BBGuy Essentials 044CE:
What I Wish I Knew! with Pat Kopko

Joe Chaffin: This is the Blood Bank Guy Essentials Podcast, episode 044CE!

[INTRO MUSIC]

Joe: Hi, everyone, welcome back to the Blood Bank Guy Essentials Podcast! I am your host, Joe Chaffin. This is the very first episode of 2018, and I've got lots of great stuff to share with you today, including a fabulous conversation with my dear friend Dr. Pat Kopko from University of California, San Diego.

So, this IS a continuing education episode, so that means we've got a few housekeeping items to cover. So I hope you'll bear with me for just a moment.

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You know, there are certain people in your life that you feel like you've known forever, and while that's not *literally* true with Dr. Patricia Kopko, it's not TOO terribly far off! Pat and I are med school classmates, and she has gone on to have an outstanding career as an authority in Transfusion Medicine. To be honest, I'm really proud of her, but don't *tell* her I said that, OK? Pat is a professor of pathology at the University of California, San Diego, where she is also Director of Transfusion Medicine. For this episode, she and I decided to have a conversation about the *essential* things we wish we would have known back when we started on our respective paths to being blood bankers. Pat and I get really, really practical, and give you tons of useful information, including tips, memory tools, and facts presented, hopefully, in a memorable way. This episode is one for all of you who don't do blood banking every day: Residents, medical students, clinicians, non-blood bank pathologists, nurses, non-blood bank laboratory scientists, and anyone else who doesn't live in our world all the time! So, pull up a chair, put on some headphones, and just eavesdrop on two friends talking the "Essentials," and enjoy!

Joe: Hey Pat! Welcome back to the Blood Bank Guy Essentials Podcast!

Pat Kopko: Thank you, it's good to be here.

Joe: You know, you are one of my two first guests on this podcast, and I still get TONS of great feedback from that platelet refractoriness episode. So, you made quite an impression on people with that one, nice job!

Pat: Well, thank you. It's good to be remembered, I guess? [LAUGHS]

Joe: Well, yeah, speaking of memories, it's funny, when you and I go down memory lane, it's a really long road, Pat. Let's just put it that way: It's a REALLY long road! I was talking with you earlier today and I'm going to throw this out to you: August 11, 1986. OH MY GOD. What do YOU remember about that day?

Pat: It was a very interesting day, and I'm sure that it is first time I ever met you.

Joe: Yep, and we've got to tell people why we happened to remember that it was that particular day. It's not like it was so memorable meeting me that you were like, "Oh my God! The angels wept," or something like that!

Pat: No, I think that's what it was, wasn't it? [LAUGHS]

Joe: Somebody wept, that's for sure! So everyone, Pat and I are being silly, obviously, but we met on our very first day of medical school on August 11, 1986. I have to tell you, my first impression of Pat was that she was brilliant, which turned out to be true. I'm pretty sure that her first impression of me was, "I wish that joker

in the back row would stop throwing paper airplanes at me." So, something along those lines. Is that about right?

Pat: No, I can honestly say, no, I knew you were pretty smart when I met you, that's for sure. And then, the other thing is, I realized that of all people in blood banking, I've known you the longest.

Joe: I know, it's the same here! Same here, and from that exact same day. Actually, I think what's cool about that is that you and I, though our careers have differed in a lot of ways, we took different pathways, I went down that Anatomic Pathology road for a while, which I know is SO appealing to you...

Pat: You mean that mistake you made...[LAUGHS]

Joe: [LAUGHS] That! Yeah, we'll just not talk about that. But, the fact that we're now, oh my god, 31 years later, kind of "veterans" in blood banking, I think in a way, it gives us a little bit of a unique position, Pat. Because we were kicking around what we could talk about, and we want to do a "What We Wish We Knew" kind of episode. And what's your perspective on how, I mean, obviously, things have changed ENORMOUSLY since that day in 1986 when we knew nothing of blood banking, but what's your perception of how that time has passed?

Pat: In some ways very quickly, in some ways very slowly. And as we were talking about earlier, think about, in 1986, the concept of even doing a podcast!

Joe: A "Pod-WHAT?"

Pat: Exactly.

Joe: Yes, for sure! Things have changed so much, but I think that you and I can give a little bit of perspective to folks. I think what we want to do today, everyone, and we want to be really clear with this, we're going to cover a lot in the next hour or so. So, by definition, we're not going to be able to go into enormous detail about anything, but this is the kind of episode where we're going to hit you with some oversight stuff, some general thoughts on things that have plagued us over the years, and really, things that we wish we knew back when we started. With the idea of just giving you some tools in your toolbox, no matter where you are in your blood banking career, or if you're a clinician, or if you're a nurse, or if you're a laboratory student, these are tips that are going to be useful for you. We've learned them, in many cases, the hard way over the years. But I think we've gotten to the point where we can get a little bit of perspective. So Pat are you ready to rock? You ready to do this?

Pat: I'm ready.

Joe: All right so Pat and I are going to cohost this episode today. So, I'm going to start and I'm going to ask, Pat what is your number one? Your first thing you wish you knew?

Pat: [00:07:40] OK, so the first thing I came up with was, when I first started in medical school and even early in residency, I had a hard time remembering, "OK **which is the DAT and which is the IAT?**" And then, I remembered a memory device: The DAT, you're testing for antibodies sitting directly on the red cell.

Joe: Tell us what those abbreviations mean before you go one step further.

Pat: Direct antiglobulin test and indirect antiglobulin test, and for the longest time, I had to stop and think, "OK which is which?" But then when I forced myself to remember that the DAT was testing for antibodies sitting DIRECTLY on the red cells, well, then the IAT, you're testing for antibody NOT sitting directly on the red cells. So the DAT: Antibody directly on red cells. IAT: Antibody in serum.

Joe: Does the IAT go by another name for us in the transfusion service?

Pat: Yeah, the “antibody screen.” Obviously, it has other purposes, occasionally. But yes, when you do an antibody screen, you are doing an IAT.

Joe: Before we move on, Pat, how do you use a DAT? What is that? Just thumbnail it for us; what things would make you think, "Oh, I need a DAT?"

Pat: Good question. Of course, any time you have a new antibody that you haven't seen before, you want to do a DAT to see if you've got, particularly in patients who've been recently transfused, if not only do you have a new antibody, but you have antibodies sitting on those red cells that you have transfused. You use it (often it's ordered clinically) to see if somebody has a hemolytic anemia. And one of the things I always tell my residents, I have this equation that I've written on this post-it and I pull it out occasionally, and it is, "DAT does not equal warm autoimmune hemolytic anemia." Common misconception is that if you have a positive DAT, you have warm autoimmune hemolytic anemia. That's not what it is. We could do a whole podcast on the causes of a positive DAT [LAUGHS].

Joe: No doubt, no doubt. Let's not, today!

Pat: Let's not.

Joe: We've got other stuff to cover. All right, cool, I like it: DAT, directly on the red cells. Fair enough. Let's roll.

Pat: OK. You're up.

Joe: [00:10:25] Oh I'm up! Oh geez, wow; I'm not used to getting queried on my own podcast! So my number one is, "**It's radioactive**." It's radioactive. So, what I wanted to talk about briefly is the fact that SO many people misunderstand irradiation of cellular blood products. What it means, what it's used for, and what kind of comes with it. Really, when you think about it, there is really only one big reason to irradiate cellular blood products, and that is **to prevent transfusion-associated graft versus host disease**. It's a horrible, nasty complication of transfusion. Thank God, it's really rare. It's caused by transfused T-lymphocytes cruising into someone else's body and attacking them, and the body not being able to fight back. That's the "in a nutshell" version of it. But clinicians often get confused about what irradiation is, what it does, like as if it's some magical thing. I've had people call me and say, "I want irradiated red cells because my patient is having allergic transfusion reactions." MMM, not so much, it's not going to do that! Again, really only one main reason, and that's to prevent transfusion-associated graft vs host disease. I think of TA-GVHD, Pat, I've taught it for years this way, as just the idea that when you get a transfusion from someone who is not genetically identical to you, and has different HLA antigens on the surface of their cells, white cells are really good at recognizing self from non-self, so those transfused cells come into your body and they start doing what white cells do. Those T lymphocytes say, "Hey, this is not me! I'm going to attack these tissues." But fortunately, most people are capable of saying, "No, not so much. I'm going to counter-attack against you transfused white cells and get rid of you." But occasionally, you'll see people, especially people that have T cell immunodeficiencies, patients with Heme malignancies like leukemia/lymphoma, one of the big ones is patients that have had stem cell transplants and are really immunosuppressed, they just don't have enough soldiers to fight back. And so they're really at risk. And Pat, as you know TA-GVHD is nasty! It is a nasty, nasty disease that is almost always fatal. People's bone marrows just get wiped out with TA-GVHD. So it's a great thing to prevent, it's a lousy thing to diagnose, and that's the reason that in someone who is at risk, you want to irradiate those cellular blood products just to make sure that they are not going to make that initial attack.

A couple of things just for boards purposes, for those of you studying for boards; just a couple of things that people forget a lot. For those of you pathology residents, for those of you that are laboratory medicine students, first, the thing that people always forget to irradiate, at least theoretically on tests, is products from family members or products that are "HLA-chosen" to be close to someone HLA-wise, whether that's HLA-matched or HLA-similar, whatever. Those products can mount an attack and may not be recognized by the recipient as needing to be counterattacked. There's a lot more to say about that. The other thing that people forget about is that when products are irradiated, they change their expiration date. For red blood cells, you have a maximum of 28 days after the irradiation before that

product will expire, so it's going to knock the expiration date down of products that are stored longer than 28 days.

Pat: So there's two things that you said that I'd just sort of like to add a little to.

Joe: Yeah, bring it!

Pat: One of them is the concept there is only one reason that you irradiate any product, and it's absolutely true. And you mentioned that there are misconceptions. I have seen people have the misconception that it prevents graft versus host disease from transplantation. It does not. I have seen a misconception that irradiation prevents disease transmission, including CMV. It does not. And the other thing that people forget to say that needs irradiation, it has to do with a misconception. And that is, if you were using granulocytes, they need to be irradiated! Some people have a misconception that if you irradiate the granulocytes, they won't work. That is not true. You do not give enough irradiation for the granulocytes to not function. You give enough radiation for white cells not to be able to multiply and the very group of patients who get granulocytes are at very high risk for transfusion-associated graft vs host disease.

Joe: You bet. Absolutely yeah. That is a great point. The family members, the HLA products, and the granulocytes; you are 100% right. That's something people forget about all the time and on examinations. Did you have another point, or was that the...?

Pat: Those were the two points.

Joe: Got it. Those are awesome! I think that really helps. Cool. Okay, you are up. What is your number two, Pat?

Pat: [00:16:05] Number two is, "**Rh switching**." When you first have to switch somebody who you would ordinarily think that you would give an Rh negative product to...so for example, if you were at a trauma center, and someone comes in, and you're kind of short on your Rh negative supply, you may have to switch to Rh positive. And that, when you first do it, makes you very nervous. The reality is that you don't have to be nervous about it, you just have to choose wisely who you switch. In general, males and women over 50 you are completely safe switching to Rh positive products, even if you don't have a blood type on them. And the thing is, switch early! Don't go through 50 units of O negative on somebody is going to use a hundred units of blood before you switch them. The only time this can come back to haunt you is if your patient who is, typically it would only be in a trauma where you didn't have a blood type yet and you're releasing blood products, if it turns out that they ARE Rh negative, and they've been in a similar situation before, and have

made an anti-D. Statistically, that is very, very low probability, and the one thing you don't want to do is run out of Rh negative for people who need it.

Joe: I love that point. And can you talk about two things, Pat? Because these are the things that I get asked a lot: Is there a published risk? Because in the old days we used to hear about, "If you're Rh negative and you get an Rh positive unit, boy, you've got an 80% chance of making anti-D." So that's question 1, and question 2: What if in that situation, you find out later, "Oh crud, this person WAS Rh negative," and someone calls you and says, "Well, how much Rh immune globulin do I need to give this guy?" How do you handle those two questions?

Pat: OK, very good questions. Let's start with the Rh immune globulin: the answer is: NONE! [LAUGHS]

Joe: WHAT? Hang on... [LAUGHS]

Pat: Because you would have to give so much Rh immune globulin to overcome even one unit, that your patient would feel like they were a human pin cushion! So that's the first reason you don't give it. The second reason is, you're going to make them hemolyze all of that blood.

Joe: Oops!

Pat: So you really don't want to do that. What you have to do, sometimes you have to hand hold with clinicians that, "No, it's going to be OK. We're going to switch back to Rh negative now, and now that the great amount of blood is not being required, we'll switch back to Rh negative." Now, the other question was, what chance do you have of making anti-D? That depends on what you gave the red cells for. As you alluded to, we used to think there was about an 80% chance of making anti-D if you got Rh positive cells and you're Rh negative. Turns out that's not so true. Those studies were done on volunteers, who got small amounts, like mL quantities of Rh positive red cells. Turns out that if you give them a whole unit or more, maybe overwhelm their immune system, because only about 20% of those patients make anti-D.

Joe: Big difference.

Pat: Then it turns out, the other place where we switch early and we switch often is if you have a liver transplant patient whose needs in the OR could be great because they're having a liver transplant, and you know that you're going to switch. Why wait to switch? Start them from the beginning with Rh positive blood. Now, it turns out, because those patients are on immunosuppressive agents and get a great big dose before they do the transplant, pretty much almost none of those

patients make anti-D, because they're on immunosuppressives and they're going to stay on immunosuppressives.

Joe: Got it. Got it. That's awesome. Those are great. Those are great, great tips. Very cool. Anything else on that, Pat?

Pat: No, I think we covered all of that. So I think you're up next.

Joe: [00:20:58] My second one is what I call, "**Let's be CMV-free**." That's a slight overstatement, but the whole point is to discuss what we do to prevent CMV transmission. So let's go back to the beginning. CMV stands for "cytomegalovirus." Most everyone has heard of cytomegalovirus. It's a DNA virus, it's actually a herpes virus. As time goes by, especially in urban areas, the majority of us, the significant majority of us have had CMV at one point in our lives and probably never knew anything of it. Because in healthy people, it just causes a cold basically, pretty much the symptoms of a cold. It can be a little more significant than that, but usually just pretty much a nothing burger. But in people who are desperately sick, in people who are seriously immunocompromised, CMV can cause really, really nasty stuff, some major, major clinical complications that, in fact, can be fatal. So, there's been a longstanding interest in blood banking circles to try and prevent the transmission of CMV from a blood donor to a recipient. So let's thumbnail this for you.

Bottom line: There are two main ways of trying to prevent CMV transmission. The first is to test your blood donors, and **test them for the presence of CMV antibodies**. Remember, CMV is lifelong. Once you get infected with CMV, generally speaking, you're going to have CMV antibodies forever. Okay, great. So if you get someone who's CMV negative you can theoretically assume that they haven't been exposed CMV (more and that in a second). The second option, in blood bank world, we realized that because CMV, after the acute part of the infection, it kind of goes and hides out, primarily, we think, in the monocytes, but certainly primarily in the white cells, if we get rid of those white cells through **leukocyte reduction**, would that functionally take the CMV load down to a non-infectious potential? And that's been the argument that's gone back and forth for a LONG time in blood banking, on what the right choice is, or if there is a right choice. Well, again, I don't want to take up too much time with this, but the short version is that most of us in blood banking world (and it's been held up pretty well by some of the older studies, which used older technology filters that didn't work as well, as well as some more recent studies in stem cell transplants) that these two were primarily equivalent. Yeah, you'll see some slight differences. But the most important thing that I tell clinicians is: Either one is not perfect! There's still a risk with either one, and there's a lot of thoughts behind that, Pat, and again, I don't want to go into this in too great detail, but for those of you listening, the basic idea is CMV, in the very early stages of infection, has a period where leukocyte reduction won't work because the virus has not gone

into the white cells yet, and testing the donor won't work because the donor's in the window period. So in an acutely infected donor, you could get a CMV negative unit or you could get a leukocyte-reduced unit, either one wouldn't necessarily prevent CMV transmission. So again, most people believe, and Pat, I know you believe this, because I've had this conversation with you before, that leukocyte-reduced units are essentially equivalent to CMV-seronegative units in preventing the transmission of CMV.

Pat: Okay so, as you know I agree with you. My question to you is, logistically, what is the benefit to going with leukoreduction?

Joe: That's a great question and really important. So I mentioned that the majority of people, especially in urban areas, are CMV positive. So when you put yourself in a position where you are ONLY going to use CMV-seronegative units in patients who are at risk, you are significantly limiting the potential pool of products available to you. Well, I'll put it to this way: In my blood center, roughly 70% or so (I'm in an urban area outside of L.A.), roughly 70% or so of the people that I test are CMV positive. So you're immediately taking 70% of the possibilities out of circulation right away, and you're making it much more difficult to transfuse your patient.

Pat: So, those are the logistics at the blood center level. What are the logistics at the hospital level?

Joe: That's a really important question as well, Pat, because when you're dealing with things at the hospital level and you're suddenly having to keep two separate sets of products when, as you know, blood centers leukocyte reduce everything pretty much every cellular product on your shelf...not just pretty much, EVERY cellular product on your shelf is going to be already leukocyte-reduced and can be called "CMV reduced-risk" already regardless.

Pat: And additionally, making your patient wait hours for something that really is already available on your shelf is probably not the best idea.

Joe: Completely agree! Let us move on to your third one. Fire away!

Pat: [00:26:20] OK, my third one is, "**Treat all transfusion reactions like they are an acute hemolytic transfusion reaction until proven otherwise**." And the reason I say that is, like with most things, I see that sometimes with my residents, after a few months, when they start to know what they're doing, they sometimes will say, "Oh it's just febrile nonhemolytic transfusion reaction, it's ok." Don't ever, ever, ever, ever do that! The reason we do the workup we do after a transfusion reaction, except for the mild allergic ones, the reason we do the DAT, the reason we look for hemolysis, the reason we re-type the patient is, we want to make sure that they did not have an acute hemolytic transfusion reaction! Until you have those three points

of data, plus the clerical check on your unit, you have not ruled out an acute hemolytic transfusion reaction. And the last thing you would ever want to do is say, "Oh it's OK, it's just a febrile nonhemolytic transfusion reaction. You can give more blood." If you haven't ruled out an acute hemolytic transfusion reaction and you do that, you could then give more of the WRONG blood. So treat them all seriously, treat them all the same. When you get the four points of data, those being: Clerical check is negative, the patient types the same post-transfusion as pre-transfusion, that the DAT is negative, and that there is no hemolysis in their sample when they spin it down, then is the time you can say, "OK it was just a febrile nonhemolytic transfusion reaction." But don't make that decision too quickly, because you could make a huge mistake and have a patient have major consequences because of it. And one of the things I realize has changed a lot since we were in residency, because most hospitals have a two sample policy now, you don't have as much acute hemolytic transfusion reactions. When you don't see something, it can be to hard to be ever-vigilant for it.

Joe: Oh, man! I love that point. That's so true. And I completely agree with that. However, I will say, there have been some publications in recent years suggesting that you can look at "high risk fevers" and "low risk fevers," and I've heard people passionately defend that. What I say in those cases (like there are certain temperature elevations that make it more likely and so you work those up and others you don't etc.), I personally, Pat, completely agree with you. And that's the way I practice. I am a part of that. I will admit is colored, well, you mentioned, we've both been hanging around blood banks for a long time. I have had to make the call to the FDA to say, "Oh, hello FDA! We just had a fatality in our hospital because someone chose to ignore a fever and transfused through it." So I am very strongly influenced by that experience. And I completely agree with what you just said.

Pat: I haven't had the experience of somebody ignoring the fever and transfusing through it. I have had the experience of having to interact with the FDA because somebody got the wrong unit of blood and had a negative outcome. And, to me, it does not take that long, or if it does take that long to do the workup, you need to figure out how to get the workup done quicker. Because, except in an emergency...now if it's emergent, and the patient needs the blood NOW, you have to be a doctor, and you have to make decisions. And in that case, you can always give group O.

Joe: I'll close it with this: What I tell clinicians all the time when they argue with me about working up things like this is, I tell them, "You know what? Chances are, you are probably right. You are probably right, but when you're wrong, you are going to deeply regret it."

Pat: Exactly, don't become complacent.

Joe: It's just that simple to me. Yep. OK, good deal. I think I'm ready for my number three. You ready for it?

Pat: Sure!

Joe: [00:31:05] OK here's my number three: "**What the heck is Cryo**?" I love that...what the heck is Cryo? Cryo is probably the most misunderstood blood product, and of course when I say "Cryo," I'm referring to the blood product which is more formally known as "Cryoprecipitated antihemophilic factor," which nobody calls it anymore. Everybody just calls it "cryoprecipitate" or as I said, just "Cryo." OK, everybody, so here's how cryo works: Cryo is a product that is made from fresh frozen plasma, meaning a product that goes into the freezer, a plasma product that goes into the freezer within eight hours of collection. Fresh frozen plasma products are about 250 CC or so, somewhere in the ballpark, and the "Cryo" part is when that plasma is thawed slowly in a refrigerator overnight (not like you're going to transfuse it when you thaw it at warm temperatures, but you thaw it slowly), and a little bit of crud precipitates out across the bottom of the bag. Just about that simple. That's a low-tech way of putting it, but you end up with an individual bag of Cryo that contains roughly 15 CC of product (most of that is just residual plasma that suspends that precipitate). The precipitate contains five main things, only a couple of which we care about, but there are five main things: There is factor VIII, there's fibrinogen, there's von Willebrands factor, factor XIII, and then a weird protein called fibronectin that we're not completely sure what it does. But nowadays, though Cryo was initially developed to treat hemophilia A (factor VIII deficiency), nobody uses it for that anymore, unless it's an, "Oh my god emergency," and for some reason you don't have factor VIII concentrate. It's primarily used in the United States to replenish fibrinogen and that's the big deal. A couple of numbers for those of you preparing for exams: You have to have at least 150 mg of fibrinogen in each individual bag of Cryo and at least 80 IU of factor VIII in each bag of Cryo. So, it's primarily used, as I said, in the United States, to replenish fibrinogen in situations of big-time bleeding in cases like massive transfusion from traumas to some extent, obstetrical hemorrhage is a big place where it gets used, liver transplants, cardiac surgery, things like that where fibrinogen levels dropping can be a big deal and replenishing that fibrinogen can help the patient do better. One last thing, before I move on from this, is I want to make mention of the fact that Cryo, as I said, comes in little tiny bags, 15 CC or so in a bag. Nobody wants to transfuse Cryo one bag at a time! That's dumb, unless you're talking about a really tiny patient that is only going to get one bag. So, nobody does it that way. Everybody pools the Cryo, and the great thing is that virtually every blood center I know of nowadays can actually do that work for you. So by the time the Cryo gets to your transfusion service, it's already been pooled. So, you don't have to waste time pooling it yourself and decreasing the time that you have to transfuse it from six hours (which is Cryo's normal shelf life after you thaw it) to four hours after you pool it, generally speaking. So you really...if you're in a transfusion service, and you're not getting pooled Cryo,

well, why not? It doesn't make any sense to pool it yourself. It's crazy, and especially if you're doing cases, if you're sending it out in cases like trauma cases or obstetrical hemorrhage cases, in particular, where you've got to get that product out there in a hurry! You do NOT have time to pool! You want to get it from the blood center that way and go ahead and transfuse it again for those fairly narrow indications.

Pat: So, Joe, I think that was a fabulous review of Cryo, and that last thing that you talked about, to me, is the MOST important. We all know, as a group, blood bankers have a tendency to be parsimonious, and because we are parsimonious, we tend to not want to pay for things we can do ourselves. The problem is, when you're dealing with a trauma or an obstetrical hemorrhage, literally seconds matter, and you never want to say, "I don't want to spend the extra hundred dollars or whatever it is for the pool because I can do it myself," and make a woman who is massively hemorrhaging after giving birth wait 30 minutes for somebody to pool that Cryo. That is not a good use of funds because, 1) You're putting a woman's life at risk, and obstetrical hemorrhage is still a major cause of death in the United States; 2) You're costing yourself money, because she's going to use more blood! [LAUGHS] So, you're NOT saving money, whereas the pooled product could save a life. And then the other thing that I wanted to talk about just briefly with that is, if you ever want to look like a complete and total genius to somebody, I've gotten a couple of calls, particularly when I was in my blood center days, from hospitals panicking because they've got somebody in the OR that they can't get to stop bleeding. "We've tried everything! We can't get them to stop bleeding! What do we do?" Your response should always be, "Have you given any Cryo?" Close to 10 times out of 10, the response will be, "No." The answer is, give them two pools, and in California, we tend to do pools of five. The standard answer is: Give them two pools of Cryo and see what happens. And every time, I've gotten a call back later telling me I was a genius! [LAUGHS]

Joe: [LAUGHS] I have to write this down. "Pat's a genius." OK. Wow. I knew that already, though...

Pat: Yeah, right! It's not genius, but the thing to remember is, it goes back to something you said at the beginning, we don't use it for Factor VIII anymore. So there's very limited use for Cryo now. Physicians forget it exists.

Joe: All right. I love that. OK so, we've done six of them. We've got a little ways to go, so let us let us move along. What is your number four, Pat?

Pat: [00:37:45] OK. The one that always confused me when I started out was the whole "**Keep the line open**" business. You will see, every time somebody has a transfusion reaction, they're saying, "Keep the line open, keep the line open, keep the line open." Why do we say that? The answer is easy: When you are having a

patient that has a transfusion reaction, you do not know what that transfusion reaction is. And there are certain transfusion reactions that if you lose vascular access, you may never get it again. And those are: Anaphylactic transfusion reactions, septic transfusion reactions are the big ones, but any transfusion reaction where a major component can be hypotension, you can lose that line and never get it back. And in everything you read, they'll tell you to keep the line open, but they won't tell you why.

Joe: That is so darn practical and important that I don't think I can add a darn thing to it [LAUGHS]. I completely agree, and it is something we say all the time, and clinicians and nurses kind of look at us as like, "O-K." Dead on right. I can't think of anything to add to that, Pat!

Pat: You know, I meet with residents on a daily basis, and they ask me the most interesting questions, including, "Why?"

Joe: Residents are good for that: The "why questions," to make you think about stuff. All right, good deal: I like it. All right. So, mine won't be quite as quick, my number four won't be quite as quick as yours. Are you ready?

Pat: Yeah.

Joe: [00:39:34] So you kind of previewed it a little bit, and my number four is, "**Oh my God, it's ALL positive**!", and that's the situation that you alluded to a little bit, where everybody starts to panic, because everything on a particular patient is coming up positive. The antibody screen is positive, the antibody panel is positive, everything looks incompatible, nobody knows what's going on. And of course, those often happen in scenarios where the patient has a hemoglobin of 3, and the clinician is freaking out about transfusing. So this is a topic that I could, in fact I HAVE in some cases, talked for an hour on. I WON'T do that today, but I do want to kind of thumbnail it for you, and think about a couple of things. And the first thing, I tell residents this all the time, and I tell my blood bank staff all the time, the very first thing to do, the VERY first thing to do, is to CALM DOWN!

Pat: It's not panic? [LAUGHS]

Joe: It is not panic time! People may be panicking around you, but you gotta calm down, because you CAN think about this rationally, and you CAN come up with a logical and reasonable solution for these patients. Panic is not your friend here. What I always do in situations like this is, I try and assess what we have. I try and assess what information we have available. Has this patient already been transfused, either recently or remotely? What do we know about the patient? Have we ever done, have we ever TESTED this patient before? Do we have a phenotype on this patient to see what antigens this patient carries? When you look at the

reactions, how do they look? Is everything positive in exactly the same way? Do you have a lot of varying strengths? What do we know, what are we seeing? And finally, the other thing that I ask is, "What does the autocontrol show? If we have a DAT, what does it show?" Because essentially, in cases like this, you're usually dealing with one of two things: Either you're dealing with something like a **warm autoantibody** that makes EVERYTHING incompatible, and your goal in that case is to make sure you don't have any other antibodies aside from the warm autoantibody, or do you have **multiple ALLOantibodies**. Has this patient been transfused previously, and he's made a whole bunch of antibodies against a whole bunch of other people's red cell antigens? So all of this goes into the "mix and the stew." And you've got to breathe for a second so that you can figure this out.

Pat: Absolutely. Can I stop you, because I have a third one?

Joe: Yeah, you can, sure!

Pat: The patient is on **daratumumab**.

Joe: Oh yeah! That is absolutely true. So those of you that are listening, I did a podcast on this earlier with Rick Kaufman about the Myeloma medication daratumumab that makes everything positive as well. Thank you, Pat. You're totally right on that.

The short version of how I approach these, Pat, is pretty simple, and I'll be interested in hearing the way you approach them. But for me, when I have a situation like this, I am always wanting to talk to the clinician and assess the urgency of the transfusion. Because the bottom line with this is that if it comes down to the fact that this patient HAS to get transfused right now or this patient is going to die, then I'm going to transfuse the patient. I'm going to deal with the consequences of it later, because the reality is, in settings like this, the risk of this patient having an acute immediate transfusion reaction, if you give, for example, Group O to these patients, the risk of an acute immediate transfusion reaction is incredibly small. The risk of a delayed hemolytic transfusion is more significant, but I always tell people, "A delayed hemolytic transfusion reaction is better than being dead!" It's pretty simple to me. If the clinician's judgment is they've got to transfuse, then, by God, we're going to transfuse! If we have time, then we're going to approach this wisely. For example, we're going to look at things like, we're going to say, "If this patient has one of these particular antibodies, their patient is at greater risk of something urgent and immediate and acute," For example if someone has Kidd antibodies, those are much more commonly associated with ACUTE hemolytic transfusion reactions than delayed. And those are significant and dangerous. Kell antibodies, anti-K is the most common antibody other than anti-D. I'm going to look for those. I'm going to gradually work my way towards, while the sample is oftentimes being sent off to a reference lab and they're figuring it out, I'm going to

work my way, as best I can, towards something that's the safest possible product with the information I have at that particular moment. And again, it's a long lecture to pull in everything, but the bottom line is, I'm going to try and make this as safe as I can with the information I have at the moment. I'm going to reassure clinicians about patients with warm autoantibodies in particular (most of them can be transfused without a problem), and assess the patient to see if this patient really needs to be transfused, which I will do rather than let them die. So what did I miss, Pat?

Pat: You know, one of the things I always say is, "You never let somebody die because you do not have the perfect product." Sometimes you just have to suck it up and transfuse them. And in a large way, you're having to treat yourself, because you don't want to do it! But sometimes, you just have to get over that and say, "I am not going to let somebody die because I don't have the perfect product." And so, the other thing that we do always is, if we have somebody with a warm autoantibody, if it is a "significant" warm autoantibody (so what I mean by "significant" is 2+ or higher, or we can't get rid of it in LISS or PEG), we will phenotype that patient the first time we see them. Either by serology or molecular, whichever one we can do. And that way, if they come in at 2 am, and they're in that situation that you described, which happens a lot, they're 2 am, it's Saturday morning, it's a long holiday weekend: I've got a phenotype on them, and I can find blood much quicker, and just give as antigen-matched as I can give, and get them through the immediate crisis.

Joe: Love it. Love it. Totally agree. So Pat, we are ready to move onto your number five.

Pat: [00:46:14] OK, my number five is, "**Platelet refractory workups: Just say yes!**" I have a good reason for this. For patients who are platelet refractory, there is this algorithm that many people recommend that you go through to prove that they're really refractory before you order the testing. And that is, you have to get a post-transfusion platelet count between 10 minutes and 1 hour post-transfusion, and you have to calculate corrected count increments, and if you show that twice with ABO-compatible platelets, you then order the workup. And so, to me, that was valid when HLA testing was very much more difficult than it is today. That was valid when it took DAYS to get HLA antibody testing back, when you had to thaw cells to do HLA antibody testing, when HLA typing was so much more difficult than it is today. I say: That is no longer valid. I say that if you just look at the chart, and it just looks like, "Yeah, okay, they're not getting immediate post-counts, but their platelet count hasn't gone above 10,000 the whole time they've been here." Well, wouldn't you want to know if you need special platelets? If you, on a Wednesday, decide you're going to make them give two more transfusions and "prove it," you can delay getting special platelet products until the next Monday. If on a Wednesday, you say, "Yeah, okay, it doesn't look like they're getting really good bumps, let's draw the

testing," and do the testing for HLA antibodies and anti-platelet antibodies, and get that back on Thursday, by Friday, I can get the patient the correct platelets they need instead of waiting until Monday. The testing is very inexpensive. It is, in most cases, it is cheaper then the platelets that you're giving them! And so, to me, I think it's more important to get the platelets, the correct platelets your patient needs quicker than it is to make them prove it.

Joe: Yeah. I love that. I think we used to have the idea of the blood banker standing at the door of the transfusion service with a flaming sword saying, "You can't have your work up until you convince me!" Right?

Pat: Yes. But that was related to how cumbersome that testing was. Now you can have the testing back in hours.

Joe: A lot more options and a lot easier, I agree, than before. Awesome. Awesome. OK. All right Pat. So we're going to fly on these last few so I'm ready for my number five, are you ready for mine?

Pat: Yes, absolutely.

Joe: [00:49:23] So my number five is actually a pretty quick one because it's been talked about a lot, but it is a big change in those 30 plus years that we've been involved in this, and that's, "**Know your 7's and 10's**." In the old days, I remember very well during our medical school days, Pat, being on duty overnight, for me, it always seemed like it was the V.A., because, whatever the rotation was, I was always at the V.A. So I'm at the V.A. in the middle of the night, and I would have some resident who really didn't know a whole lot about transfusion, but he would tell me, "You've got to get that guy's hemoglobin over 10." And I remember very well saying, "Why? What's so magical about 10? He's at 9.7. Why is that bad?" "Uhhh, it's got to be over 10. Just get it over 10!" And that was about the level of scientific discussion that we would have on that, and really in the old days, people used to think that the threshold to transfuse red cells was to get the patient to a hemoglobin of 10 or hematocrit of 30%, and for platelets, for prophylactic platelet transfusions, the patient was in danger if that platelet count dropped below 20,000. I'm sure you remember those days all too well, Pat, right?

Pat: Absolutely.

Joe: So what we have now, and again I'm not going to beat this to death, because I've talked about this in previous podcasts, is that we have great data for red cell transfusions, relatively great data, I mean, it's not as great as it could possibly be, but it's relatively good data that suggests in non-bleeding, hemodynamically stable patients, that **you can use a threshold of 7 g/dL in most patients for hemoglobin and they do just fine**. For patients who are having significant

surgeries like orthopedic surgery, cardiac surgery, and have underlying cardiovascular disease, 8 g/dL for hemoglobin may be a more appropriate threshold. And honestly, we're not totally sure in patients with things like acute cardiac syndrome, patients that are chronic transfusion dependent, etc. But those numbers, while they are numbers that are considered reasonable thresholds, I do want to emphasize this, because just as I thought it was dumb to say, "Hey, this patient at 9.7 or 9.8, why do we have to get them over 10?" I also think it's dumb for us to adhere too rigidly to the 7, for example. Say someone's at 7.1 and they're having clinical symptoms, "Well gee, no, sorry you're over 7." That's just as dumb to me as transfusing to just get over a number. Withholding transfusion just because someone's just over a number is equally silly to me. So again, these are clinical judgments that can be guided by some of these thresholds that we are aware of. The other thing is, for platelets, it's been shown fairly clearly for prophylactic platelet transfusion, that the 20,000 number in most cases and in most situations is too high. That **you can reasonably use a threshold of 10,000**, and in fact some patients do just fine lower. But again, those are numbers. Patients are patients, and make that treatment individual for your patients.

Pat: So I have one question for you. What do you think of single unit red cell transfusions?

Joe: [LAUGHS] Yeah, single red cell transfusions. Wow! You know, I remember I think my very first transfusion committee meeting, when I was the medical director at Walter Reed. I remember having as a list in the transfusion committee all those doctors who had committed the SIN of transfusing one unit of red cells!

Pat: And that's why I'm asking you!

Joe: How DARE you transfuse one unit?

Pat: It used to be a sin, and now it is considered *noble* to only use one unit.

Joe: Exactly. And honestly, it makes more sense, to tell you the truth. You transfuse one unit, you see how the patient's doing, and if it's effective, then why give more? I mean, to me, it's just the same argument as using the minimum dose of a medication that's going to do what you want it to do. Why give more than that? It's the same thing. So it makes total sense to do it. It's just funny because of where we came from and how horrible we used to think that was to use just one unit, but absolutely, now, I think it's the best practice.

So you have number six. What is your number six?

Pat: [00:53:39] OK, my number six is, particularly for people starting out, that you should absolutely know is, "**The blood center is your friend**!" And I say this from

the perspective of, when I was a resident, I used to call the blood center, and Dr. Joy Fridey would always take my calls and always be wonderful. And I just used to be so amazed at how helpful she was and how nice she was. And after having spent almost 15 years at a blood center, and now being back at a hospital, you need to know: This is what the blood center is there FOR. So if you call the blood center as a resident, they're not going to be upset with you. You're not going to be bothering them. In fact, a lot of the time, they would rather they get the call from you so they can know what's going on. It often helps the blood center to have additional clinical information on the patients, so that they can understand what you need and why you need it. And then, once the blood center has jumped through all those hoops and gotten you the things you need to take care of your patient, it's always great to circle back and let them know, "Hey, thanks, and just wanted you to know, the patient's gone home and is doing fine," because that really gives people at the blood center an uplifting moment that, "OK, this work I do day in and day out is very important."

Joe: That's the role I'm filling now and I know the role that you filled for a number of years. We LOVE doing that! Blood centers LOVE hearing from hospitals, and we love helping hospitals with difficult cases, so right there with you on that! Absolutely!

Pat: OK. What's your last one?

Joe: [00:55:38] So my last one is one that we probably couldn't make long but we're going to make it quick. And that's "**Whither plasma?**" Whither plasma? I actually want to say that again, because I like seeing the word "whither": Whither plasma! It's simply the discussion of this, and that is: A lot of plasma that gets transfused would be just as effective if it were poured down the drain. A lot of plasma that's transfused in the United States, and from what I understand, internationally, is simply not effective because the patients don't need it.

Pat: Right! And in addition, my smart aleck way of saying it is: "In addition to it's not needed, you're giving a homeopathic dose!"

Joe: Yes! See, that's the thing. That is exactly the thing. Let's be clear: What we're talking about is in those patients that have the low level, generally speaking, INR elevations, because that's how people look at it (even though INR is not intended for that but whatever, people typically use the INR because it's easy to understand), and they see INRs of 1.3 to 1.5 or 1.6 or so and they go, "Ooo, I have to correct that." And they think, "Oh, let me give a unit or two of plasma and that's going to make things all better prior to this patient's procedure." You mentioned A) It is a homeopathic dose; that's not NEARLY enough! Here's here's my dopey illustration for that, Pat: What I tell people is, that's like sitting in a bathtub full of ice water and pouring one glass of warm water in and expecting it to change the temperature! Right? It's just not going to DO anything. It's not enough! You need much, much,

much, MUCH more plasma to make an impact on that. But further, why do you even need to do that? When you look at how the coagulation system works, you really don't start having issues with bleeding until that INR gets to a significantly higher level, typically 1.8 or more. And when you transfuse them lower than that, not only are you wasting your time because you're not giving them enough to move the needle, that's number one; number two, there's no predictive value that the patient's going to BLEED from INRs at that level; and number three, the few studies that have been done (and they are admittedly few and they're mostly observational) show NO benefit from transfusing plasma in those situations. So my bottom line with those is that with low grade PT/INR elevations, plasma is wasted! How do you feel about that?

Pat: So, there's two things I want to add to that, and you can see, I'm talking over you I'm so excited about it!

Joe: It's alright! Go! Go!

Pat: The first is: You can give your patient a horrific reaction from giving a plasma that is not needed. You never know which unit of blood your patient is going to a horrible reaction to! The best thing is, don't give it less it's needed, and in this example, it is not needed. The other thing is, I think there's a misconception out there that the INR of FFP is 1 and it is not!

Joe: What? Wait a second! Tell me. [LAUGHS]

Pat: OK. So, as you are very much aware since you're now the one works at the blood center, you don't take plasma off of somebody and directly put into the freezer. In fact, if you're doing a mobile a hundred miles from the donor center, it could take 12 hours to get that plasma into the freezer, and it's not FFP, it's "plasma frozen within 24 hours of phlebotomy," or what we all call "FP24." And so, it does not have an INR of 1. It typically will have an INR somewhere between 1.1 and 1.3. And so, if you're trying to "correct" an INR of 1.3 with FFP, it's not going happen.

Joe: So I guess my illustration would be better: It's like sitting in a tub of ice water, and pouring a slightly lukewarm glass of water in and expecting it to change the temperature. Is that better? [LAUGHS]

Pat: [LAUGHS] Or *more ice water*, depending on what your patient's INR is. If your patient's INR is 1.3 and you happen to be transfusing with an FP24 that has an INR of 1.3, it's like putting in more ice water!

Joe: You're absolutely right, and we're shocked when it doesn't work (GASP).

Pat: Horrified.

Joe: Yes. Oh man. Pat, my goodness, there is obviously a lot more that we can talk about, and I would love to pick your brain for another three hours! But because we're on podcast time, we got to shut this down. I cannot thank you enough, my friend. I will tell you, it has been an honor knowing you for these 31 plus years, and you are just the absolute best. I love talking to you! Thanks so much for hanging out with me.

Pat: I feel the same about you.

[CLOSE MUSIC]

Joe: Thanks for listening, everyone! Just a reminder: Go to **wileyhealthlearning.com/TransfusionNews** to get CE credit for this episode, both for physicians and laboratorians! Also, I want to hear from you! Visit the show page at **BBGuy.org/044** to leave a comment, which I will definitely see and read, and very often respond to.

Time for me to go! As I leave you today, my wish for you hasn't changed: I hope you smile, I hope you have fun, and above all, never EVER stop learning! See you next time.