

**BBGuy Essentials 069CE:
Preventing TRALI with Beth Shaz
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Beth: Hi! I am Beth Shaz and this is the Blood Bank Guy Essentials Podcast.

Joe: Hi everyone, welcome to Blood Bank Guy Essentials, the podcast that has one goal, to help YOU learn the essentials of transfusion medicine. My name is Joe Chaffin, and I am your host. I'm very excited to share this interview today with Dr. Beth Shaz from New York Blood Center on how we've done over the years with all of our efforts to prevent Transfusion-related Acute Lung Injury.

I'm going to get to that in just a moment, but first you should know that this is a continuing education episode and the free continuing education credit is provided by Transfusionnews.com. Transfusion News is brought to you by Bio-Rad, who has no editorial input into the podcast. This podcast offers a continuing education activity where you can earn several different types of credit, including one *AMA PRA Category 1 Credit™*, one contact hour of ASCLS P.A.C.E.® program credit, or one American Board of Pathology Self-Assessment Module for Continuing Certification. To receive credit for this activity, to review the accreditation information and related disclosures, all you have to do is visit www.wileyhealthlearning.com/transfusionnews, and I hope you do that.

Over the past 10 to 15 years, I think it's been fairly widely known and understood that Transfusion-related Acute Lung Injury (or "TRALI" as it's called). It has been not only a leading cause of transfusion-related fatality, in fact it's the MOST common if you look at that 10 to 15 years as a block. It's killed more people than any other transfusion complication. A lot of people outside of our world don't necessarily know that (and you should know by the way, if you're a student, that very recently Transfusion-associated Circulatory Overload in the last couple years has been a little more common than TRALI in terms of causing fatalities). At any rate, blood centers and transfusion services have undertaken tons of different efforts to try and prevent or what we call it, "mitigate" TRALI. We've done things like tried to collect plasma from predominantly male donors (thinking that female donors who have had pregnancies or babies in the past are at greater risk of being immunized and causing the problems), we've done HLA antibody testing, we've done a whole bunch of different things. But what hasn't been super-clear is exactly how well those mitigation strategies have worked.

Well, Beth Shaz from the New York Blood Center and a group of her colleagues have undertaken a very large look at this in a new study that's coming out soon. They have looked at over ten million transfusions over a ten year period, from 2007 to 2017 in nine different states, and tried to really quantify how much impact have these efforts that we've undertaken actually had? They have some very, very interesting data and I'm going to let Beth share it with you because I'm very excited for you to hear it.

A little about my guest, Dr. Beth Shaz is Chief Medical and Scientific Officer and Executive Vice President at New York Blood Center. Beth is responsible for all kinda things at New York Blood Center, including all the medical and scientific activities throughout everything that they do. There's too much to go into but they do a ton of stuff. She also is leading New York Blood Center's Comprehensive Cell Solutions, which is focused on facilitating the next generation of cures in transfusion medicine, cell therapy, regenerative medicine, etc. So lots of great stuff going on there. She was previously an Associate Professor at Emory School of Medicine as well as at Harvard Medical School and worked at Beth Israel Deaconess Medical Center in Boston.

Dr. Shaz is significantly involved with the American Association for Blood Banks, okay, AABB. She is the President-elect of AABB and the Previous Chair or a member of many, many sub-committees. She's also an Associate Editor of Transfusion and an editorial Board member of the journal Blood. She's an author of more than 135 peer-reviewed publications, more than 60 book chapters, and also she is a primary editor of my current favorite transfusion medicine textbook, outside of the Technical Manual, it's called "Transfusion Medicine and Hemostasis: Clinical and Laboratory Aspects." It's now in its third edition and it is a terrific book for those of you that are looking for something outside of the Tech Manual, as a resource. So I can't wait for Beth to share her thoughts on prevent TRALI with you today, so here's my interview with Dr. Beth Shaz.

- Joe:** Well, hey Beth, Welcome to the Blood Bank Guy Essentials Podcast!
- Beth:** Thank you and good morning.
- Joe:** Great to talk to you. This is a first for us, to actually talk face to face. I actually think we met at one point at an AABB meeting a long time ago, but it's certainly our first opportunity...
- Beth:** We did. We did, I remember Chris [Hillyer] introduced us.
- Joe:** That is correct.
- Beth:** Years ago.
- Joe:** I'm honored that you remember. Well, I am so excited to get the chance to talk to you today about Transfusion-related Acute Lung Injury. I think your expertise on this and some of the current work that you and your group are doing on this is really interesting and exciting. I wanted to start by really just taking it back a little bit and starting with just the "essentials," if you will, of Transfusion-related Acute Lung Injury. As we start this talk on TRALI, let's just start with the bare definition. How do we define Transfusion-related Acute Lung Injury? What is it?
- Beth:** Well, the definition that is used is that it's an acute lung injury that starts within six hours of transfusion. The patient has hypoxia and importantly, there's no evidence

of other reasons for acute lung injury. There's no evidence of cardiac, so it has to be non-cardiogenic.

- Joe:** What's the deal with that six hour thing? People ask me that a lot, why does it matter six hours versus not six hours, do you have any insight on that?
- Beth:** Well, I think because if you get longer out then other factors come into play, but it's not a crisp and clear six hours. So it's not that if it's between six and 24 hours you say this is definitely not TRALI. I mean TRALI remains a clinical diagnosis.
- Joe:** Oh and that's huge. Hold that thought, you said a phrase, "acute lung injury." Is there a definition for that? How do we make that call that someone has acute lung injury?
- Beth:** The definition that was really developed out of the Canadian Consensus Conference is hypoxemia defined as PaO_2 over FIO_2 less than or equal to 300 mm Hg or an oxygen saturation of less than 90% on room air. In addition, is a chest x-ray that shows the bilateral infiltrates.
- Joe:** You said something a minute ago that I want to make sure that we really emphasize and you said that TRALI is (I'm paraphrasing because I can't remember the exact words that you said), but you said TRALI is a "clinical diagnosis" basically. What do you mean by that? I mean, hey, we're laboratorians for crying out loud, don't we make the diagnosis in the blood bank?
- Beth:** Well, I think that a lot of individuals and groups have tried to look for specific changes in patients to say, "Oh, that's TRALI," but there's not a clear, like if you do a BNP that it's elevated, that makes you think of circulatory overload. But there's not any laboratory test that says, "Wow, this is TRALI."
- Joe:** Those things that you were talking about, the presence of hypoxemia, the timing, the six hours or so and the radiographic evidence of...the chest X-ray stuff, the radiographic evidence of bilateral infiltrates; without that stuff I can't help myself but make that point that without that stuff, we're kind of left up the creek for trying to actually make a definitive diagnosis of TRALI. Is that a fair way to put it, Beth?
- Beth:** Yeah, that is. I think that's why there's these "probable TRALI" and "possible TRALI" diagnoses.
- Joe:** I definitely want to get to that. You had mentioned also the no evidence of heart issues, like left atrial hypertension. Why is that such a big deal? I mean, so what if somebody has pre-existing heart failure? What does that do to try and diagnose someone with TRALI?
- Beth:** Well that makes you really think that the person has "TACO," so transfusion-associated circulatory overload, that their heart can't withstand the volume of the transfusion.

- Joe:** So Beth, we've described how TRALI happens, what the presentation is, the definition, etc. Before we move on to some more stuff can you tell us, do we have an idea what the mortality rate of this is? How do people do after they get a diagnosis of TRALI?
- Beth:** The mortality rate remains about 10%, and I don't think that that has changed over time. The data is not great. They get supportive care, oxygen, intubation, others...we don't have any definitive treatments for TRALI. There's no magic drug and I think without understanding better the pathophysiology, drug development will be hindered and then the mortality rate is about 10%.
- Joe:** You mentioned that there were different things that lead to different degrees of certainty and you threw out a couple words like "definite" and "probable" and "possible" and things like that. Can you talk about that a little in terms of, well first, I guess backing up for just a second, you had mentioned that this is how TRALI is defined. You talked about the Canadian Consensus Conference from a number of years ago, in the United States, is there a standard way to diagnose TRALI today, in 2019? Is there some place we can go to find a listing of the things that you need to make this diagnosis?
- Beth:** What we rely on is the CDC has the National Healthcare Safety Network Hemovigilance Surveillance protocol, which defines TRALI.
- Joe:** That's not just for TRALI, right? That's for really any transfusion...
- Beth:** For all transfusion complications, correct.
- Joe:** Got it, okay. Everyone, I will put a link on the show page at BBGuy.org/069; on the show page, I'll put a link to those criteria that Beth was just mentioning from the CDC, the National Healthcare Safety Network. Sorry Beth, just wanted to make sure everyone can know that they can go and take a look at that.
- Back to that definition, again, you had mentioned definite, probable, possible, etc. what are those breakdowns according to the NHSN?
- Beth:** So "definite" is that there's no alternative risk factors for TRALI. So other alternative risk factors are pneumonia, trauma, almost drowning, shock, other injuries, drug overdose. There's a whole list of things that could put patients at risk for acute lung injury. So they can't have any of those things, because otherwise it's possible TRALI.
- Joe:** I see, okay. What about the "probable" term?
- Beth:** Well, the probable term, as we mention in our paper, has really come from the blood centers. Part of it is it goes to the pathophysiology of TRALI where there is HLA antibodies or HNA antibodies between...the donor has the antibodies and the recipients have the antigens in most cases. You could say oh this is more clearly definitely TRALI if your donor has an antibody that the recipient's positive for. Well

we're not always able to do that testing, and we don't always find these correlating antibodies so then we use the term "probable."

- Joe:** I think it's important for us to make that point now because when we talk about the data that you guys are trying to record, even though probable is not specifically, well it's listed as an N/A in the NHSN, right? I think that's what they say, N/A.
- Beth:** Correct, yes.
- Joe:** But it's really common to see that in blood center world, I completely agree with that. It's a term that while it's not defined by NHSN, we tend to use it often. All too often, sadly.
- Beth:** Yeah.
- Joe:** Got it, okay. I assume that other categories like doubtful, etc. are just lower degrees of confidence in the diagnosis, right?
- Beth:** You're correct.
- Joe:** All right, fair enough. So we won't take the time to go over those, but I do want to take a few minutes here before we, again before we get into the data that you guys pulled together. Now that we know what TRALI is, how it's defined, can we spend just a few minutes talking about, well, how it happens? I think that's really important if we're going to talk about how to prevent it and the strategies that have been implemented over the years in terms of how to prevent it, we need to understand a little about the pathophysiology. Beth, I ask you this knowing...I mean, you and I have both been doing this for a little while, and you and I have both seen, I'm sure, many iterations of "how TRALI occurs" and our thoughts have evolved, I think over the years. But from your perspective now with the data that's available and the thoughts that have been developed over the years, how would you describe the basic pathophysiology of Transfusion-related Acute Lung Injury?
- Beth:** I think that you're right, I mean it's been, I think TRALI mitigation is one of the Transfusion Medicine success stories and we're still learning. It's still evolving. But as I was speaking to, most cases are really thought to be that the donor has a white blood cell antibody, so an HLA or an HNA antibody that binds to the recipient's white blood cells and that then causes the acute lung injury. Now, more data has come out over the years to look at that the recipient needs to be "primed", the "Two-hit hypothesis." So the first hit is that the recipient has underlying inflammation. One of my favorite manuscripts is by Pearl Toy et al, where they look at these risk factors, you know, such as shock, liver surgery, history of smoking, other things that prime the recipient so they're more understanding, it's like their neutrophils and other inflammatory cells have more antigen binding sites. When they get the antibody, it really is... they're primed to be set off, that causes lung injury.
- Joe:** You gotta "make the neutrophils mad" first in other words, right?

- Beth:** Exactly. You gotta kinda activate them and make them mad. Now, there are some cases where, if you get so much antibody, and particularly with the HNA antibodies, if you get so much of them, they will cause TRALI, even in a recipient that isn't already activated.
- Joe:** Beth, before we move on from that, I just, for some of my listeners that may be sitting there going "HLA versus HNA?" Sorry, could you give us the 30 second thumbnail on the difference between those antibodies?
- Beth:** Sure. HLA is the human leukocyte antigen and HNA is the human neutrophil antigen. So HNA is on the granulocytes and HLA is expressed by more tissues.
- Joe:** Got it. TRALI, as I recall Beth, was initially defined, the antibodies that were the riskiest ones were initially defined as HLA's, but over the years we've certainly seen lots of cases, in fact, lots of nasty cases with HNA's, right?
- Beth:** Yeah. I think, in this month's Transfusion, there was a really nice article even highlighting, again, that we may have not respectful enough for the HNA and the HLA class 2 antibodies.
- Joe:** I will put a reference again, on the show page at BBGuy.org/069 to that article that Beth is talking about cause you're right that is a little scary, quite frankly.
- Beth:** Well, part of it is that we've not really had great tests for HNA antibodies and to screen donors and recipients. They're not, you know...now we have high three part tests for the HLA antibody screening but we don't have it for the HNA.
- Joe:** More of a specialized lab thing would you describe it as rather than something being mainstream?
- Beth:** Yes.
- Joe:** Yeah. Okay, that's probably a topic for another day, so we'll just leave that one, but thank you for helping me define those for everyone. Going back, you were talking about the "two-hit model" where the first hit is something to aggravate the endothelial cells and the neutrophils in the lungs, so that's the priming event. And the second hit, as you mentioned, was for the immune cases anyway, a transfusion of plasma-containing blood products with anti-HNA's or anti-HLA antibodies. Is there another mechanism, I mean is there something where you could get to TRALI without those antibodies?
- Beth:** Yeah, so probably about 20% of the cases, they can't find these antibodies, so there are a couple of other ways. One is, there's this term that we used to call like "inverse TRALI," basically the recipient has the antibody and the donor has the white blood cells. So maybe that happens a few percentage of the time. Then there's these non-immune, meaning, so non cases where there's antibody and antigen that we don't, there's a lot of studies, but I wouldn't say that we have a very good sense of the causes. You know, they could be these you know, CD40 ligand, or phospholipids or things that are related to storage age. We have not

been able to so clearly define them and they work in the murine model but not so much in the clinic.

Joe: I mean, I guess I would describe that as somewhat frustrating, right? I mean you've got cases that certainly appear to be TRALI without the antibodies and trying to figure out exactly what has done that, I have been frustrated by that in the past, certainly. As you mentioned, a lot of work on that, but translating that to actual something we can do about it, I think has been a struggle as you mentioned, Beth. There wasn't really a question there, I was just agreeing with you really.

Beth: Yeah, I know. I mean I think that you're right in that where we see this residual risk from red cells, from red cell products with very little plasma, but they still have a TRALI rate of let's say one in a hundred thousand transfusions. Until we kinda understand what else is going on, I think it'll be hard to make a dent in that.

Joe: Yes. Boy, I agree with that. That actually brings us around to, I mean we've talked about what TRALI is, we've talked about the general pathophysiology of it. Again, everyone, the two hit model, something in the background first for the patient and then transfusion of antibody-containing products in the most common mechanism of TRALI. So Beth, when we talk about prevention, I'm going to assume, because we just talked about the fact that the non-immune stuff has been difficult to put our fingers on, I'm going to assume most of our prevention efforts are, as we like to use the term, mitigation efforts, have revolved around preventing those antibodies. Is that an accurate way to put it or am I missing something?

Beth: No, you're completely right. I mean, I think all of them really are about the donor antibodies. All the mitigation strategies that AABB has put in the standards and through association bulletins, the only one that's kinda not is if a donor's implicated in a case of TRALI, they're now deferred from donating. That's the only where you don't have to show that there's an antibody response.

Joe: Well, I think it's a fair time now to talk a little about what those mitigation strategies have been over the years. I would love it if you would take us on a little bit of a "history tour," Beth. I love history when I can remember the things that have happened! I think I'm going to remember all of these. Can you take us through just what the AABB has done to try and prevent, or to mitigate, TRALI?

Beth: Well, I think, first of all, I think your history comment is really important. I think as a resident, as a junior faculty, seeing cases of TRALI and how detrimental they are...you would have TTP patients who are getting daily plasma exchanges, they would get a case of TRALI and they would be like set all the way back. This is how far we have come. So starting in 2005 really, is when AABB put together its first Association Bulletin...so, just to kinda pause at that, AABB puts together these association bulletins, they are not "standards," meaning you do not HAVE to implement them, but they educate on risks in the blood supply, primarily in what actions you can do to prevent them. Then they eventually, most of the time will lead to standards as well.

The first round of recommendations was really focusing on plasma components and preparing plasma from male donors. I guess to educate the audience, the male donors, most HLA antibodies are formed in response to pregnancy. Women that have been pregnant are the ones at highest risk for making HLA antibodies, so some countries have moved to complete only plasma from male donors. Then that was really the first set of recommendations, was plasma from male donors or never-pregnant females. Then as the HLA antibody screening test became improved we could add that, so females that were pregnant, we could screen for the HLA antibody test. The big issue was AB plasma, and so meeting the demand for AB plasma took a little while to transition. I think we are now at a point where even AB plasma is appropriately screened for TRALI, for donors at risk for causing TRALI.

Joe: I hope so.

Beth: Yeah, I know. I hope so. I mean they are supposed to be.

Joe: Yes.

Beth: Yeah. The next wave of recommendations was on platelets. So again, apheresis platelets because apheresis platelets are suspended in a fair amount of plasma since these antibodies are in the plasma of patients so they are also a high-plasma component. So again, the donors can be male, never-pregnant female or HLA antibody-screened previously pregnant females. That really was mandated in 2016 through AABB Standards.

Joe: So we've kinda had several waves of it, right? I mean as I recall, everything but the initial push to do predominantly male...am I remembering this right Beth, that was implemented in 2008/2007 range, somewhere in that ballpark?

Beth: Yes.

Joe: And then eventually we moved forward with the AB plasma and finally the AABB Standard in 2016 as you said. But we've had multiple waves of, in the United States, of strategies to prevent TRALI, right?

Beth: Yeah and I think that every blood center has taken it's own steps in time. By 2016, everyone had to be on board.

Joe: So with that, as blood centers have taken steps to try and decrease the risk of TRALI, I know that you and your group have put together a look at large number of transfusions and a large number of reports of TRALI and probable TRALI. I want to give you the opportunity to go through what you guys found when you were analyzing data from your centers and your associated centers. Before we do that, Beth, one quick question: In the United States is there a national reporting of cases of TRALI, whether they're fatal or non-fatal? Is there a way for us to look at that and see before what, discussing what you guys found in your centers, do we have data to suggest that any of this has worked so far?

Beth: Well, so I think you're asking just for really good hemovigilance program. The U.S. is a little fragmented so as we talked about, we do have these definitions, these surveillance definitions and hospitals can put their data into it and that is periodically published. Our other mechanism that we use, well we have two other mechanisms really. Another mechanism is the National Blood Collection Utilization Survey, which also every other year, hospitals put in their data on blood use in adverse events. That was recently published with 2015 data. None of these are perfect, but the last way is the REDS program now is putting together donor/recipient databases. Right now there are four hubs that put their data in, so they're periodically also reporting out complications, but none of them are comprehensive like the UK SHOT, Serious Hazards of Transfusion, which has done a phenomenal job of collecting... Again, I mean it's all passive reporting, but at least it's MANDATED passive reporting. They have shown really drastic low rates of TRALI in their most recent 2017 report.

Joe: Those are great mechanisms. What about the reports to the FDA of fatalities, has that shown any impact?

Beth: All transfusion-related fatalities have to be reported to the FDA, who annually puts out a report, and they have shown that the TRALI-related fatalities have dramatically dropped off. Although, I mean, notably TRALI still remains one of the major causes of transfusion-related mortality, it is much less, as are all transfusion-related fatalities.

Joe: Yes. Okay. All right, so we have teased this enough, and I would love to hear about what you guys looked at and what you guys found in your look at cases of TRALI in centers that you were involved in. So why don't you just give us the background on what led you to do this and where you looked and what you found?

Beth: Okay, so what led me to do this was because the U.S. does not have a great formal hemovigilance system, I wanted to look at our blood center. Our blood center consists of New York Blood Center, as well as our affiliates. I wanted to look at our TRALI rates to see, how are we doing? Which it was a good quality improvement project to see are we at where we think that the rest of the country and the world are at. In particular, there hasn't been a lot of data on the residual risks for platelets and red cells.

Beth: We looked at data from our blood center and our affiliates from 2007 to 2017, so ten years. We had 104 TRALI cases reported in a little over ten million components distributed. We had a TRALI rate of about one in a hundred thousand components. Then we looked at the rate of TRALI, over those ten years and the effect of putting in these mitigation measures. So we nicely were able to show a figure that starting in 2007, our rate was about 2.8 per hundred thousand components distributed and that really dropped to about 0.5, and how with each measure there was a decrease in our TRALI rate.

The other thing that we looked at was the difference between females and male-donated products and those affects on TRALI. Now, us, like others, the TRALI rate

due to plasma, really has gone down with all the mitigation strategies. So that's consistent with other places. For the platelets, there still seems to be a higher risk with female donors than the male donors. However, for both of those it's gone down with the implementation of the mitigation strategies. It's unclear why that is.

- Joe:** So just to be clear, I want to make sure I understand this, because I think it's an important point, with current strategies for testing or for TRALI mitigation for apheresis platelet in the United States, you're still seeing a significantly higher rate of definite and probable TRALI with female donors than with male donors?
- Beth:** Yes.
- Joe:** That doesn't sound good. I'm worried.
- Beth:** Well, it's much better than it was.
- Joe:** Okay.
- Beth:** You know, then the question is, why is that? I don't, at the moment... I can *hypothesize* about it, and you know, it's unclear if what we're seeing is the same as what other blood centers are seeing. So is it related to HNA-antibodies? Should we be using more platelet additive solution that takes out a little bit of the plasma? I think this is an area that we should still look at. I mean, I think what was promising or when these platelet apheresis mitigation strategies came into being, we had predicted a decrease of about 60% of the TRALI cases. And that is what the American Red Cross showed in their publication, and that is what we also saw. The strategies are working as predicted, but we may need other strategies on top of this.
- Joe:** That makes sense that there may be more work that we have to do. That was actually where I was going next, these numbers that you're mentioning and you had talked about the UK and the Serious Hazards of Transfusion reports and other reports in Europe, how do your numbers compare to what has been seen internationally?
- Beth:** Yeah so UK, they've had ten components for about ten million transfusions in the UK. We've been in discussion to find out why that is and, so some of it is they use different products. I know they use buffy coat platelets, but at the moment, I don't know if they screen with HNA antibodies. I don't know, I haven't gotten enough direct dialogue. Or is it different reporting, because those systems use passive reporting. But I can say this, that there have been no cases of TRALI with SD plasma. I do think that is consistently published and seen throughout the world. Countries that use more SD plasma, do have lower rates of TRALI.
- Joe:** We talked earlier, Beth, about the stages of TRALI mitigation that were utilized in the United States with the different mandates from AABB... Sorry, "mandates" is too strong a word, as you said. They don't necessarily come out as "you've gotta do this," but strong suggestions at least and in some cases standards at least with the 2016 implementations. But over the years, as we've implemented these different

strategies, did you guys see in your data, step-wise affects of those different strategies?

- Beth:** Yes, we did. With the biggest drop was moving towards male-predominant plasma products. Another big drop was HLA antibody screening of parous female platelet donors, were really the biggest drop in the TRALI rates.
- Joe:** That makes sense. That makes sense, but Beth, I have to ask you, and this kinda goes back to what we talked about at the very beginning. Well not necessarily right at the beginning, but when we talked about the residual risks. So as I look at your data, and you have a really nice table that I hope we'll be able to at least, maybe not share definitively, but at least describe. But when we look at that figure, showing the residual risk, despite all these mitigation strategies, and you mentioned the issue with female donors in particular. But it doesn't go down to zero, any thoughts on that? I mean, for goodness sake, we're doing all this stuff, is there a role for those, going back to those nonimmune things that we talked about. Is that maybe why we're not getting down to zero? Or do you have any hypothesis on that?
- Beth:** If you think about the majority of the blood components we transfuse are red cells. With the red cells, if we don't have a rate around one in a hundred thousand or 0.5 in a hundred thousand. It's difficult to imagine that the 10 mL or so of residual plasma with the antibodies in it, so I think that really understanding these other reasons for TRALI. I've also been a big component of understanding the recipient risk factors for TRALI. That's why, I mean I think these vein to vein donor to recipient databases and these studies are coming out from these, will help us understand the recipient risk factors and maybe with certain recipients you have to be more vigilant about the transfusions.
- Joe:** That's really interesting. Do you foresee a day when we're able to, I mean obviously this day is not now, but do you foresee a day when we might be able to screen a patient for being at risk for TRALI?
- Beth:** Yeah, I do. I think we have some clinical risk factors and then, nicely presented in, so "Blood" has a review series. A Transfusion Medicine review series and one of the manuscripts is on TRALI and TACO [NOTE: Link at BBGuy.org/069] they go to highlight the measuring of interleukin-8 and interleukin-10, as ways of suggesting that a patient may be at risk for TRALI. Because again, the idea that it's the IL-8 where this is a marker of being an inflammatory state.
- Joe:** The thought of being able to have those tools available is interesting and it would lead to an entirely different conversation about TRALI, wouldn't it? I mean, I think we've said for years, it seems like there are certain cases of TRALI, that the only way to prevent it from occurring would've been to not transfuse the patient. I'm sure you've had those conversations at some point in the past, and that might change things.

- Beth:** Yeah and I think that, why I'm so excited about the future of transfusion medicine, both from the blood center and the hospital side, is as we have more data and more information, we can really be more thoughtful of the products that we transfuse. Potentially, if you have a patient that is a current smoker and maybe in shock, then you want to choose the male donated product, or that's who you're going to give the solvent detergent plasma to. I think only when we start doing these things can we say oh well, maybe... or you use a washed product. We don't know enough.
- Joe:** Somewhere Neil Blumberg is smiling because you just said "washed product."
- Beth:** Yeah. I know. I'm always, I mean, this is a total sidenote, but with all these red cell additive solutions, I'm like, "We could just rejuvenate them instead of having to do all these things and then we can stop doing all these studies. We have an answer if we really think it's a problem."
- Joe:** There you go.
- Beth:** But that's another episode...
- Joe:** It is.
- Beth:** That's another conversation.
- Joe:** It is, for sure. Well, one more thing Beth before we close this out, that I just wanted to ask you. And I think you talked about this a little in the report that you're working on, as far as this goes, is it possible that these residual numbers that we're seeing and in particular the female versus male issue in terms of higher risk apparently for female platelets in particular, female-donated platelets in particular, is it possible that our answer to this is time? That over time, that everything may continue to decline and that maybe some of this residual risk that we're seeing is just, we haven't been doing this for very long in the grand scheme of things in terms of the most recent mitigation risk? That's a long question, I'm sorry, but is it possible that the answer to this in part could be just wait and see?
- Beth:** It's possible.
- Joe:** [Laughs] That is an excellent answer, thank you! I asked you the longest question in history and you gave me an excellent answer. So we'll see I guess, right? That's the key.
- Beth:** Well, I think importantly, what you...is making sure that we keep watching it and tracking it. I think on one hand, my reason for asking for us to do this is to say, "Oh wow, how far have we come! Wow, we've come really far, but how far more do we need to go?" I think trying to keep, there's a lot of research going on about TRALI and lung injury and the roles of the platelets and neutrophils and red cells and other monocytes and macrophages. So I think as we were learning more about these things, can we start saying how do a better job of a preventing it. I think one of the things we haven't discussed much because there's not much to discuss, is

how do we treat this? That really...right now, we do supportive care. Actually, when I was a resident and junior attending, in particular the junior attending for TRALI, I kinda waited to see how the patient did over the next 72 hours to figure out was it TRALI or...

Joe: I understand.

Beth: Or ARDS, you know?

Joe: Right.

Beth: Some of these cases, yeah. I think that a lot of work is being put into this and we've come really far in ten years and I think we're going to keep moving forward.

Joe: Beth, as we close our time, I wonder if you would just take a couple minutes to thumbnail for us what you hope people will take away from this data that you guys are presenting in this paper regarding the look at the last, the ten years from 2007 to 2017 with TRALI in the centers that you're affiliated with. What do you hope that people glean from this paper?

Beth: Yes, I think that two points are, one, that we've made substantial progress in decreasing the rates of TRALI over the last ten years. One of the goals that AABB had was that TRALI would be rates should be less than one in a hundred thousand and we've really been able to meet that goal overall. But, however, there's still more work to be done and we're going to keep trying to find ways to decrease the rates of TRALI.

Joe: This has just been a blast! I've really, really enjoyed talking to you about this. Thank you for the work that you're doing and that you are reporting on TRALI, I think it's really interesting and exciting to see that the mitigation strategies that we've been working on are actually having some affect. So thank you so much for being here.

Beth: Oh thank you. Thank you for having me. It's been a pleasure speaking with you.

Joe: Well, my thanks again to Beth Shaz for being with me on the podcast today. I hope you learned from that. There was a lot of great information there. Please remember if you are a physician or laboratory professional you can go to www.wileyhealthlearning.com/transfusionnews, get your hour of totally free continuing education credit. While you're there you can find a lot of other episodes, a lot of other things that you can listen to and get equally free continuing education episodes. My thanks for that as always to Transfusion News, Bio-Rad, who brings you Transfusion News and Wiley Health Learning from bringing you all of that continuing education for free.

Joe: Again, the show page for this episode is at BBGuy.org/069 and you can find all kinds of links there, including links to previous articles on Transfusion-related



Acute Lung Injury, as well as AABB references, for those of you who are AABB members. I really recommend you check some of those out, it's very, very interesting.

Joe: You've heard me say this before, but please, please, please go to Apple Podcasts on your computer, give this podcast a rating and review. Those ratings really help more people be able to listen to and notice the podcast, which I'm really trying to do.

Joe: I have some other great episodes coming up, including interviews on neonatal platelet transfusion, interviews on pathogen reduction, lots of really cool stuff coming up. So I hope you stay tuned to that cause it's coming very soon. But until that day comes my friends, as always, I hope that you smile, and have fun, and above all, never, EVER stop learning! Thank you so much for listening, I'll catch you next time on the Blood Bank Guy Essentials Podcast.