathered on that, but there are reports coming out where people have started using that drug.

Jay: Most of the time, I'm seeing these, these antibodies, some are Duffys, Kells, and an increasing number of Kidds. In the setting of the Kidd antibodies, that has been always in the back of my mind for a suggestion, because they're more likely to get complement activation in those particular settings. Because it's so expensive, there does have to be a significant justification for its use.

Joe: First, I will, once again, re-emphasize what Dr. Hudgins is describing here is a scenario where he's having communications, challenging conversations with docs. The first time that you have a tough conversation with your doctors, can't be, in my opinion, in a time of crisis. You've got to establish that credibility beforehand. And I know for a fact that Jay has already done that in his setting. So learners, please keep that in mind, again.

The only other thing I would add is just a re-emphasis of what you both have mentioned before, which is that these incompatibilities, especially in the Rh system, are not typically associated with massive immediate hemolysis. And you usually have some more wiggle room than you think you do. As learners, oftentimes we think it's a catastrophe any time somebody gets incompatible blood. Obviously, we don't WANT to do that, but again, with most of these antibodies, you do have a little more wiggle room than you thought you might have.

Okay, Mark, your last case, case number four: You have an emergent aortic dissection repair, and it looks like this patient might bleed, as they often do. Unfortunately, you find out that your patient is blood group AB, and there are only eight units of AB plasma in the hospital, and you're

anticipating that you might end up needing to use more than those eight. What do you do?

Mark: Sure. Our go to, and actually in our inventory is to no longer stock group AB red cells. And so I make it very clear, "This patient gets only group A red cells, A, nothing else. No AB," with the intent that we're going to eventually run out of the AB plasma. And so by the time we run out of the AB plasma, we've tanked this patient up with only A red cells. And so that then I can safely switch to group A plasma, which is what we would do. The other thing is I also tell, particularly since this is an aortic repair, they often will want to use a cell saver in the room with the perfusionist, and I tell them to NOT use the cell saver, because I don't want them to recycle that AB red cell back into circulation. I need all of that B antigen gone. So then when I switch over to A plasma, we would be safe. And there are studies to show that when you use low-titer group A plasma, or even if you don't titer it, in the trauma situation (this is the STAT study) that that's, that's fine. There's been no instances of harm.

Joe: This is one of those cases where we're actually telling them NOT to use the cell saver. And that probably seems bizarre to people, right? Mark, that's absolutely counterintuitive, but I totally hear what you're saying. You don't want that B antigen in there. Jay, do you have anything to add to that one?

Jay: I would say that I would just start off with the A plasma, because we're dealing with that daily, with our traumas that are coming in. There's a low percentage of B individuals in the hospital, but weirdly enough, they do show up as traumas and they're getting A plasma. And I have not seen a case of hemolysis. Dr. Shulman has talked about one that has previously happened. We are using low-titer plasma in those emergent situations. So that does sort of correct, at least in part for that.

Joe: We have to move on to the next case, but Mark, I'm going to give you, I'm going to give you about 45 seconds to answer this question: What if we changed this case scenario? Because this is one, I hear a lot in blood center land, and instead this was a patient who has TTP, thrombotic thrombocytopenic purpura, and they're needing a plasma exchange, and they're group AB, and you don't have the AB plasma. Would you consider switching them then, or what would your options be?

Mark: Oh, gosh, I guess that's where you would have to use the low-titer A plasma and also with the TTP, I assume it's emergent at the time. Yeah. I think you have no choice. You'd have to switch to the low titer...I would use the low titer A plasma.

Joe: Jay, have you had that situation?

Jay: I have not had that situation, but I think the mortality associated with not treating TTP in emergent settings is high enough that I would, that I would use the...I would use low titer A plasma.

Joe: With the TTP, I've spoken with physicians that do a whole lot more exchange transfusion than is my expertise, who have started those patients with group A plasma and just continued on to do it, with success. But I don't think there's a lot of data to support it.

All right, Jay, here we go. So a 54 year old male is being wheeled to the OR for a redo four vessel coronary artery bypass graft. So as learners should know, those tend to bleed a whole lot more than the initial ones. So it's a redo four vessel CABG. The anesthesiologist calls the transfusion service, just to help, just to be courteous, just to let you know, and say, "Oh, by the way, this patient is IgA deficient, IGA deficient, and they are only going to be accepting IgA deficient blood products." And they're on the way that the OR, Jay! What do you do?

Jay: Okay, yeah. So this literally happened my first week of fellowship. I never had a heart attack more than at that moment in time. So in my fellowship at the Cleveland clinic, we had a cell washer, so we were able to get back all the cellular products and wash them and then provide them to them so that they would still be able to do the surgery on that day. Not every single hospital has that advantage. The Los Angeles County hospital does not currently have a cell washer on campus. So there are not a lot of good options in that particular setting. Now, I will always promote cell saver for these sorts of situations in order to be able to have those red cells that will be present and unlikely to have any sort of sequela from those transfusions. In this particular setting, this is one of the only times where I might suggest acute normovolemic hemodilution as a potential use for helping them to bleed more dilute blood during the procedure as well.

Generally speaking, the first thing that I would do is try to see whether or not this was an emergent surgery, or is this something that we can take time to prepare for? Because the likelihood is that this person is going to need plasma products, which then becomes much more difficult, right? We're going to need IgA deficient plasma products if the person has had anaphylactic reactions in the past. Now, one of the problems with IgA deficiency,, selective IgA deficiency in and of itself is that we are not really concerned with people who have just low levels of IgA. We are concerned that people who have nearly absent levels of IgA, less than 0.05 milligrams per deciliter. And the frequency with which selective IgA deficiency happens within the general population is somewhere between 1 in 300 to 1 in 600. The frequency of individuals that have anti-IgA antibodies, which are primarily IgG, but can be IgE, and that might mediate this type of transfusion reaction is 1 in 1200 of those individuals who have selective IgA deficiency. And then the frequency of anaphylactic reactions is 1 in 20,000 to 1 in a 100,000.

So the real question is, is this person really at risk for having an anaphylactic reaction? And I don't think that we would know that unless the person had previously been transfused and had an anaphylactic reaction. Now, the way that the case is presented would suggest that they

have, so I would probably stop at that point in time and try and get them to stop, unless the person absolutely needed to go to surgery at that moment in time, prepare the products ahead of time, and then bring them back to surgery.

Joe: So first make sure that the patient is actually going to need them through a combination of finding out history and perhaps some more lab tests, if possible, and then make a plan. I totally, totally agree with that. I think you made some great points there. Mark, do you have anything to add to what Jay said?

Mark: No, those are, those are key points. I think history is very important because as Jay pointed out with all those numbers, the reality is even of patients that have IgA, true IgA deficiency with the higher sensitivity assay that our reference lab runs, and actually even of those patients that have an IgG against the IgA, most of them will not have an anaphylactic reaction. So these are patients oftentimes because of other studies that are being done are incidentally found to be IgA deficient, and it causes much alarm for us because we think we need to use IgA deficient blood. But if you look there's, I think there's at least once editorial or some kind of article by Gerald Sandler to this point, that even questions, whether IgA deficiency anaphylaxis is a true entity.

Jay: Anti IgA antibodies are not uncommon. They are found in elevated concentrations in normal healthy individuals, too. So it's not like the presence of these antibodies immediately confers the risk of anaphylaxis.

Joe: If you would like to hear Dr. Jerry Sandler talk about his feelings on IgA deficiency and anaphylactic reactions, I did an interview with him last year, and you can find that at BBGuy.org/066. And you're 100%, right: Jerry is not convinced.

Guys, this has been just fantastic. You've both made some really great points and helped us work through some SCARY situations to a point where I think we're all a little bit better prepared to deal with some of these things. So thank you both so much for being here. I can't tell you how great this has been. I really appreciate your time.

Mark: Well, thank you, Joe. It's always a lot of fun to be able to hang out with you and to work with Jay on these really tough cases.

Jay: I really appreciate the opportunity to be on the podcast. And you know, it's always good talking to you and I'm always happy to discuss like any sort of interesting or difficult case because it gives me more information to deal with it at a later point in time.

****

Joe: Hey everyone, it's Joe with just a couple of quick closing thoughts. I want to thank both Jay Hudgins and Mark Fung for joining me, and to Mark again for the great idea for this episode!

I want to mention one more time that this is a continuing education activity. So if you're a physician or a laboratorian, don't forget to visit wileyhealthlearning.com/transfusionnews and you'll get your hour of totally free continuing education credit. Can't beat that! My thanks for that, as always, to Transfusion News, to Bio-Rad who brings you Transfusion News, as well as, of course, to Wiley Health Learning.

If you have a minute, please go to Apple Podcasts and give this podcast a rating, a review, and even subscribe if you want to. I really do read every one of those reviews (even a recent one that made me laugh where the person said I talk too fast, which is absolutely true!). I really appreciate all of you that have gone and have given ratings and reviews already.

And last, you may have noticed that I've not released many episodes this summer. 2020 has been a trip for me, as I'm sure it has for each of you. To all of you who have suffered losses of any kind in this bizarre, ridiculous, insane year, I send you my heartfelt best wishes for comfort and recovery (whether that's physical or mental). I am doing my best to get more episodes out before 2020 ends, including upcoming episodes on donor infectious disease testing, transfusion in thalassemia, transfusion in ITP, and some more details on working with autoantibodies.

But until then, my friends, I hope that you smile, and have fun, tell the ones that you love that you do, and above all, never, EVER stop learning. Thank you very much for listening. I'll catch you next time on the Blood Bank Guy Essentials Podcast.