



Joe Chaffin: Welcome to the Blood Bank Guy Essentials podcast. Today's guest is a good friend of mine, Dr. Kevin Land is here from Blood Systems. Kevin, welcome to the podcast!

Kevin Land: Hey, thanks Joe. Glad to be here!

Joe: It is awesome to have you, my friend! I just want everyone to know a little about you. Dr. Kevin Land serves as the Senior Medical Director for Field Operations for Blood Systems. He is the Chief Medical Officer for UBS Rocky Mountain and Dakotas Region, which includes North and South Dakota and Wyoming, but that's not where his influence is limited to, that's for sure. Kevin is a clinical informaticist and a patient-oriented transfusion medicine doc and he has spent much of his career on systems design and process improvements. He has—boy, I don't even know where to begin with you, Kevin! There's so much that you have done, so much that you have contributed to in areas, including donor hemovigilance, among many, many other things. So Kevin and I have, actually in full disclosure have overlapped in a couple of places where we've been and we actually currently work together as part of his employment and my affiliation with Blood Systems. So Kevin, again, it's great to have you! I wanted to explore first with you, something that I tend to explore with everybody that comes on this podcast because I'm curious. What was it, with your background, obviously you're a pathologist, you're also a clinical informaticist, what is it about blood banking that got you excited and what is it that keeps you going there now?

Kevin: Oh, great question. So, it starts a long time ago when I was a kid. My dad actually worked at a blood center in Dallas, in a research department. And as a seven and eight year old, I'd walk through the blood center there, on the way to the elevators to go to his lab and I would see all of these people donating blood, right? This is the '70's we're talking about, right, early '70's! You're hearing stuff about racism and inequality, and you know, I'm a seven year old, I'm hearing Walter Cronkite talk about it, but I don't really understand what it means, because I didn't live in that kind of family. But here I am looking at these round tables, where you have an elderly African-American, a younger Asian woman, a middle-aged Latino woman, and then Caucasians, just all sitting around a table. They're holding one arm up for 15 minutes, and the only way they can have a snack—because if you remember back then—there's these big five pound jars of peanut butter and these big huge containers of Ritz crackers and restaurant style carafes of apple juice, orange juice, whatever! So if you wanted anything, somebody next to you had to help you either pour it or

hold the Ritz cracker while you slather it with peanut butter. So one day, I said, "Dad, if everyone just donated blood, there wouldn't be any of this problem of people not trusting one another!" So, it sounds kind of campy, but that really kept through me all the way through college and medical school. I was going to be a forensic pathologist or a Pedi Heme/Onc doc, and my wife was pregnant and I had a lot of patients, dying on the Pedi Hem/Onc floor, about the time we were making the decision—"what's my career for fellowship and moving on?" I did a forensics rotation and—well, it's forensics, right? So, there was a lot of stuff you don't wanna talk about! I just found out it was a baby girl, right? We had just done the ultrasound and I'm like, "I can't bring my daughter, ever, to ANY of this." So I said, "You know what? I've always kind of liked blood banking, I had a great mentor in Hal Kaplan, and I had an open fellowship position there. I decided, "You know what? Instead of helping people recover from their worst, transfusion can help people be their best for the day." And I decided that's where I want to spend my career.

Joe: That's awesome. Well, as I've said, your contributions have been great! I know you're modest about them, but realistically, you've made an enormous impact in our field and you continue to. So, I'm proud to be your friend! Today, Dr. Land and I are going to have a fun conversation about a topic that I've heard him speak on before—it's such a great topic! We're doing "MythBusters" today! "MythBusters" as you may know, was a television show that ran from 2003 through just earlier this year, 2016, Discovery Channel I think, I could be wrong about that, but I think it's Discovery. In the "MythBusters" show they would focus on, well, one or two popular beliefs which may be true or may not be true. And they would take you through all kinds of fun stuff! They did things like toilet bombs, and cell phones exploding gas stations and stuff like that! Basically, with an eye towards just answering the question: Could this really happen? Is this really true? And that's what we're going to talk about today because there have been, over the years, a lot of beliefs that people may have, both clinicians and blood bankers, about things in transfusion medicine that may be true or may not be true. And we want to tackle a few of the more common ones. So, Kevin, are you ready to go? You ready to bust some myths?

Kevin: Absolutely! (laughs)

Joe: Alright! So let's try myth—well, we'll say, statement #1 and you'll tell us whether it is a myth or not.

Statement #1: The biggest risk of transfusion or from transfusion is getting a viral disease.

How do you respond to that one, my MythBuster friend?

Kevin: Well you know, I've given this talk a couple of times. The first time was actually in your neck of the woods, a couple of years ago. And I've given it to some residents and I asked them the question. And they said, "Well, it depends on what you mean. If it means the one where everyone is the most worried about vs the one that's going to kill you the quickest, it's a different answer." And I said, "OK, well, the let's move on to the next section!"....(laughs) So, that's actually correct, right? Like you, I'm kind of a life-long teacher, I love teaching all sorts of level residents, medical students, primary care docs out there, and over and over again, I've seen—just like you probably have—that when people talk about risk, they always focus on HIV, HCV, HBV, the hepatitis', the HIV; because those were so scary in the '70's and definitely in the '80's. And when you ask doctors today, you say, "What's the residual risk?" And they say, "Oh—maybe 1 in 1,000, 1 in 10,000." And I go, "Ummm—have you thought about what that means at your hospital? If it's 1 in 1000, and you transfuse 20,000, that means you'd get 20 HIV cases a year!"

Joe: (laughs) Yeah, they don't like that a lot, I'm guessing!

Kevin: And they're like, "Oh! Well we haven't had one, EVER!" Oh, okay. Well, if you're doing 20,000 and it's been ten years, or twenty years I guess now, thirty years, that's getting on the order of 1 in 600,000. So, now we're getting kind of into the realm of where infectious disease risks are now, right? So, as you know, if you look at infectious disease testing that we do today, we do testing based on the antibody, based on the antigen, and based on nucleic acid material of many of the different pathogens—trying to get the diseases in different stages, early infection or chronic infection, primarily. And for the big three: HIV, HCV, HBV, we're on the order of 1 in 1,000,000 to 1 in 2,000,000. And to put that into prospective, try to figure out, you know, what's somebody trying to think about that would put you into kind of that same category. And I found, that if you were to take a coin and flip it, randomly, twenty times in a row and they all came up heads or they all came up tails, that's about the order of risk for those pathogens.

Joe: Yep, pretty small. But Kevin, let me interject, for just a second. I think that even that may mislead people a little bit, because when you look at the statistics and you say, "Okay, 1 in 1,000,000 or 1 in 2,000,000, but we're transfusing like 14 million units or however many millions units in the United States a year. Does that mean we're getting 14-15 HIV infections?" And I think generally the answer to that is, No! As far as we know, right? Even that doesn't necessarily, accurately estimate the risk.

Kevin: No, you're right. So, the risks that we publish are based on population-based statistics, looking at incidences of new HIV or hepatitis, and looking at the window between infection to when we can reliably detect it. So, for HIV for

example, there's about an 11-12 day period, right? Between when you're infected and you can reliably be detected as being HIV positive by samples. You might be detected earlier, but reliably. Every time you go in you'll be positive. It's about 11 days. So, we try to calculate on that 11 day window, what's the residual risk? But in practice, to your point, we only see, one every, what—5 to 8 or 9 years in the U.S.? And we know from several publications that 50-70% of people who get a transfusion live a year beyond their transfusion event (that's not related to their transfusion, it's more related to their underlying medical condition). So that by itself isn't enough to say, "Oh, well so many people are dying because they're sick." The risk is so low because everyone else is too sick to be tested later. No, I think the reality is, is to your point, the realistic risk is on the order of 1 in ten's of millions, but we state this just because we can count the numbers and we can estimate using data that's been fairly well vetted by FDA and the industry.

Joe: Yep, yep. So if we're not talking about a very large risk from viral diseases, then what should we be worried about, Kevin? If the biggest risk isn't getting a viral disease, what are the other things that are potentially a problem?

Kevin: Great question. So again, going back to what I said at first, probably most people are really worried about HIV, right? There's a lot of stigmata unfortunately, still, about having that disease, so they may be more concerned about it. But if you google "FDA and transfusion fatalities", you can see the list—it's public record of transfusion related deaths and I think they go back to 2008 and I think they have the 2014 data up, recently. And you can see that the biggest reasons for death, following a transfusion, are TRALI, TACO, hemolytic transfusion reactions—whether they're related to ABO or non-ABO red cell antigens. Microbes that aren't viruses, you know, the stuff in platelets, *Staph aureus*, *Klebsiella pneumoniae*, *Babesia* was in there as well, or anaphylaxis. These are the things that most likely will result in acute death but are largely forgotten when we talk about transfusion risk.

Joe: Yes, for sure. And just for the trainees that are listening to us, TACO and TRALI, those are acronyms standing for "transfusion associated circulatory overload" and "transfusion related acute lung injury," in case anybody missed that. Sorry to make sure everyone is aware of that, Kevin!

Kevin: No and I think that's a good idea! Quite honestly, we don't know a lot about what those really mean, right? They're both lung-associated injuries, following transfusion. One is volume overload, predominantly, right? And one is actually, an acute lung injury as it relates to the transfusion. Unfortunately, which is beyond the scope of this talk, I guess today, or this conversation—it's hard sometimes to tease out, which one is which. But still, there's still a significant cause for morbidity and mortality in our patients.

Joe: Sure. So other things you've mentioned the ones that are fatal, obviously there are also things that are not fatal. Do you want to mention those, real quick, before we move on? Because I think we've pretty much busted this one, Kevin.

Kevin: Yeah, I think we've pretty much busted...obviously, you can have—are you talking about like febrile non-hemolytic transfusion reactions? Things like that?

Joe: Sure, things like that.

Kevin: Yeah, there are definitely other things that can happen when you have a transfusion won't result in death, but would result in discomfort, right? If you get a fever, if your getting a local or systemic allergic reaction. Those can be uncomfortable. We spend a lot more time signing out those cases. But one of the things that I think your audience should be aware of that is, if you're not getting enough of those in your hospital, then you'll never get the other ones. Right? Because you'll see 20, 30, 40 of those sort of reactions, febrile non-hemolytic transfusion reactions, before you'll see a TRALI, right? TACO is on the order of 100 transfusions, probably a little higher, if we're being honest. But if you're not getting any, and I oftentimes, I'm sure you hear it as well. You hear hospitals say, "Oh, I haven't had a transfusion reaction in five years." Well—that just tells me nobody is reporting anything.

Joe: Yeah, they say it as if it was a point of pride, when actually it's a scary point, right? (laughs) Don't brag about that one!

Kevin: (laughs) Nope!

Joe: Okay! So I think we can put that one "to bed". The biggest risk from transfusion is getting a viral disease. We would call that one? BUSTED!

Kevin: Busted!

Joe: Okay, so with that one out of the way, let's move on to the second one, Kevin. And that is this one:

Statement #2: Blood donors that are type O negative are universal blood donors and their blood is safe for everyone.

That sounds reasonable, come on, right?

Kevin: Oh—absolutely! And quite honestly as an “everyday watcher of TV,” that’s what they tell you, right?

Joe: Yes, they do!

Kevin: I mean, if you remember some of the “Chicago Hopes” and some of those, if you were O neg and a resident in the ER, chances are you are being stuck right there, and blood is going to be drained from you so you could save a patient’s life!

Joe: (laughs) Yeah...yes! Fresh whole blood, baby, bring it on!

Kevin: (laughs) Fresh whole blood, baby! So, of course, for many emergency transfusions, right? Whether that’s due to trauma, due to GI problems, or an obstetrical patient who’s bleeding, those are the three most common areas for uncrossmatched emergency-release blood. O negative blood works very well for those patients. But the reality is, there’s more on a red cell than just A, B, and H, right? There’s no O on there, for those of you residents that are taking your boards. What other things are on there? Turn and asking you a question.

Joe: You’re asking me a question? Boy, we’ve got all kinds—it’s a “sea of antigens” on the surface of a red cell, Kevin. Just a “sea of other antigens”!

Kevin: A “sea of antigens”! So, that’s of course, is true. But not all of them are the same, right?

Joe: Right.

Kevin: Some of them are worse than others. And so, one of the things I may have heard from you, when I was taking my Osler Course? That Kell and Kidd Kills, Duffy Dies, Lutheran Lives, and of course, Rh—those are bad actors, as well. So, the ones that we’re really worried about, the clinically significant ones are Rh, because about 80% of them result in developing an antibody, you got Kells - about 10%, you have c and e - which are about 3% risk of developing an antibody, and then, Duffy and Kidd at less than 1%, but still important. So, the point is, that if you look, and I think there’s an article from American Journal of Clinical Pathology from 2010, where it’s just one hospital’s experience, They found that, if you looked at all their patient’s who received emergency-released units—O neg trauma units—a significant number of them actually had alloantibodies, underlying alloantibodies and it’s kinda of scary. I don’t know if you’ve seen it, but it said, I think about 11% of the patients had some antibodies that weren’t A or B related.

Joe: I can’t remember the exact number, but it’s in that ballpark.

Kevin: Yeah, so like 5-6% had a clinically significant antibody, you know, the ones we listed. And they actually found that they had 15 antigen incompatible units transfused, right? And seven of those 15 had clinically significant antibodies, one of them had a hemolytic transfusion reaction. And so, it's a lot more common than we care to think about. Fortunately, most hemolytic transfusion reactions don't necessarily result in death, but we're not here to avoid death! I mean, that's a pretty safe thing, "Well, I didn't kill anybody today!"

Joe: Yay! (laughs)

Kevin: Yay! We try to do a little better than that and best practices, right? If it's your mom, if it's your daughter, if it's your wife or the reciprocal, you know, you would want your clinical staff to avoid as much as possible, developing the antibodies to begin with, and #2) exposing your loved one to a potentially incompatible unit. Clearly, even in the small retrospective study of like 1,000 units, there were 10-11% that had antibodies that would not have been protected against just by going with O neg units.

Joe: So what does that practically mean for people that are working in hospitals, Kevin? I mean, I know this is something that you are passionate about because I've heard you speak about it before, "The Intelligent Use of O Negative Blood." It's maybe slightly off-topic from what we're discussing here, but I think it's important for people to understand, how can they help safeguard the O negative supplies and only give it when it's appropriate?

Kevin: Oh thanks! (laughs) What a leading question, right baby?

Joe: Yeah! That's a softball, right there!

Kevin: Yeah—that's an under-handed pitch! I think I might be able to hit that! So, I know you're aware and I'm hoping most of your audience is aware, that a few years ago, AABB put out a "Choosing Wisely" Campaign, right? Where they went out and said, "These are 5 questions that all patients should really discuss with their doctor" So the "Choosing Wisely" Campaign is a large campaign from the what—American Board of Internal Medicine Foundation that really helps cut through some of the myths, or some of the misperceptions in medicine, and the 5 that came about from AABB, 1) Don't transfuse more units than absolutely necessary, that makes sense, right? You should get all you need, none that you don't. 2) Don't transfuse red cells for iron deficiency without hemodynamic instability. Give them iron, give them EPO, there's other things to give them, right? 3) Don't routinely use blood products to reverse warfarin. 4) Don't perform serial blood counts on clinically stable patients. That's a great way to give a transfusion later on, is to draw a whole bunch of blood the preceding days. I

think there's a study that showed that in some ICU/CCU areas, up to a unit of blood was being collected everyday just to test the patients.

Joe: Incredible.

Kevin: Yeah. And the 5th one, is the one that you're referring to: 5) Don't transfuse O neg blood except to O neg patients and in emergencies, for women of child-bearing potential, with unknown blood group. We have a crisis, right—in the world, not just in the U.S. And it's sort of a good problem to be in, in the sense that, we have a lot of great literature that's come out in the last 10-15 years on understanding the “Goldilocks Principle of Transfusion”—not too much, not too little, just right. And most institutions, worldwide, have noticed, as they have adopted these best practices, many people call it, “Patient Blood Management”—but it's really just adopting the best practices. They've seen a decline in transfusions on the order of 10, 15, 20, 30 up to 40%! The problem is that the decline in blood usage hasn't been across all blood types. So A and B and O+ have declined but the rate of use of O neg has actually gone up. I recently published study with Mark Yazer and Neil Beckman, from Australia, Mark is at ITXM in Pittsburgh, you know, that looked at this across a couple of countries and it's pretty staggering. The scary part is if people don't quit using O negs inefficiently, we're not going to have enough for those that actually need it.

Joe: Right. That's so important and I talk to people all the time about this and basically, unfortunately, we can't make O negative out of nothing. We can't fight population genetics, try as we might. There's only a limited number of O neg people out there and it's gotta be used intelligently.

Kevin: Absolutely! And the reason why this is relevant to our conversation today, is that one of the inefficient uses of O negs is using O negative units for adult males. When you talk to these hospitals, usually the blood bank or the director or the lab supervisor, they are so worried, right, about giving an Rh positive unit to a Rh negative adult male, who then comes back having formed an anti-D and then you give them another emergency O pos unit and then they have a hemolytic transfusion reaction and die. So, I did a little “napkin calculation” of that, and I'm happy to supply you—it's 9 different steps. I put references off to the side, so if anybody has a better reference, they can update it. This isn't to prove a point. This is to make sure that we have the right information to make informed decisions. So if you start off with 41,000,000 trauma patients per year—well step 1. And you go through, how many of them require red cells? How many of them survive? How many of them are Rh negative? How many of them are male? How many of them are over 18 y/o? (assuming that everyone less than 18 y/o is probably getting Rh negative O neg units) Has ANOTHER trauma, after developing an antibody, and then, has a hemolytic transfusion reaction,

right? So we go from 41,000,000 patients per year in the U.S., down to 236 patients.

Joe: (laughs) Tiny odds!

Kevin: So that's MUCH less than 1%, obviously. But yet, we're okay giving "unsafe" blood, 10-11% of the time, for things that aren't ABO or Rh.

Joe: uh hm, yep. You mentioned Mark Yazer, I had him on the podcast a while back and he and I were discussing the—not quite that very issue, but something similar, and one of the things that he pointed out that I know you're very well aware of, is that old 80% thing that people have said for decades about the risk of making an anti-D, is well, certainly in hospitalized patients much lower, and probably in trauma patients, even lower than that, right? Doesn't that even add more to your argument?

Kevin: Yeah, we actually have had a nice debate over a pint of beer, on what's the likely risk of developing an antibody in trauma patients. Don't know, but I think it's easier to say though, from the AJCP paper, that people who present, because we're already—a lot of places west of the Mississippi, already give Rh negative units to everyone—it's an oversimplification. But most of the hospitals east of the Mississippi give Rh positive units to males in trauma. A lot of hospitals, west of the Mississippi, either haven't or recently within the last few years, have moved to that. So we kind of know what percentage of patients present, and that's on the order of 10-13%.

Joe: Got it. Yep, okay. We could go on about this one, Kevin, I know we could! It's a hot button for both you and I, especially in our role as blood supplier it's obviously very, very important. But we better leave this one alone. So how would you categorize this one? Donors with O negative blood are universal blood donors and their blood is safe for everyone.

Kevin: Yeah, whenever you see "always" and "everyone" and "no one," that's pretty easy. So I would say that this is busted!

Joe: Busted! Alright, but it's not quite as simple as the previous being busted, right? There's more complexity to it. Okay, but we've gotta move on. So let us go to the next one. So here it is. You mentioned, one of the magical buzz phrases that's cruising around transfusion medicine world right now, and that is "Patient Blood Management." And one of the things that I think people may have gotten a misperception about, is the following statement. Let me read it to you.

Statement #3) Blood is bad. Transfusing leads to increased mortality.

How would you like to take that one on?

Kevin: Boldly! (laughs)

Joe: (laughs) I would expect nothing less from you!

Kevin: So, the thing is that we know blood isn't entirely bad because we kinda of need it to live!

Joe: Yeah, a little, yes! (laughs)

Kevin: A little bit, right? And we also know, from Carson and others, that if you look at the Jehovah's Witness literature, when you start getting below 5, mortality starts going up, with maximum life-threatening levels reaching about 3 or less, and you know, zero hemoglobin is incompatible with life right now. So we know, that **no** blood is bad. But that's not really the point, is it? They're just saying, "Blood is bad and the transfused unit—there's maybe storage lesion, there's maybe some sort of manufacturing defect, blah, blah blah...that results in a unit that actually causes more harm than good." That started from well-meaning folks that looked at retrospective studies, right? Because that's the first thing you do usually when you're exploring, you look at retrospective studies. But you say, "Okay. What happened to all my patients that received blood?" Well, the problem with that question is, there's a lot of associated risk in there that unless you correct for that, are you really measuring or evaluating death, as the result of the transfusion? Or are you just measuring a blood transfusion as a surrogate for the other risks? And so, sick patients are more likely to get blood. Older patients are more likely to get blood. Sick patients are more likely to have complications, right? People with 20 underlying diseases are more likely to have a bad outcome, than somebody that just comes in with a simple, you know, broken ankle or something like that. Unfortunately, many of the observational studies early on did not adjust for that. And so, you started seeing reports in literature that said, "Blood transfusion is associated with increased mortality." Well, the problem is, when you see the word "associated", we think "causation", right?

Joe: "Causation," right.

Kevin: But it really should be interpreted as "prediction." It predicts. And if you want me to, I have a really good informatics story from Target, that has nothing to do with blood banking or medicine, but shows what "causality" vs "association," really puts it into perspective that most people can go, "Oh, I get it."

Joe: Okay, it's a podcast. Bring it—bring it, man!

Kevin: Okay, so a few years ago, Big data, is a big deal, everyone's trying to get everyone's data to figure out stuff about you. Google does it, Amazon does it, any website you go to collects data about you, okay? Well, Target was trying to figure out, "Okay. What is the best category of customer I can get, that could be life-long customers that would spend a lot of money here? These people are going to be spending money already, so they might as well spend it with Target." And they decided that young families, specifically, pregnant moms are a great group to target. No pun intended! So they have a registry, right? A Target new baby registry and they actually ask you, I think, when your expected due date is. This was ten years ago or so, they started capturing all this data and then they went back and said, "Okay. What were all the purchases they did leading up to the delivery? And could any of those predict, if a woman was pregnant, if they weren't in our registry, if we didn't know that they were pregnant?" And they came up with 5 items that if were purchased, in a certain order but in general, these 5 purchases. They had a 87% predictive rate of identifying a pregnant person—could actually get pretty close to when the due date was, in a couple of weeks. That's pretty scary, isn't it?

Joe: That is scary.

Kevin: And if you don't believe me, you can go Google it! I think it was in Forbes or Harvard Business, because it was a pretty big case study. What they used to do is, they would say, "Okay. We found somebody and now we're going to send them some targeted email. Here's a brochure about all this baby stuff." And they would even be so bold early on, as to say, "Congratulations on your new pregnancy! Here's some coupons to help you out." Well the problem occurred, because they sent it to a teenager and it arrived at the house. The father sees this thing saying, "Congratulations on your impending delivery! Here's some coupons."

Joe: (laughs) Ouch!

Kevin: Joe, you're a father, right?

Joe: Yep!

Kevin: So, like just about any good father would do, after he had a conniption fit, right? He calls Target and says, "What in the world are you doing? She's a teenager, you do not know what you're doing!", and just berated them. Target apologized and apologized and whatever. Well, apparently, he was the only one in the house that didn't know that she was pregnant.

Joe: (laughs) So often that happens that the dad is often the last to know, right?

Kevin: So, the 5 products did not **cause** her pregnancy! Do you know what the 5 products were? But they were **predictive** of her pregnancy! But do you know what those 5 products were?

Joe: Please, tell me!

Kevin: Large, generic bags of the puffy cotton balls, large amounts of multi-vitamins, a bag that could be used as a diaper bag, but doesn't have to be a diaper bag; big, nice, ultra-soft towels, like you would use to wrap a baby or swaddle and unscented lotion.

Joe: Those five things, clearly cause pregnancy! (laughs)

Kevin: Now, even if the unscented lotion was KY-jelly, that doesn't **cause** pregnancy! (laughs)

Joe: (still laughing) Wait! We gotta stop going down this pathway! Time out! Hold on—Danger, Danger, Danger! PG-rated podcast, dude!

Kevin: Well, we just got to the edge of PG. So anyway, that's my kind of silly, but real-life story of how observations, because that's all that is was a retrospective observational analysis, only gives you things that have an association or predictive ability. It doesn't give you a "causation." I'm sure you've reviewed articles through the years, I've reviewed articles for several different journals. People are publishing these studies, and if you look in the studies, they haven't even normalized their data for severity of illness, for underlying or co-founding medical conditions, for the number of other blood products besides red cells that they might have gotten. Not all of them, I'm saying some of them, right? They haven't looked at the volume of blood products that they got. So when you start adding all this stuff up, how in the world can you say that this one red cell that you got was the cause of their death when probably 20,000 things occurred to the patient, inside the hospital, and that patient is already sick? So when you move to the newer data or reports, there are randomized controlled trials where they try to control for all these confounders. And so far, every single one of them has said, "Mm, no. Really haven't seen a difference." Blood used *appropriately*, confers no extra risk. Now I would argue, and I think you would too, that, even though blood is safe, we've already talked about there being other risks. Do you really want to roll dice with your patient, if they really didn't need the unit?

Joe: Yep, right.

Kevin: So one final thing, that if you look at the health care utilization product (HCUP) data from HHS, during the time where transfusions—and it's freely available, if you want to be an informatics nerd, you can go find it and download a lot of data—that during a ten year period of time, red cells doubled in usage to the point where it became the #1 procedure performed at hospitals. During that time though, mortality, across all of the big cardiac, pulmonary, things that you would think that would be at-risk for dying, especially if they had a transfusion; the mortality for all of those severe diseases decreased. If you look at the Nareg study from Kaiser Permanente, it was in JAMA 2014 - "Decreased Red Blood Cell Usage and Mortality in Hospitalized Patients," he's got a great graph that showed that as the transfusion incidence went down (if you looked at controlled patients; he controlled for as many variables as they possibly could, patients transfused, patients untransfused but otherwise matched by age, severity and disease, etc.), their mortality decreases over time from 2009-2013, but you couldn't tell from one to the other which line was the transfused patient, which line was the non-transfused patient. They both had essentially the same mortality risk.

Joe: Right. Yes, I've seen that, in fact, will make sure that we put that reference on the show page for this episode, so people can make sure to check that out. We might even have a slide, we'll see about that. So, since we are running a little bit short on time, let's just bring it to the conclusion. So I think I know where you're going with this. If I say, "Blood is bad", what would you say about that one?

Kevin: (chuckles) Well—busted!

Joe: Busted! Yeah, no problem. Agreed. But I think you made some really good points about that, though Kevin, and I think it's essential for the audience to remember, that doesn't mean that either you or I is advocating, "Oh well, it's totally cool! Just do what you want!" You still should transfuse intelligently and for proper indications. But in that setting, there is little evidence to suggest that we're doing anything other than helping people.

Kevin: Correct, and if you've heard enough people talking about this, especially in the patient blood management world, there are some CMO's that would say, "We started off when the 'blood is bad' camp, and we think it swung too far over where there were a couple of cases where patients nearly died in their hospitals, because they're exsanguinating and people were worried about giving them blood."

Joe: Yep. And that is not the outcome you want, that is for sure! I think we have time for one more, Kevin. We'll have to do this one fairly quickly. I love this one, so I wanna make sure we hit it. And that is this:

Statement #4: Younger, fresher blood is better than older stored blood.

Kevin: It is a sexy statement, right?

Joe: (laughs) Why thank you! I feel better about myself for having said it! Even though you wrote it, I feel better about myself for having said it! Sorry! (laughs)

Kevin: (laughs) It kind of goes with this whole milk meme that we have when I go to the grocery store, I look for the gallon of milk that has the longest outdate and I grab the one in the back of the refrigerator, not the front, etc. Well, the problem is, there's a little bit of disconnect between a unit of blood and a gallon of milk, right? A unit of blood comes from one donor who meets pretty rigorous set of questions. You know, your audience should be very familiar with the FDA layers of safety on testing and etc. We also know that milk is pooled together, where as blood is from one unit. So what am I trying to get to? That it's a good meme in a sense that in general, you want the freshest you can get, but the reality is if you use it correctly and you just grab it in a "first in, first out," it works just fine for the vast majority of people in the U.S., *just like blood does*. So, we have some studies recently, RECESS and ABLE, and things like that, that have really shown us, because we're only looking at randomized controlled trials, that if you look at blood that is released as standard issue; You go into a hospital, you ask for a unit of blood, it's going to have an average age on it, right? That age is anywhere from 18-28 days, in most institutions. The older that is, does not necessarily reflect the fact the blood center is giving you older units. It might, but it also could mean that your hospital is carrying too much blood on their shelf.

Joe: Right.

Kevin: So, I really think this is a really good indicator for both the blood center and the hospital to work together to find a comfortable range of the mean age of transfusion. The reason I say that is, the studies are showing that if you compare "fresh blood," three, five-day old blood that's transfused, with standard-issue blood, there's no difference in morbidity and mortality. And some pretty sick patients, right—ICU patients, cardiac patients, pediatric patients—the ones you'd think that would be at most-risk at having an adverse event. The outstanding question, though, is that the absolute oldest blood, 41-42 day, we don't know whether those units are as safe as the freshest unit. And the reality is that's a pretty complicated question. There's some pretty big ethical concerns. You know, it's like giving everyone a glass of milk that's expired today! Some of it will be spoiled. So I think that will be hard to get past an IRB. I do want to say though, that a lot of the things we think about when we think about old blood vs. new blood, come from some recent studies that are looking at what we traditionally would think of as storage lesion, effects, genomic effects, proteomic

effects of blood as it ages over time. And I think we were starting to talk about this before we started the podcast, but a recent study came out that looked at blood processing methods and how it affected microparticles. Some of these things that they looked at, historically, have been thought to be storage lesions: microparticles, MTDNA, increases in the blood supernatant. And Canadian Blood Services and BSRI recently published in *Vox Sanguinis* that those things may have more to do with the processing methods, how you manufacture the blood than actually how long the unit's been stored in a refrigerator before it's transfused. So, do I think it's important to give units that are as fresh as reasonably possible? Yes. But for every unit that you give as fresh, the FDA did an analysis of this, every other unit you give is going to be older!

Joe: It's kind of automatic, right?

Kevin: It's automatic. So if your average is 20 days, and you're giving all of your in-utero patients 3 or 4 day old blood. Well, those 3-4 day old units aren't sitting on the shelf to keep your numbers down. So then the average age for everyone else becomes 22, 23, 24, 25...

Joe: You got it! Yep!

Kevin: So, for every group of patient that you think it's so critical to give them the freshest blood, you make it older for everybody else. So, I think in general, it's important to consider, if it's good for one patient group, it's probably good for all groups. I think in-uterus, I'm okay with giving fresher units, just because of the risk inherent. You don't want to give multiple transfusions. The second thing is, we should probably understand a little bit more about what's causing the bad effect, if anything. And just because we can see a difference—I've published with Chris Silliman on proteomics of plasma and red cells—and things go up, things go down over time. But we don't know what that means.

Joe: That's the problem. We're still guessing and I think that you raise really good points about RECESS and ABLE and the studies that have been done. And I just want to reemphasize that to the audience. You will hear sometimes people saying that those studies have been put everything to bed, but I don't think they quite have. But they have answered the question pretty clearly, of whether the way we're doing things routinely now is safe and that answer is pretty much a resounding—yes!

Kevin: A resounding yes!

Joe: Yep, okay. Alright, Kevin, I think we're going to have to close with that one. Maybe you and I can get together another time and do another set of "potential myths." But let's go over real quickly what we've said:

#1) The biggest risk from transfusion is getting a viral disease.

We consider that one?

Kevin: Busted.

Joe: #2) Donors with Type O negative blood are universal blood donors and their blood is safe for everyone.

Kevin: Busted.

Joe: Thank you!

#3) Blood is bad. Transfusing leads to increased mortality.

Kevin: Busted.

Joe: Thank you! And finally:

#4) Younger, fresher blood is better than older, stored blood.

Kevin: Plausible.

Joe: Yes. Can't quite say busted on that one, right?

Kevin: No, but if we were to say, "Younger, is better than standard-issue," then that would be busted.

Joe: Agreed. Alright, my friend, is there anything that we've missed that you wanna bring up just in closing?

Kevin: No. Ya know? This has really been fun! Thank you for inviting me.

Joe: It is my pleasure! Thank you for being here and I think that we can plan something further down the road. Thanks again, Kevin.

Kevin: Alright.