Joe Chaffin: Hi, everyone! I am so glad to welcome you back to the Blood Bank Guy Essentials Podcast! My name is Joe Chaffin, and I'll be your host.

Today's episode is a really interesting conversation that I had on March 15, 2016 with Dr. Anne Eder. Dr. Eder is the Chief of Blood Services at the National Institutes of Health in Bethesda, MD. She was kind enough to share her expertise on septic transfusion reactions. Now, septic reactions may not be familiar to you, but they are scary, sometimes fatal things that occur when a blood product (which is usually platelets, for reasons that Anne and I will go in to) is contaminated with bacteria. We have made lots of progress in the past few years in terms of reducing these really nasty suckers, but we really still have a long way to go. I mentioned the date of the recording for a specific reason: The day before we recorded this podcast, the United States FDA issued a second draft guidance on detection of bacterial contamination (and it was their second one in 4 months). We stayed pretty much clear of the draft guidance, because FDA has already shown that they can and will change their mind on platelet bacterial testing, and neither of us know where things will shake out (you should check out the draft, because it has some VERY substantial changes!). Depending on when you hear this podcast, the FDA may have already issued a final guidance that will change the things we discussed; just check the show page on the Blood Bank Guy website (bbguy.org/podcast) for more information.

Dr. Eder wanted it to be known that she has no financial disclosures for this episode, and neither do I. She also reminds us that the opinions she expresses are hers and not those of the US Government or the American Red Cross. Likewise, my comments and opinions are not necessarily those of any organization with which I am affiliated.

OK, so enough of that! On to Episode 003, with Dr. Anne Eder!

I am delighted to introduce to you today, Dr. Anne Eder. Dr. Eder is the Chief of the Blood Services section at the National Institutes of Health in Bethesda. Before that, she was vice president for National Medical Affairs at the American Red Cross. Dr. Eder has a lot of great things going on: she's an adjunct Associate Professor at Georgetown and in addition, she serves as an Associate Editor for a couple of the major journals in blood banking—-both *Transfusion* and the ISBT

Science Series of *Vox Sanguinis*. Dr. Eder is board-certified in Clinical Pathology as well as Blood Banking/Transfusion Medicine and she trained for both of those at the University of Pennsylvania. She's also an MD/PhD, you over achiever, you! (laughs) and she got both her MD and PhD at the University of Iowa. What I find with Dr. Eder is that her information is useful, it's helpful and it really just, it hits things in way that's easy to understand and is just spectacularly great. So I am honored beyond belief, to have Dr. Eder here with me today. Anne, welcome!

Anne Eder: Thank you, Joe! And I have to say it is a huge honor for me to be here, because I and many other people…I mean I studied for my CP and blood bank boards with what might have been one of your first study guides, and I passed my boards and I don't think that was a coincidence. So thank you for that and thank you for inviting me to talk today.

Joe: It is my pleasure to have you and my honor. I have to say, I always ask my guests this right up front, just because I'm really interested in what gets people interested in blood banking? And what is it for you in your career, as you were coming up, as you were in your pathology training, what was it about blood banking that just kinda grabbed you? What keeps you doing it now?

Anne: What's not to love about blood banking?!? So, I really enjoyed my training, but I'll share with you a true story that I carry with me. So very early, in the first days of my medical training, when I was covering the outpatient clinic, a man with non-Hodgkins Lymphoma was getting a platelet transfusion and within a few minutes, he became very uncomfortable and his temperature started rising and he turned a horrible shade of ashen grey. He was known to the unit. He was getting platelets once a week, and he often had febrile reactions. That day he had been pre-medicated—-and you know, it was kicked around that maybe it just hadn't kicked in yet. It was 5 o'clock, probably on a Friday (I don't remember), but nobody suspected that he was having a septic reaction. We did stop the transfusion, but we resumed it, to see if was just febrile reaction…

Joe: Oh boy.

Anne: …and his clinical condition precipitously deteriorated. His temperature climbed to 105, his blood pressure dropped, he had rigors, he had to be admitted to the ICU. Thankfully, he recovered—-no thanks to the transfusion. But needless to say, that episode stuck with me. I carry that with me. So a major career goal has been for me, transfusion safety!

Joe: Wow, so you got the experience that I dare say a lot of us with pathology backgrounds don't necessarily get, the experience of seeing things in transfusion from the other side, and what can happen. I'm sure that woke you up and probably scared you a little bit I'm guessing, right?

Anne: It was, yes! (laughs) I thought I was watching…I carry it with me. And at the time, what I most recall is—-we brought up, I mean the team discussed possible sepsis, but the discussion as I recall was— we've never seen it, it can't be that, it must just be a febrile reaction. You know, "let's get moving. We want to go home." (laughs)

Joe: (laughs)

Anne: Unfortunately, so there was, but common sense…

Joe: Uh. Wow, that is scary. Well, you know, the fact that you share that story is actually—-it's probably more than a slight coincidence, since we are gonna talk about blood safety today. But we're going to talk about it in a way that's going to surprise the listeners, I think, maybe just a little bit. As I look out my window, I can see across the street from the blood center, where I work— a Target. And I promise you, if I went over to that Target and just asked lay people when they were coming out of the store or if I asked 100 people in a row: "What would scare you about getting a blood transfusion?" I'm sure, 90+ of them would say HIV, right? And a few of them might talk about, oh that weird virus that they're talking about on the news…the one with the funny name, what is it? Zika? Something like that, yeah well, we're not really going to talk about Zika today, but I'm interested in your perspective on Zika, just because, well, first before I ask you the question, let me make it clear, we're recording this in **March 2016 [Note: I know, I said "2015"]** and we're right in the middle of two very interesting things happening with blood safety. We'll talk about the second one in just a little bit, but the first one is, a whole lot of interventions that the blood industry is doing, to prevent the theoretical (or I guess maybe slightly more than theoretical), but still fairly theoretical risk of Zika getting into our blood. So, do you mind just taking a brief moment to talk about Zika and what we are doing with it?

Anne: Oh sure. Zika virus is in the headlines everyday. It is the scariest new virus on the scene. Most people infected with the virus don't know it. They don't become symptomatic, but 1 in 5 will develop symptoms. They're usually mild. They usually last only a few days. They include: fever, rash, joint pain, conjunctivitis, and headache. But what's got people's attention is that Zika virus has been associated with pregnancy complications, fetal microcephaly, and Guillain-Barré Syndrome; neurologic complications, after infection. And there have been 2 likely cases of transfusion-transmitted Zika, described in the press in Brazil, and cases of sexual transmission by men who were infected with the virus. So, it appears—those were, it's interesting, those were just in the press. But they sound like they're confirmed cases of Zika virus transmission. So, FDA and AABB have taken swift action and require prudent precautions to protect the blood supply. They are appropriate and impressive, that is, another—-I think the second FDA guidance on Zika virus came out today. The ides of March. (laughs)

Joe: yes (laughs)

Anne: So, what are we doing about it? Well, as a precaution, Zika virus infection occurs not in the U.S. mainland yet, but in Puerto Rico, in the Virgin Islands. So, there have been imported cases from travelers. So what are we doing about it? Well, blood centers in areas, in the U.S., that are not infected by the Zika virus, must directly question prospective donors about travel and for those who have been to Zika-infected areas for 4 weeks. And in addition, we are providing donors information so they can self-report and self-defer if they've been traveling in an area or if they've been diagnosed with Zika virus infection, if they've been in affected areas and have symptoms or if they've had sexual contact with men who are infected with the virus—-and we're asking them **not** to donate for 4 weeks. And Zika-affected areas—I won't go into it—but really unprecedented actions are being taken to take precautions in those areas to protect the blood supply. And of course, the race is on for a screening test for the blood supply! And all of those actions are prudent and necessary, BUT other infectious risks of blood transfusion demand at least equal attention.

Joe: That's a great summary and you took something that's pretty complicated and made it simpler. I don't know if it's possible to make it "simple" because there's a lot of rules there. I know you well enough to know that what you just said, the "other" infectious risks, in the face of all this that we're doing for Zika, nothing against Zika, nothing against the precautions, which I agree with you are necessary; but, we've got other stuff going on that we KNOW causes more problems right now than Zika, and we haven't been able to stop it yet! So, how do you feel about that, about the "other stuff" going on?

Anne: Yeah, well it's a hot topic for me. It's like the fear of flying, when the greater danger is in the car ride on the way to the airport (laughs)! So it is quite a coincidence that it is getting attention. There was the FDA draft guidance just released on March 14 [2016] about measures to take to control bacterial contamination in platelets. So, if we think about infectious risks, I agree that most people will still convey that their greatest fear is the risk of AIDS, getting AIDS with a blood transfusion, but the risk of transmitting HIV or Hepatitis B or Hepatitis C through blood transfusion is less than one in a million, and it's much lower than that based on results of "lookback" and investigations. But, the risk of septic transfusion reactions after apheresis platelets is much higher, at least an order of magnitude or two. So, that occupies my mind…

Joe: I understand completely and since we are talking to students in part at least, I want to clear up two things. A student hears something like, "one in a million," and while that sounds like that's pretty rare, I think it's important that they understand that doesn't mean that every one million transfusions in the United States, someone gets HIV! It's a statistical thing, right?

Anne: Right! Not nearly! So, that's exactly right. There are about 14 million transfusions in the U.S. each year. I was giving this talk/lecture once, and someone in the audience said, "Well, that means that 14 people each year get AIDS," and that could not be farther from the truth! We just don't see that. If that were happening, we would see that…I mean, we would be picking up some cases, and we don't. So, in fact, that one in a million estimate is from a mathematical estimation that makes a few assumptions and takes "worst-case" and is probably or almost certainly a conservative estimate. When you look at what's actually identified, since 2000, when blood centers started nucleic acid testing for HIV, there have been six documented window period transmissions of HIV in the U.S.

Joe: Just 6?

Anne: Just 6. There might be a couple more identified through lookback that weren't reported in the literature, but you can count them on two hands. So contrast that with the observation that there are at least that many septic transfusion reactions each year. So, we are talking about at least one or two orders of magnitude higher, and measurable. It's something that we get reports, you know, Red Cross distributes about 800,000 apheresis platelets and we see about 8 cases a year, and a fatality about every other year. So, that's tangible and measurable. Window period transmissions are still *possible*, but extremely unlikely.

Joe: Got it. So, let's take a step back for just a second again, keeping in mind that not everyone that we are talking to today has an automatic understanding of what a "septic transfusion reaction" is; we're blood bankers, we like to toss around words and phrases like that. So, just stepping back for a second, can you tell us, just describe for us what we mean when we say that someone has experienced a septic transfusion reaction?

Anne: Sure. Well, a septic transfusion reaction typically presents with fever, but so does a febrile non-hemolytic transfusion reaction. Criteria that are commonly used to identify septic reactions are fever more than 39°C (so a relatively high fever, 102°F), or an increase in temperature of more than 1 or 2°C depending on how you define it (or 2-4°F). Usually it has rapid onset, but we'll talk about how symptoms onset might be delayed. So, usually it's within minutes, it can be within minutes, it's usually within an hour, it's usually within 4 hours but it can be delayed. It can also present with "rigors," blood pressure changes (either increases or decreases, and usually more than 30 mm Hg), tachycardia. And what *clinches* it is when it's investigated, when you culture the residual blood component, if you take the residual volume out of the apheresis platelet component and culture it, you grow bacteria, and sometimes when you culture the patient, you grow the same bug, and you show identity between the strains.

That's what we call a "definite" reaction. It's confirmed. Clearly the bacteria is the same. Often though, patients are on broad-spectrum antibiotics, and their cultures are negative, but the component is floridly contaminated. We would still call that a septic reaction, we would just classify it as a "probable" reaction. So those are the definitions that we use when we described our case reports to our hemovigilance program, but really, sepsis should be suspected with *any* change in condition or suspicion. It's a clinical judgment call. If fever is increasing one degree or a little bit more than one degree, you have to use your clinical judgment. But febrile non-hemolytic transfusion reactions don't take the same course as septic, and are usually more mild. It's always a judgment call.

Joe: Understand. So, I should point out to everyone that Dr. Eder has been very kind to lend us a few slides that illustrate some of the points that she is talking about. What she just described in terms of the criteria for septic reactions, that among other slides are available on the show page for this particular episode. Just go to BBGuy.org/podcast/ and look for Dr. Eder's episode and you will find a whole bunch of illustrations. Forgive me for that interjection. So, "Bugs in the Bag!" Bugs in the bag that cause somebody to get sick, and you were specifically saying "platelets," so I'm assuming that platelets are the most likely culprit, though I don't think they're quite the *only* culprit, right?

Anne: Right. Platelet units are more likely to cause septic transfusion reactions, so that's the focus of the FDA's draft guidance, that's the focus of prevention, and that's because platelets are stored at room temperature, with gentle agitation. So, it's perfect growth media for bacteria compared to the refrigerated storage for red cells. But, septic reactions can occur with red cells, but are less likely. And when you think about plasma, that's stored frozen, and septic reactions are rarely if ever observed with plasma. Having said that, somebody will show me a case report, but I haven't seen it.

Joe: Right! OK, so platelets are a big issue, and we know that; that's fairly well-recognized. So, what do blood centers do to try and prevent first, bugs from getting in the bag, and second to detect the bugs once they *do* get into the bag? How can we stop this from happening?

Anne: So the effort has been to **limit and detect** bacteria in platelet units.

What do I mean by "**limit**"? Donors are screened, they have to feel healthy and well, they have to have a normal temperature, and that's less than 37.5°C or 99.5°F. They can't be taking antibiotics or other treatment for infection. So we're questioning the donor, we're qualifying the donor. In addition, of course, all of the equipment and solutions that we use are sterile and pyrogen-free. We use single use equipment, of course. We scrub the skin with chlorhexidine or povidone iodine, and that's been shown to reduce the burden of bacteria on

your skin. But, most of the bacteria…your skin is SKIN, and it can't be "sterilized." We can "disinfect" it, but there's still…deep in the deep layers, there can still be bacteria. So that's why we also divert the initial volume of blood after you stick the needle in, divert the initial volume of blood, and that diverts skin bacteria that might be still there, and pulls it away. So that inline sample diversion, or "diversion" you'll hear people saying, diverting the initial sample is *very* effective, and has been shown repeatedly to reduce contamination. So that's a way to reduce contamination. So that's how we try to limit it.

And then since 2004, blood centers have been using culture-based methods to **detect** bacteria in platelet apheresis donations. There's two methods that are FDA-approved: The BacT/ALERT, by bioMérieux, and eBDS, by Pall Medical. The BacT/ALERT involves incubating culture bottles and monitoring them continuously through the five day storage of the platelet unit for growth, and it's detecting increased CO_2 production that's produced if there are bugs growing in the bottle.

Joe: Anne, forgive me for interrupting, but that's just the same BacT/ALERT that gets used in micro labs all over the country, right?

Anne: Yeah. And eBDS is based on a different principle: It's based on inoculating and detecting growth after 72 hours based on the consumption of oxygen. So one is looking at CO_2 production; the other technology is looking at consumption of oxygen in the space of the pouch. So, both are approved and cleared, and those are the culture-based methods. The platelet pheresis donation is sampled, it has to be after at at least 24 hours, so you collect the platelet unit, you wait 24 hours, and then you sample the collection. And then you inoculate your bottles, and then you hold the components from that donation…and keep in mind that there might be one, two, or three; often there are two platelet components prepared from one donation. That's important to keep in mind because if the donation is contaminated, there could be two contaminated units in play, or three contaminated units in play. We hold the components for at least 12 hours, and that's when most positives come up, and that's when we detect most positives. But then we distribute the platelets for transfusion, but continue to monitor the cultures. If there's a delayed positive, we contact the hospital, immediately tell them not to transfuse it if they haven't already. Oftentimes, they *have* transfused it, but those delayed positives are not what we've seen cause septic reactions. What we've seen cause septic reactions are units that completely escape detection. So, the testing is *good*, and it has made a huge safety improvement. It detects about one in 5000 apheresis platelet donations are contaminated, but the ones that are causing reactions that get reported to us are just negative. They are false-negatives, they never grow. They escape detection.

Joe: OK, there's a couple numbers that you mention there that I think we should just talk about for a second. You said "one in 5000 units," please tell me that one in 5000 units is going out loaded with bacteria!

Anne: Right..no…it's not, but it's complicated! It's a moving target, right? It's a moving target that grows exponentially (laughs). So, if you sample on day one, you are going to detect what you can detect when you sample on day one! So, if it's very low level, what you can detect are those one in 5000, so it's detecting the fast-growing gram negatives. But, it is missing, some people estimate that our day one testing doesn't pick up half of contaminated units. When you do the cultures at outdate or at five days, it's had five days to get out of log phase and take off, so it is true that the testing does not detect every contaminated unit. Contaminated units still get out, but what *is* clear…if you look at the FDA fatality report before testing, there were 6-8 deaths each year from contaminated platelets, and most of them were gram-negatives. So those are deaths, not infections! But if you look at the last five years, with the culture-based testing that's been performed by blood centers, there's one death per year on average. So, it's been a 90% improvement, but not 100%.

Joe: So you would expect those significant pathogens, especially those gram-negatives to grow generally speaking, quickly enough so that they can be detected by the cultures? Is that the supposition?

Anne: That's right. So some of them escape even, but most of those are effectively detected and not distributed. It's still those skin contaminants about 80% of septic transfusions reactions are now skin contaminants, the gram positive, the coag-Negative Staph, Staph aureus, and Streptococcus species are 90%. So it's still what's on the skin that gets in at very low levels, has a long lag phase, but once it takes off it takes off. So that by day 5, where we see most of the reactions or all of the reactions on Day 4 and 5, you know you've got a contaminated unit on your hands. And you might have more than one, you might have 3 from the same donation….but

Joe: And that's scary…oh no you go ahead, that's my fault. You go ahead Anne.

Anne: But it's also interesting, this is little consolation. But about half the time you get lucky and a unit with—-and you know this isn't acceptable, this is by no means acceptable! But it's also known that about half of the units with bacteria will not cause a reaction. And that's been shown many, actually a couple different ways. But we'll see it among the studies we will be talking about. So half the time, even when there are bacteria, and usually it's under a certain level, a patient won't have a reaction to it. So it's complicated. (laughs)

Joe: (laughs)

Anne: But the other half of the time, they do and the treatment shouldn't make you sicker.

Joe: So you said a couple things that worry me a little bit, I mean one thing that obviously I think everyone should be worried about is those contaminated units that escape detection that do have the potential to cause harm. You already said that some of them that escape detection, no big deal because they're not going to hurt anybody. But the ones that do escape, and can cause harm, are obviously, that's something where we're focusing and obviously the FDA is focusing based on their new draft guidance. But what can you tell us about that? Why does that happen? What do we know about that?

Anne: Sure. So the reactions that we see are from bacteria that completely escaped detection. All of the cases that we've seen have been from units from culture tested apheresis donations that have been negative. Most of them are these Gram-positive bacteria that have very low levels and long lag phases. And almost all of them almost occur on the 4th or 5th day, so sampling on, after 24 hours…they just have time to get up to levels that cause a reaction. And based on the reporting, what we've seen, is a risk of sepsis of about 100,000 units. And all of them—for more information, you can look at the slides that I provided, but in ten years, 81 reactions from 8 million distributed apheresis platelets, 80% are the coag-negative Staph, the Staph aureus, the Streptococcus species that escaped detection. Now it's clear, and I do want to emphasis that the routine culture, and this is the primary testing culture-based testing of platelet pheresis donations, has improved safety. We've seen before culture—-unfortunately, we don't have a great estimate of baseline risk. But, we've seen at least a 50% reduction and then further improvement when we made changes. I mentioned the diversion of the initial sample. Several years ago, that wasn't universal, so some of the collections didn't have that. So by introducing sample diversion of every collection, and increasing the volume for culture to increase the culture sensitivity, that's caused more improvement. But the risk has been constant, and it is about 1 in 100,000. We know that that's an underestimate, because sometimes when we investigate a septic reaction on Day 5, when we look back on the co-component from that donation, we found reactions that occurred on another patient on Day 4, that weren't recognized or reported. So we know, in our own data, that we're not getting all of the reports. A study out of Michael Jacobs Group at University Hospitals Case Western, suggests that it might be 1 in 10,000. So I can tell you about what he found. He has been taking a small volume, so even after the primary testing for more than 10 years he's been taking—doing what he calls "active hemovigilance," taking a small sample and culturing it, at the time it's right before transfusion. So before it's transfused, so on Day 4 or 5, a small plate

culture. And they identified 5 septic reactions in a 7 year period, and that was about—-they had transfused about 51,000 platelets, so about 1 in 10,000. They actually identified 20 contaminated components, but only 5, when they looked back at the patient records, saw that the patients had symptoms. In four of those cases it was confirmed. So the component in the patient grew the same culture. So those are definite septic reactions, but they commented that this estimate is tenfold higher than what we see with hospital-based reporting because they're doing a test on every transfusion. So, you know, depending on how you define the reaction and how you look at it, almost certainly the risk of sepsis is real and measurable and much higher than any other risks people worry about.

Joe: Well I sense a buzz word coming because you're dancing around the buzz word, Anne! And that buzz word is—-everybody ready? Here it goes: Hemovigilance! Hooray! So you raise a really interesting point, and it's something that we in the United States have been debating back and forth for a long time, that if we had "active hemovigilance" like say some other countries do, active hemovigilance programs, would that put us in a better situation vs. "passive hemovigilance"? How do you feel about that? Would that help us? Do you think that the active numbers are more realistic than the 1 in 100,000 that you gave before?

Anne: Yeah, you have hit a buzz word, as if all programs were the same.

Joe: Right.

Anne: You know, I would argue that some active programs are really retrospective and don't provide you real-time information and some passive programs are really active, because somebody is at the bedside recognizing and immediately reporting. They're monitoring every reaction and immediately reporting and other programs really are very passive. So, I think, it's important to understand what it is you're talking about and any risk estimate is going to depend on your methods and the definitions used for reactions and the intensity of your activities. So they're all informative, they're all sort of telling us the same thing. The one really interesting aspect of the case study was that—-so they identified 5 reactions in a 7 year period—all of them had onset after 9 hours. So between nine, symptoms weren't immediate, the onset was—-between 9 and 24 hours, was delayed. And they commented that often, transfusion was in an out-patient setting, they went home and when they came back, a different clinical team was taking care of the patient. So it wasn't appreciated, but the transfusion, 10 hours earlier could have caused that reaction. So it really was informative from that perspective. But with any study, it's just important to understand methods and definitions they're using and how… I do think that the most important type of active hemovigilance occurs at the bedside…

Joe: Yes.

Anne: …with close observation of every transfusion and immediate, recognizing…and of course, stopping the transfusion. Providing supportive care, of course. Notifying the transfusion service, investigating and then immediate notification of the blood center, because again, two more units might be in play. I also should mention, if your hospital is splitting platelet units or making pediatric aliquots, the first thing you should think about is, "is there another aliquot that's about to be transfused to another patient that could be contaminated?"

Joe: Right. And you're 100% right! Hospitals often times have a hard time remembering that, blood centers are usually pretty well-trained to think about other components or co-components, but hospital transfusion services sometimes miss that.

Anne: Yep. I include myself in that (laughs) because my time at Children's Hospital, I can say that, yes—-I mean that should be the first thing you think about is could there be another component in play that you need to go after.

Joe: I want to just circle back for just one second because you talked about the study that described the "Delayed Onset of Septic Reactions" and that's—-I wanna emphasize that to the students listening, because when I teach about septic transfusion reactions, I tend to teach them as a fairly cut and dried, very early in the transfusion, kind of cataclysmic type thing. But that just really illustrates, if we don't have a high index of suspicion, you can miss the diagnosis easily.

Anne: Right, yeah. And they're harder to investigate because the unit might have been taken out with the trash! So you can't filter it to investigate it.

Joe: Absolutely!

Anne: It just happens that the way that this group was doing the cultures, was they had that information. But often times it is possible, and I think most reactions will be within 4-6 hours, but it is important to appreciate that reactions can be delayed. You know— 9 hours, 24 hours.

Joe: Sure. Well Anne, we're running out of time but I wanted to touch on a couple of things very, very briefly before we close, and we don't have time to talk about either Pathogen Reduction or the kind of point of care Rapid Bacterial Detection testing, but can you just take 30 seconds and give me the thumbnail on both of those? They're not widely used yet, but we're gonna be hearing more about them in the future.

Anne: Definitely. Yes, this will be the time for pathogen-reduced platelets might be coming to your hospital. The FDA Draft Guidance identified them as an acceptable risk, of course they're approved, the amotosalin-treated platelets are FDA-approved in the U.S. and recognized in the FDA Draft Guidance as an acceptable risk control strategy. Also recognized is secondary testing and using the rapid tests on Day 4 or 5 and, also in the draft guidance, are considerations for how to extend storage to 7 days, and that would require to insure microbial safety and the additional things that would have to be done to get to 7 days. So I do think, with the Draft Guidance released yesterday, with pathogen reduction starting to be on the upswing, with some of those other strategies that can be used, things are happening.

Joe: Yes, they are.

Anne: This is getting attention and it's really important.

Joe: Thank goodness.

Anne: Because you know, the treatment shouldn't make you sicker…from where you were to start with!

Joe: Agreed! That's the worst! That's a blood banker's worst nightmare, isn't it? You know this thing that we take so much effort and time to try and make right and to have, I like you have had the experience of seeing one of these things in person and it's the worst feeling in the world! It really is awful. So as we close, I wonder if you wouldn't mind, just giving us three quick ways that blood bankers and clinical staff can kind of work together to help make sure these things get recognized and we keep people as safe as possible?

Anne: The most important thing is to **maintain a high index of suspicion**. And you know, act on the side of caution. So often it is a judgement call but stop the transfusion and investigate. Consider whether your hospital has a clear protocol for investigating clinical signs and symptoms that suggest sepsis. And that includes, changes that…it doesn't have to fit exactly the definitions that we use for the final classifications. So if the condition is changing, any change in clinical condition during or after the transfusion, could lead to a suspicion of sepsis that should be investigated. And then, **immediately report suspected septic transfusion reactions to the transfusion service and to the blood supplier**, even if you're uncertain, even if something is not quite, not quite all the criteria are met. Because the symptoms, you know, we've talked about the delayed onset of symptoms, some patients won't have a fever, but other signs could suggest. And I guess the third thing would be—-well, can I have 4 things—-but the third thing would be to **think about co-components** or think about whether the unit could

have been split and a unit from the same donation that cause a reaction could be still on the shelf somewhere, and retrieve it and prevent it from being transfused. And **if hospitals start to do secondary testing, to remember to immediately report the results of those tests back to the blood center**. Because again, there might be another unit in play that needs to be intercepted. So that's what I would like to leave people with.

Joe: I like it! So let's just to summarize: 1) Maintain a high index of suspicion. If you're in doubt, work it up. 2) Immediately report (from the clinical side) anything suspected to the transfusion service. 3) Isolate co-components as quickly as possible. 4) If you're doing secondary testing, make sure that the blood center knows about confirmed positives. Does that summarize it? Did I get that right?

Anne: Thank you! Perfectly. (laughs)

Joe: Excellent! I love it when I get things right. I passed the quiz! (laughs) Well, Anne, it has been an incredible honor to have you here. I thank you so much for taking your valuable time to meet with us and to give all of this great information about Septic Transfusion Reactions. I **know** that the people listening to this will benefit from it, so again, thank you so much!

Anne: Thank you, Joe! It has been an honor for me as well!