Joe Chaffin: Hi everyone, and welcome to episode 001 of the Blood Bank Guy Essentials Podcast. My name is Joe Chaffin and I am your host. I'm very, very grateful that you are willing to take the time to check out this podcast. I hope you'll find this interesting and informative. I'm super excited that you're here and I'm very glad to share my conversation from January 2016, with Dr. Mark Yazer. Dr. Yazer works at The Institute for Transfusion Medicine and the University of Pittsburgh, and he and I are going to be discussing **the use of apheresis-derived vs. whole blood derived platelets** and the relative challenges that come with each of those products. I think you'll find it very interesting—I hope so, anyway. Just a couple of things to start off with: I have no financial disclosures for this particular episode and neither does Dr. Yazer, though he wanted it to be mentioned that he is on the Scientific Advisory Board for several companies including Terumo, Macopharma, Grifols, and Octapharma. Also, the opinions that Dr. Yazer and I express in this podcast are our own, and may not reflect those of the organizations for which we work. So without any further adieu, I am proud to introduce episode 001 with Dr. Mark Yazer.

Hi Mark, and welcome to the Blood Bank Guy Essentials Podcast! I'm really really happy to have you here. I want to introduce you first: Mark is with The Institute for Transfusion Medicine, ITXM, in Pittsburgh. And from what I can tell, Mark, you have various titles. Can you summarize for me a little bit what you do at ITXM?

Mark Yazer: Well, at ITXM, I'm one of the medical directors of the transfusion service. We provide transfusion medicine expertise to over 20 hospitals now in Pittsburgh and the surrounding area. So a lot of in-hospital patient management stuff with transfusion. We're very active with patient blood management. And then, on the University of Pittsburgh side, I'm a Professor of Pathology and do a lot of research around transfusion medicine, blood group genetics, patient blood management, trauma resuscitation, that sort of thing.

Joe: Awesome, awesome! Well, before we get into what we are going to talk about today, I'm always interested what gets people interested in transfusion medicine in general. We've all got our stories and things that kind of put us along this pathway. What was it for you? What kind of pushed you in that direction and what keeps you there?

Mark: Yeah Joe, I wish I had a good answer for this…but the truth is, I've always liked hematology, I've always liked morphology. My training was in hematopathology, so I spent 4 years looking at red cells and various other cells under the microscope. But it was the transfusion bit that really got me because I

saw what a—-a sort of "black box" transfusion was and how a lot of the stuff we did relied heavily upon magic. And I thought that we could, you know—really bring some light and some evidence to our practice, so it struck me as really a part of medicine that needed some research, and where somebody with an inquisitive mind could go to and to ask some questions and to move the field.

Joe: Very nice! I actually did not realize that you were a hemepath doc. I don't know, we may have to stop the recording right now, dude, I'm not sure!

Mark: I'm trying to think of who the enemies of Hematopathology are! (laughs)

Joe: (laughs) That's a great point! Not a lot I'm sure! That's a really good point!

Mark: I tell you what, if you told me you're a Toronto Maple Leafs fan, I'm hanging up right now!

Joe: Ok well, see, now that— I wasn't going to get into that, but you are clearly —obviously you're…I don't want to say because of your accent, but I know already before that you're Canadian…I actually grew up in Detroit, so I'm a huge Red Wings fan. So can we still be friends?

Mark: Yeah, "Hockeytown"—Original Six—-no problem with the Red Wings.

Joe: Okay…we can do that! Alright, fair enough!

Joe: Well, I'm really really glad to talk to you today, Mark—-in large part because, well not just because you're a great expert in the field, but I heard you give a talk at the AABB Annual Meeting a few months ago in Anaheim. And, I was way in the back of the room it was awesome! It was—-I guess I could describe it as super heretical…and you could see all over the room, hackles were being raised, if that's the right phrase, and people were like, wait, wait—-wait a minute! And so, I got really happy, by the way, when I heard the talk so I wanted to talk to you about it today and just kind of go over, some of the things that you went over today. And I have to say right from the beginning, you hold a belief that I think is not incredibly common among blood bankers anymore. And maybe not even among clinicians, in fact, probably not among clinicians. So before we get into the specifics of your heretical beliefs, let's talk about—just for the people that are listening to this podcast, that are beginners, that are starting off—can you summarize for us, in a nutshell, the 2 main options for how we provide platelets to patients that need platelets in the United States?

Mark: Sure. Well there are 2 ways, as you say. One is to buy a nice comfortable chair, a great LCD TV—equipped with all the best movies, and convince

somebody to sit there for an hour and a half or two hours, and donate only their platelets. So, this is not somebody that goes in and donates whole blood, like most people do. They're hooked up to an expensive machine, and the machine takes whole blood out of the donor, but it spins it and it can take only the platelets out, and give everything else back to the donor. And this is called the platelet pheresis procedure and the platelets that come from that are called apheresis platelets or single donor platelets. Those 2 words are synonymous…that's the majority product. About 90 percent of the platelet transfusions in the USA are apheresis platelets. The other forgotten about platelets are called "whole blood platelets" because they are derived from whole blood donations. So, you know, when you go into the blood blank and they put the needle in your arm, and red comes out—that's a whole blood donation. And you donate. You know it takes a half hour on the chair. So it's not long enough to watch a feature like movies. So get a magazine or something. (laughs) Short-story podcast, like this?

Joe: Yeah!

Mark: And so what we do at that point is we take the whole blood, and again we spin it, but now the blood is—it's permanently out of the donor, so it's not going back. We spin it and we take the plasma, fraction away that plasma—- will be full of platelets—and then we spin it again and we can separate just the platelets, with a little bit of plasma.

There is another way of producing whole blood platelets, it's called using the "buffy coat method" that they do in my home and native land, Canada, and through much of Europe. It's a whole blood donation. Again, it doesn't use the apheresis machine, but it involves different spinning and it's a different bag—in fact, that allows for this buffy coat to be produced and it's not FDA approved, in brackets, yet…with a question mark, in the USA.

Joe: That's actually something I wanted to just briefly explore with you, the buffy coat deal. So you say it's not FDA approved in the US, which is obviously true. Does that mean, just because something's not FDA approved, can we NOT do it? Is it forbidden for us to do that in the United States, to make buffy coat platelets?

Mark: Ah—well, I wouldn't…I wouldn't produce a buffy coat platelet and try and use it on a patient if it's not FDA approved. I think that's the mark of acceptance, you know it's gone through the regulatory process. It's been shown to do what it says it's going to do and in the absence of it, unless there was some experimental reason to do it, I wouldn't make a routine habit of providing products that aren't FDA approved.

Health Canada, you know…the company has gone through the regulatory steps in Canada and in Europe. But the FDA….you know we're a very small market here when it comes to whole blood platelets…and so, I think we're not as advanced in terms of whole blood platelets technology as they are elsewhere.

Joe: So just for, again just for clarity purposes—-and if you said this, forgive me, I may have missed it—-but an apheresis platelet product, quantity wise vs. a whole blood derived platelet product—-they're not exactly the same, are they?

Mark: Ah, very good. So that's a great point Joe, and you're right. An apheresis platelet is sufficient for 1 adult dose. So an adult gets 1 bag of platelets, comes from 1 donor and it's sufficient for the adult. In terms of whole blood platelets, you're right; What you get is between a fourth to a fifth of an entire adult dose and so, for whole blood platelets, be they buffy coat or platelet rich plasma platelets, we have to pool them. So we're going to have to pool 3, 4, 5 platelets together to make a dose suitable for an adult. For a little baby, one whole blood platelet dose is enough, right? We say 1 unit per 10 kilo, so if you're less than 10 kilo and you need platelets, then you have a single donor in there, but for everyone else we have to pool them.

Joe: Got it. And I believe that's the term that doctors that have been around for a long time will throw out the term "Six Pack"…and I know that—-well, it is 5 o'clock in the evening for you in—on the eastern part of the country. I'm in California, so it's only 2:30 or so, but—-"Six Pack" is an old term for whole derived blood platelets, correct?

Mark: Well, I think the "Six Pack" referred to the number of platelets, the number of donor platelets that had to be pooled together to provide a quantity platelets to be suitable for an adult. Plus it's sexy, right? I mean…"I want a Six Pack from the blood bank!"

Joe: (laughs) It sounds great! But unfortunately…

Mark: Just don't drink it!

Joe: …yeah—exactly! Unfortunately, it still confuses people because you have these old docs ordering six platelets, when they don't really mean six apheresis platelets, but that's a topic for another day!

Mark: You know, we get that in the blood bank, too. They'll order a "Six Pack" of pooled platelets, and that's okay. We know they really meant to order 4 platelets and so we send them what they really meant!

Joe: Right…you edit the requests slightly. I understand. So, the 2 main options we have in the United States are apheresis-derived platelets or single donors, as you mentioned, or a pool of—-between 3 and 5 or so—-whole blood derived platelets using the platelet rich plasma method, okay. So, you mentioned this, you said this already Mark, 90 percent or so, of the products in the United States are apheresis derived—it would seem to me…well, a number of years ago, Steve Jobs was talking about the operating system wars with Microsoft, and he said, "The wars are over. Microsoft has won." Wouldn't you say that apheresis derived platelets has won? What's the history of that? How did we get to 90 percent, because that wasn't always the case, right?

Mark: No, you're quite right. Apheresis technology is relatively new—-it's newer than whole blood technology. And to be honest with you, I don't really know a lot about the "platelet wars," if you will. I don't know who the Luke Skywalker and Darth Vader were, that were squaring off to make the country go towards apheresis platelets. I think, you know, I think if you think—that you mentioned Steve Jobs and therefore, iPhone…I mean, you remember back in the old days when cell phone companies first introduced cellular data, right? They spent lots and lots of money to put up these huge towers to provide data and they wanted to make all their money back so they would charge, you know, 20 dollars a meg for data, and who's gonna spend that? And so they wanted to make all their money back quickly and no one did it, and so they realized they had to take more time to get their money back. I think the same principle might be true in blood centers. They went out and spent a lot of money on these expensive chairs and these expensive apheresis machines, and DVD's aren't cheap! And so, they wanted to have a product that they could sell for a higher margin than whole blood platelets.

Joe: Okay. So, well, I mean we've been kind of moving towards this point, but, I'm just going to give you a chance to say right out what you believe in this. So the current status is as you mentioned, 90 percent apheresis derived, 10 percent or so whole blood derived—-in your opinion, in 2016, is that the right mix? If not, where should we be going? What should we be doing?

Mark: Well, you know there's nothing wrong with apheresis platelets, they're just very expensive compared to whole blood platelets, even a pool of them that's leukoreduced. And I think now, what we have is evidence to show the equivalency between these 2 products, which we didn't always have that. So now that we have evidence to show that these platelets are just as hemostatic,

don't cause as much or at least equivalent, in terms of their bacterial transmission, by terms of contamination problems, terms of their Rh alloimmunization—-so we have all this data now, so we can make a more enlightened decision as to what kind of platelet we want to provide to our patients.

Joe: Ok, then that gets to the heart of it. We're going to spend the rest our time together talking about that data and what you have to share with us that will help convince us of this heresy. And I say that tongue in cheek, as I think you are well aware.

Mark: (chuckle)

Joe: So let's talk first about, I mean really, what it comes down to more than anything else, I think, I mean all the things you mentioned are important, but the first question I think we have to ask and clarify is: "Is there a difference in how well these products work? Does one have an advantage over the other?"

Mark: I guess it depends on what you mean on how well they work. Certainly, it's been known for a long long time, that patients have a higher increment after they receive apheresis platelets compared to receiving whole blood platelets. And so, there's a research technique we can use called the "Corrected Count Increment" or CCI. And it's basically a useful tool that accounts for how much the platelets went up after the transfusion, the patient's body surface area, and how many platelets were transfused. It's a very useful research tool, for determining if a platelet transfusion was in quotes, successful or not. And it's very clear, there have been many studies, including a very nice meta-analysis from 2008, that showed clearly that patients who get apheresis platelets have a significantly higher corrected count increment compared to whole blood platelets. Not sure quite why that is but it's a repeatable, meta-analyzable finding and I think that was a large part of the advertising for whole blood platelets is, you know, don't you want your patients to have the highest possible corrected count increment? And if so, you have to give them apheresis platelets. And so, I think when that's all we had, when that was the data that we had, that was a pretty convincing case. Wouldn't you want to have a higher count? After a platelet transfusion…God forbid, absolutely you would! And so, it's correct, it's scientific, it's proven and it tugs at the heart strings of what kind of platelets you want to provide.

Joe: So that's one thing—the CCI is one thing, which by the way, honestly, I'll just ask you this: In real life, how often do you actually do CCI's, Mark?

Mark: Well, I guess it depends on how much I like the fellow? (laughs)

Joe: (laughs) That was fantastic! Thank you for that! Ok, oh man, so that was the quote of the day! So alright, that aside, CCIs aside, but what about function? Do we have data to talk about how well they prevent people from bleeding or stop bleeding?

Mark: Well, isn't that the reason why we transfuse platelets—this is the key. We don't transfuse platelets to make the piece of paper look nice, in the morning with the patient's lab results. We transfuse them to stop the bleeding or to prevent them from bleeding and now we do. You know, there was a large study called the PLADO Study, the determination of the optimal prophylactic platelet dose strategy to prevent bleeding in thrombocytopenic patients (and I had to read that, I haven't memorized it). It was the New England Journal, a couple years ago, and it was a randomized trial that involved many hospitals in the states, randomizing almost 1300 patients with hematological problems or solid tumors, and they were randomized to get 1 or 3 doses of platelets, depending upon into which group they were randomized. And the questions was, do any of these 3 doses prevent a certain kind of bleeding, better than the other, and the answer is no. They all work just as well, the low dose is just as good as the high dose. But what was really interesting with that study was a subanalysis that was made of it in 2012 published in Blood. In that study, the authors showed that **it didn't matter what the source of the platelets were. Didn't matter if it was an apheresis platelet with their great CCI's or if it was a whole blood platelet with the lower CCI's, the development of the grade II or higher bleeding was equivalent between the 2 groups**.

Joe: OK, so I'll grant you that; that we have data to suggest that in terms of count, we are alright, and in terms of function, we seem to be ok. Yes, PLADO was a large study and a nice study, so I'll give you that one, but the thing that we said back when I first started in blood banking, which was (since I'm an older guy than you are) a little bit further back, one of the arguments we made is, "Well, doctor, wouldn't you like to just have one donor exposure vs. three/four/five/six whatever donor exposures for whole blood-derived?" That was one of the selling points for sure for apheresis-derived. How do you respond to that?

Mark: You know, I think that at certain times and in certain parts of the world, donor exposures are a very relevant thing to consider, and I think that we've done extremely well in terms of our screening and in terms of our testing to really reduce the risk of having multiple donor exposures. So, for example, it might even be advantageous in some circumstances to have a pool of different people's platelets in terms of, let's say reducing bacterial contamination. So for example, when we prepare a pool of platelets, what we've got are four or five people's antibacterial properties all acting synergistically to destroy any bacteria that might be there. Apheresis platelets are leukoreduced, so the white

cells are removed at the time that the platelet is collected. They are just removed by gravity. So an apheresis platelet doesn't really have the opportunity to "auto-sterilize." It doesn't have a lot of white cells that can fight bacteria, whereas whole blood platelet is stored with the white cells until the leukoreduction is done at the time of issue, and in all that time, up to five days, the white cells are still doing their thing. They are still looking for bacteria; they are eating and destroying the bacteria. So we actually have some evidence that demonstrates this. There was a large study, 18 hospital study in the USA, and what they did was they looked at almost 28,000 apheresis platelet units and these platelet units were cultured at the beginning of their storage (8 mL cultured on an automated machine), and each of these 28,000 apheresis platelets that were going to be issued were still negative at the time they were going to be issued. BUT, the study used a "time of issue" bacterial detection kit, a rapid assay to detect bacteria. So you take a little sample of the platelet when you are going to issue it to the patient, put it on the machine, 45 minutes later, the card tells you if there is bacteria. Would you believe that there were NINE of those almost 28,000 apheresis platelets that were negative in culture that turned up positive when we tested them with that time of issue test? So, now we can say that the rate of bacterial contamination of apheresis platelets is probably about 1 in 3000 or so.

We did a similar study with our colleagues in Seattle (we are probably two of the biggest whole blood platelet users in the country), and what we did was use the same test, the same time of issue rapid bacterial detection test, and we tested about 71,000 whole blood platelet pools over a 36 month period, and we found that our rate of true contamination was about 1 in 10,000. If you do a statistical test, you'll see that that's a statistically lower rate of contamination amongst the whole blood platelets compared to the apheresis platelets.

Joe: Wow! Well, you said a couple of things there that are a little bit startling. The first (and I don't know if "startling" is the right word), the "auto-sterilization" I believe that you said, that's a concept that i don't think that a lot of people have thought a lot about, that the white cells being allowed to stay there and not being removed right away, and when products are pooled from multiple different donors, that the white cells are policing the bacteria in the platelets. That's a new thought for a lot of people, I think.

Mark: Well, that's a great way to look at it! You know, white cells, we think of them as "evil," because they can bring certain viruses like CMV, they can lead to alloimmunization, they can release cytokines that cause fever/chill reactions. So white cells do have some negative aspects to them. But they are still functional, right? So they can still hunt down and kill bacteria where they find them. And so, if you store your platelets with white cells, the white cell doesn't

know that it's not in the vessel, it just knows its job is to find bacteria, and it's going to do that wherever it can. In fact, we even have some in vitro data that this auto-sterilization can occur. So, this notion was one of the reasons why we thought that our rate of whole blood contamination was lower than that in the apheresis platelets that don't have a chance because their white cells are taken out, like I say, as soon as they are collected.

Joe: Do you think that there's a difference now, part of the difference…we look back at the data in the past, Steve Vamvakas did a meta-analysis in 2009, and he said (I'm sure you're familiar with this data) that whole blood derived platelets are 5.6 times more likely to be contaminated. Do you think that is in part due to the way practice has changed; the fact that we are now the ones in the blood centers doing the pooling as opposed to the transfusion service? Do you think that has something to do with it?

Mark: It depends on your arrangement. In Pittsburgh, the transfusion service does the pooling.

Joe: Oh, I see!

Mark: Yeah, so it really depends on where you are and what sort of level of technologist that you have. I think we've become a lot more tuned in to bacterial contamination since then. We use the diversion pouch to divert the first 50 mL of whole blood, so that skin plug, which is full of bacteria isn't transfused. We have a lot more attention to what fluid we use for arm sterilizing and how long we put it on and what the motion is. I really think that we've become attuned to the real problem of bacterial contamination. So we've been able to drive down the risk for both apheresis and whole blood platelets, just because we are paying more attention to the problem as a whole. I think that when pathogen inactivation becomes more widely adopted here, that this discussion will become moot, because the risk will be so low for both products.

Joe: Boy, that IS a topic for another day, but you are so right about that. That has the potential to make everything we just talked about with bacteria pretty much inconsequential. So, with that being said, let's move on and talk about a couple of other things that people have mentioned in the past. One that I think we can get rid of fairly quickly, and that's the relative risk between these two types of products for HLA alloimmunization. Can you talk about that a little bit?

Mark: Yeah, sure! You know, there was a great study from last century really (laughs), called the "TRAP" study (the "Trial to Reduce Alloimmunization to Platelets" study). It was a very, very simple study but elegant. Randomized about 500 leukemia patients to get one of four types of platelet products: Non-

leukoreduced whole blood platelets, leukoreduced whole blood platelets, apheresis platelets, or ultraviolet irradiated platelets. I remember as a resident in Edmonton I would get calls from the transplant surgeons, and they would say, "Look, my patient is having solid organ transplant, and the LAST thing that I need this guy to make is HLA antibodies, so I want apheresis platelets!" And that makes a lot of sense, doesn't it?

Joe: It does! It's appealing.

Mark: You know: One person, one donor, one HLA, versus a pool. And at that point, I think we were using six pools ("six packs;" it's sexier). It made a lot of sense, because we just didn't know. Turns out, **what the TRAP study showed was that the incidence of making lymphocytotoxic anti-HLA antibodies and the incidence of becoming immune refractory to platelets was exactly the same if you gave someone a single donor apheresis unit or leukocyte reduced whole blood platelets**. So the key is the efficiency of the leukoreduction: Take away the white cells, and you've taken away the main stimulus for HLA alloimmunization.

Joe: That's something that a lot of people miss. You're 100% right on that; TRAP showed that really elegantly. So let's leave that one behind; I don't think that one's super-controversial. Like you said, "last century," so let's move on.

There is something you mentioned, the risk of RhD immunization in Rh negative [patients] who are getting Rh positive platelets. There is definitely data out there, one that's still quoted in the AABB Technical Manual, saying that there is WAY more red cell content in whole blood-derived platelets as opposed to apheresis-derived platelets. So, that would SEEM I think to people to enhance the risk for an Rh negative person getting Rh positive platelets. How do you respond to that? Do we have data on that?

Mark: Well, you know, Joe, I take it because of the fact that you and I are talking, that you didn't win the Powerball last week?

Joe: (laughs) Correct!

Mark: And, because I'm here, you can be assured I didn't win it either! You know, and whether I had 1 ticket, or 10 tickets, or 100 tickets, I still wasn't going to win, right?

Joe: (laughs) Correct!

Mark: Even if I had a HUNDRED TIMES greater chance of winning the lottery with 100 tickets, I still was just going to basically flush my $100 down the toilet, right?

So…what we've shown recently is the same is sort of true of platelets. You know, an excellent study from 2011 from my good friend Joan Cid in Barcelona showed that in an everyday whole blood platelet unit there is about 0.036 mL of red cells. It looks yellow to the naked eye, doesn't look red; there's a small, small amount, 0.036 mL of red cells. In an apheresis platelet, you have 0.0004 mL of red cells, so 100 times less or I guess fewer red cells in an apheresis platelet unit. So again, we are talking about quantities of small; 100 shades of red, if you will, in terms of splitting hairs of just how few red cells there are. And we know that in theory, the theoretical minimum dose of red cells that you need to create a primary anti-D response is about .03 mL, and so, the amount of red cells in a whole blood platelet unit is sort of in theory right at that level. But again, most of those studies were done in healthy volunteers, not sick, immunocompromised people, and so the level is different.

You know, with Joan, and with the BEST collaborative, we did a study called the "ADAPT" study, where we looked retrospectively at about 200 D-negative recipients of D-positive platelets. And what was interesting about this study was that we did the best that we could to exclude them from having ever received D-positive red cells before, so we really tried to exclude patients that would have had the ability to be tolerated to red cells. And so, in this study, what we found was of these 485 or so D-negative people, about 7 of these patients actually had a primary anti-D response. So 7 of them, or 1.4%, made anti-D. And amongst these 7 people, there was about an **even distribution among those who received apheresis platelets and pooled platelets exclusively**. It's a small number, it's a very, very small number of alloimmunized patients, that's for sure, but that number is always going to be very small. Yet, within that population there was no difference in the rate of getting whole blood or apheresis platelets.

Joe: Just a quick side question, just in terms of your practice, some of the people listening to this podcast are going to be residents who are in training and who get some weird phone calls in the middle of the night, so let me ask you this: In your practice (this is off-topic slightly), someone calls and says, "hey, we've got to give Rh positive platelets to an Rh negative recipient." What do you, when the resident calls you to ask for advice, what do you tell them about giving Rh immune globulin or how do you make that decision?

Mark: Joe, you are really going into all of the highly controversial areas today; I'm loving this (laughs). You know, in Pittsburgh, our practice is perhaps a little bit more liberal than elsewhere. We consider the patient's gender, age, and disease status, and so, if it's a male over 18 years old, and we're short of Rh negative platelets and he's bleeding and he needs a transfusion, or his count is very low and we need to bring it up because otherwise he will have a spontaneous bleed, or going for a procedure, then we'll just give it to him. We'll

do that. If it's a woman of child-bearing age, which we define as less than 50, then we would really try and move some mountains to find some Rh negative platelets for her. But if we couldn't, we wouldn't withhold the transfusion, we would recommend a RhoGAM administration afterwards. But if the patient has a hematology disease, you know if they're having a stem cell transplant or if they are immunosuppressed for that reason, then even a woman of child-bearing age, we wouldn't recommend RhoGAM. Just to finish quickly, other institutions would never THINK of giving Rh-positive platelets to anyone. That would be the most conservative approach. Others would always follow with a RhoGAM administration, but ours, like I say, we take a more liberal approach that accounts for some patient factors that are known to affect alloimmunization.

Joe: And realistically, by the way, I'm right on board with you there. It makes such logical sense that someone who is incredibly immunosuppressed is really unlikely to do something that's already really unlikely. That's the way it seems to me, too.

Mark: Well, that's right, you know, and one of the nice things about the ADAPT study was that we really didn't have a lot of exclusionary criteria. We took patients from all over the hospital with all kinds of underlying diseases. So, not just Heme-Onc patients which have been extensively studied in their rate of producing anti-D, but we took everybody, the surgery patients, the trauma patients, everybody. So, our rate was 1.4%, because, again, we are only giving 0.03 mL of red cells in a whole blood platelet transfusion. It's really not very much, especially when you consider that, for D-negative patients, not healthy people who get a whole Rh positive unit, only 20% of them are going to make anti-D.

Joe: Yes! (sarcastically)You mean it's not 80%, Mark? What happened?

Mark: Well, it is! It is 80% of normal, healthy volunteers, but we don't find too many normal, healthy volunteers in the hospital!

Joe: They are misplaced if they are there, that's for sure!

Mark: I remember something called Munchausen's disease…

Joe: Yes, you are correct.

Mark: That was years ago…

Joe: So, we are starting to run out of time, so if we can just talk about one more thing that is a little bit controversial, though the rules are changing somewhat.

Let's talk a little bit about Transfusion-related Acute Lung Injury, and again, let's step back for just a second, maybe your thumbnail on what TRALI is, though again I know it's controversial, but the bigger question is, in terms of preventing TRALI, is there an advantage for apheresis vs. whole blood-derived platelets?

Mark: So TRALI is probably an immune-mediated phenomenon whereby donor HLA antibodies (or neutrophil antibodies) bind to the recipient neutrophils, the neutrophils migrate to the lungs, the vasculature in the lungs become porous, and the patient gets noncardiogenic pulmonary edema. To red cells, the pathophysiology is probably a bit different. And so, the question becomes, well look, if you're going to give somebody five exposures, five chances to have a donor with an HLA antibody, surely the risk of TRALI is going to be higher in the whole blood transfusion than it would be with an apheresis unit. And as you say, it's been reviewed in several papers where the incidence of TRALI to whole blood platelets and apheresis platelets has always been shown to be very comparable. The Red Cross data, the Canadian data, and the study from an ICU at a single center here in the United States have always shown extremely similar rates of TRALI to both types of products, and I think that's because it comes down to the volume of plasma that you are getting. So, it's true you might get five donor exposures in a whole blood platelet pool, but you are only going to get 50 or 60 mL of plasma from any one of the donors, whereas an apheresis thing, you've got a whole lot of fluid, but it's only one chance to get a unit with a high titer HLA antibody.

So, knowing that HLA antibodies are important in causing TRALI, the transfusion community has really made important strides in mitigating the risk. The AABB has put standards in place and will put a standard in place shortly for apheresis platelets that says if you are going to transfuse plasma or apheresis platelets from a woman who has been pregnant, she has to be tested to be shown to be HLA antibody free, because we know that the greater or the more pregnancies that the woman has had, the more likely she is to have developed HLA antibodies. So what this means is that, just like the risk of bacterial contamination of apheresis and whole blood platelets, **now that we know what the source of the TRALI problem is, our risk mitigation steps are likely to bring that risk down for both products, and render any differences that there were moot** because the risk mitigation will apply to both products.

Joe: Got it. So, it is going to become shortly an irrelevant point, simply because both products are basically going to be living under the same exclusionary principles or standards for ladies who have been pregnant.

Mark: You know, there is still a debate as to what to do with whole blood platelets, whether there should be a standard imposed that requires testing for

them, because there is only 50 mL, which again is not dissimilar to the amount of plasma that is in a red cell, and there is no mandate to test for that. But certainly, if you are going to give plasma for transfusion, 250 mL, or an apheresis platelet transfusion, which can often be more, we know we have to mitigate the risk, we know we have to test the women or use plasma from women that have never been pregnant.

I'd like to make another quick point, Joe, which is, if you look at the data from the National Blood Collection/Utilization survey, over the past 6 or 7 years, there were 19 TRALI fatalities reported to the FDA. Interestingly, 17 of those 19 fatalities were caused by apheresis platelets. That's about 90%, and the other two were caused by whole blood platelets, which is 10%, which about exactly mirrors the percentage…

Joe: Those are familiar numbers…

Mark: Doesn't that sound familiar? Exactly! It just adds more credence to this idea that it's the quantity of plasma that's responsible for TRALI, and so the risks are going to be very similar between the two products.

Joe: Makes sense. So, I would say that you've convinced me, but to tell you the truth, Mark, I think I was pretty much there before we started, which is a good thing! But, have I missed anything else? Are there any other risks or comparisons between the two that we haven't been able to cover during our time?

Mark: You know, an interesting secondary analysis of that PLADO study by Rick Kaufman last year showed that the **incidence of adverse events like febrile reactions and serious adverse events between apheresis platelets and whole blood platelets were again, not significantly different**. So once again, we have this building, mounting evidence that we didn't have previously, admittedly, we didn't have all this data until just a few years ago. It's all going in the direction that there really is no reason to throw out whole blood platelets when red cells and plasma are being manufactured.

Joe: Yeah, I'm really glad that you said that, because, I'll be honest with you, one of my biggest pet peeves for a long time is the fact that, well, you know, you work in a transfusion service as well as a blood center; we, at different times of the year and for whatever reason, we so many times have "platelet crisis" and "platelet shortage" and we are literally sitting on a MOUNTAIN of platelets that we aren't even utilizing because of this whole "apheresis platelets are the only thing that's viable" thing…

Mark: And I hope that I've convinced you and our listeners that that's not true, and that given the current data that we've got, the recent data that we've developed, that whole blood platelets are hemostatically equivalent in Heme-Onc patients, and other things like HLA alloimmunization, D alloimmunization, TRALI risk; those risks are all at least similar, if not even better for whole blood platelets.

Joe: Well, Mark, I can't even tell you how much I appreciate your time for hanging out with us here on the podcast! It has been a pleasure, and you've been a delight. Thank you, my friend!

Mark: Joe, I've got to tell you, all my residents love your web site; they always look forward to your updates, and I think you are doing a great service for our trainees. And so, thank you for all the stuff that you are doing for us, as well.

Joe: You're very kind! Thank you very much, Mark. Have yourself a great day!

Mark: Thanks, Joe.

Dr. Yazer's Comparison between Apheresis and Whole Blood Platelets:

Apheresis Platelets	Whole Blood Platelets
Same hemostatic benefits	Same hemostatic benefits
One donor exposure	4-5 donor exposures
Bacterial contamination risk same or higher	Bacterial contamination risk same or lower
HLA alloimmunization risk same	HLA alloimmunization risk same
Anti-D alloimmunization risk same	Anti-D alloimmunization risk same
TRALI risk-same or higher	TRALI risk-same or lower
Other adverse reaction risk same	Other adverse reaction risk same