# BBGuy Essentials 078CE:
# Does That Patient REALLY Need Platelets? with Joe Sweeney
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**Joe S**: Hello, I'm Dr. Joe Sweeney from Providence, Rhode Island, and this the Blood Bank Guy Essentials Podcast.

**Joe C**: Hi everyone. This is episode 078CE of Blood Bank Guy Essentials, the podcast designed to teach YOU the essentials of Transfusion Medicine. My name is Joe Chaffin and I am your host.

I'm extremely excited to have you hear my interview today called, "Does That Patient REALLY Need Platelets?" with Dr. Joseph Sweeney from Brown University in Rhode Island. I really think you are really going to enjoy it.

But first, you should know that this *is* in fact a continuing education episode. The free continuing education credit is provided by TransfusionNews.com, and 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 (or "SAM") for Continuing Certification. To receive credit for this activity, to review the accreditation information and related disclosures, please visit www.wileyhealthlearning.com/transfusionnews.

I believe that WAY too many platelet transfusion decisions are made based on just simple evaluation of one laboratory value: The patient's platelet count. It's easy to get stuck with the idea that every transfusion below a particular threshold or count is fine, and every transfusion above that  same threshold is automatically bad practice. The truth is, it just isn't that simple!

My guest today, Dr. Joe Sweeney, has a long history of promoting wise choices in platelet transfusion. He is very actively involved in day-to-day practice at Brown, and as you will hear, he really enjoys getting involved in helping transfusing physicians get past a simple reliance on the platelet count in making their platelet transfusion decisions.

Dr. Joe Sweeney received his medical school and Internal Medicine and Hematology training in Ireland, followed by training in Clinical Hematology, Medical Oncology, and Blood Banking/Transfusion Medicine in New York. He has been at Brown since 1994, where he is a Professor of Pathology and Director of Transfusion Medicine and Coagulation. Dr. Sweeney has edited two books, including one of my favorites, a terrific book called, "Platelet Transfusion" from AABB Press that still sits prominently on my reference shelf. He has also written several book chapters and over 230 scientific papers and abstracts.

Two last things before we start: First, Joe and I are going to mention a lot of articles in this interview. You can find all of those references on the show page for

this episode, which is BBGuy.org/078. Second, I have to admit, this will be a little weird, since both of the people you will hear in the interview are named "Joe." It should be fairly easy to keep us straight, though, because one of us has a wonderful, smooth, magnificent Irish accent, and the other…is me! So I think you'll be ok.

Here's my interview with Dr. Joe Sweeney titled, "Does That Patient REALLY Need Platelets?"

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**Joe C**: Hey Joe, welcome to the Blood Bank Guy Essentials podcast.

**Joe S**: Great. Thank you very much, Joe, for inviting me. I'm honored to be considered one of the interviewees!

**Joe C**: You're very passionate about platelet transfusion and doing it well, obviously. So I wanted to talk to you today primarily about maybe the "not so obvious" scenarios where platelets should and maybe shouldn't be used. And in order to get to that, I wonder if we could just start off with a very high level look for the learners that are among us and for those that maybe aren't as familiar with this, just a quick look at, how do platelets work, what's the essential function of platelets? What do they do?

**Joe S**: The traditional view about platelets is that their role is in what we call "primary hemostasis." And that's basically the primary process by which breaches in the vascular system are curtailed by the attachment of platelets to expose some endothelium and subsequently the aggregation of platelets on top of that. So I think that really probably the simplest thing to think about platelets without getting into the more exotic areas is that they are involved in bleeding, in primary hemostasis, and in forming a a platelet plug, and that probably is the simplest way to think about platelets.

**Joe C**: And we're going to talk quite a bit today, Joe, about different levels of platelet counts and different, different levels of thrombocytopenia, I guess. So again, just to lay the groundwork, what's a normal platelet count? Is there variation among different people or, or what's considered relatively normal for platelet counts?

**Joe S**: Well, I think obviously there is variation. You know, to be more concrete, sometimes you'll find the normal platelet count being expressed as an interval or a "range," if you wish, with the lower threshold being approximately 150,000 platelets per cubic millimeter or per microliter, or 150 x 10^9 per liter. All of those are the same. And the upper limit of normal, sometimes that's variable, let's sort of agree to that number of around 400 to 440,000 cells/uL. So that's the number that you'll find mainly in the textbooks.

But unfortunately what the textbooks don't tell is that that's not exactly the situation. And sometimes you find... so for example, in females, platelet counts are higher than males in general. And in African-Americans, platelet counts are lower than in European-Americans. So, for example, the significance of that is that the lower limit of normal, let's say for an African-American male might be in the region of 115,000 platelets. And an important point there, not to label these healthy human subjects as having an abnormality when it's not actually present.

I think we also just need to be very careful in understanding that platelets are measured in whole blood, obviously, but they actually don't exist in whole blood. Platelets exist in the non-red blood cell compartments. So if you actually make an adjustment for the hematocrit, patients with high hematocrits will tend to have higher platelet counts than patients with lower hematocrits, because the volume in which the platelets is distributed is actually dependent on the hematocrit. That's an important point when you consider patients with thrombocytopenia due to ITP, for example.

So the last issue, of course, is the size of platelets, Joe, and I think people don't think a lot about that, but it actually is probably quite important. In normal healthy human subjects, individuals who have lower platelet counts, say in the region of 150 to 180,000 platelets/mm3 (or per microliter), they tend to have bigger platelets than healthy human subjects who have platelet counts in the 400,000 range. Their "MPV" or the size of the platelets tend to be smaller. So when we think of the platelet count, that's the number that's derived from these hematology analyzers. We're not actually counting platelets at all, as you know, we're counting particles of a particular size dimension. And hence, looking at the platelet count in isolation doesn't give you the clear picture because you really need to look at the platelet count in relationship to the hematocrit and the platelet count in relationship to the size of the platelets that are present. And we need to bear in the back of our mind the differences in gender and ethnic groups that can influence the normal platelet count.

Well again, just staying high level for just a second before we dive into this more. What are some reasons, Joe, that patients might get thrombocytopenic? What, why do people drop their platelet counts, if you will?

Well there are different ways, obviously, of classifying thrombocytopenia, you know, different textbooks give it different ways, but I tend to think of it in much more simple terms. So I think within the bone marrow, the platelet count can be reduced because we're not making platelets. That's one way. Examples of that would be aplastic anemia. An example of that would be chemotherapy-associated thrombocytopenia. So those platelets are not being produced in the bone marrow. And those platelets, in addition to being decreased in numbers, are generally small in size. That's certainly true for chemotherapy.

The second reason why patients might have a low platelet count is, of course, because of what we call "ineffective thrombopoiesis." So that's a kind of a fancy term, but what we really mean is that within the bone marrow, the megakaryocytes are trying to make platelets, but are unable to effectively produce them. And an example of that would be megaloblastic anemia and some cases of myelodysplastic syndromes. So these patients may have low platelet counts even though, for example, if you examined a bone marrow, you'll find plenty of megakaryocytes. That's the second reason.

And then the third reason is that maybe the bone marrow is making platelets adequately, but their survival is curtailed, in other words, they have a shortened platelet survival. So in the extreme situation with defective platelet survival, kind of the prototypic disorder is Immune Thrombocytopenia where we envisage antibodies being produced against platelets. So the shortened platelet survival would be common in that situation. Now those situations are typically associated with large platelets, and very commonly, there is an associated high MPV. There are other conditions where platelets are, if you like, "consumed," Thrombotic Thrombocytopenic Purpura, DIC, for example, is another example of that type of situation. And again, the bone marrow is quite capable of making platelets, it's just that the platelets have a shortened survival.

So normally platelets, you know, have a mean survival in humans of around 10 days, but there's a huge scatter there with some platelets perhaps surviving as little as one day and some maybe surviving as many as 20 days or so. And so when the platelet lifespan becomes reduced, in other words, there's a diminished survival of the platelets, then the bone marrow will attempt to compensate initially. But the degree of compensation may not be adequate to maintain a normal platelet count and the platelet count therefore will decrease. It's very similar to how you might view anemias, actually. Anemias and thrombocytopenias could be viewed in the same way of diminished production or ineffective production or shortened survival (you know, the hemolytic anemias). So conceptually it's kind of a good way of thinking of why a patient has a low platelet count. But Joe, I'd like to hasten to add that whilst what I've described seemed very simple in theory, in practice, sometimes it's more difficult to figure out exactly why an individual patient has a low platelet count. And in fact, it could be a mixture of different mechanisms in any given patient at any given time.

**Joe C**: That's a great overview of that. Everyone listening, I have described in previous episodes how we supply platelets in the United States, primarily from apheresis-derived processes, as opposed to another countries where perhaps they're more whole blood-derived. So I'm not going to take the time, Joe, to go into that with you today, but I do want to get to kind of the core of what we're here to talk about today. And that's the way that you have broken down this down in the past (and I really, really like it), is

essentially three main clinical situations where platelets are transfused. I wonder if you would summarize those three situations and then we'll go into them individually. So what are those three, Joe?

**Joe S**: So those three situations are, there are two clinical situations where platelets are transfused PROPHYLACTICALLY. So the first is where platelets are transfused prophylactically to prevent or mitigate bleeding, spontaneous bleeding, and then the second prophylactic indication is where platelets are transfused to patients prior to an invasive diagnostic or therapeutic intervention. So again, the prophylactic indications could be either to prevent spontaneous bleeding or in the second case to prevent "provoked bleeding." And then the third indication is THERAPEUTIC, that is patients, who are thrombocytopenic (and we can talk about how we categorize that), who are actually exhibiting clinical bleeding or patients with a normal platelet count who have platelet dysfunction from drugs, for example, such as the, thienopyridines, Plavix, for example, aspirin, who have normal platelet counts and may be bleeding in that context. And they are two very different situations.

What I think is probably worth commenting on at this point, Joe, is that the vast majority of platelets transfused in the United States and in resource-rich countries is for the very first indication, that is the prophylaxis against spontaneous bleeding. And then progressively fewer platelets are transfused as prophylaxis for provoked bleeding, and similarly fewer platelets for the therapeutic indication. And it's interesting to ponder on those three separate indications because we have actually reasonably good data on the first indication. We have good randomized control trials, et cetera, which can provide us with reasonable guidance about platelet transfusion therapy to prevent spontaneous bleeding. And then we have progressively much less high quality data, you could argue we have very little good data at all with regard to the transfusion of platelets in the context of provoked indications or the of platelets in a therapeutic context.

**Joe C**: I've talked a little bit about some of the, some of the guidelines for how these things are done in the past. I did a podcast previously with with Rick Kaufman where Rick went over the, the AABB guidance document that came out in, when was that, Joe? I believe that was 2015, if I remember right. And so folks, you can check out previous episodes to hear some of that. We're going to try and make this really practical. And that's one of the things that I really appreciate about your approach, Joe.

So let's start with that first indication, the prophylaxis to prevent spontaneous bleeding. In the patients where we're transfusing platelets, you know, on a purely prophylactic basis to prevent, as we said, a spontaneous bleed. Is the risk of bleeding in thrombocytopenic patients higher? What do we know?

**Joe S**: I think one has to go back really historically to the 1950s or 1960s, with autopsy studies on patients with severe thrombocytopenia, typically in the context of acute myeloid leukemia. It was pretty clear autopsies showed bleeding as a major cause of death in these patients, that thrombocytopenia was extremely common, of course, in these entities. And because of that, in the late 1950s, early '60s, people started getting interested in harvesting platelets and transfusing platelets. And that's how it all sort of got started.

And then about 1962, so it was around the same time, a very interesting person called Gaydos published, I think, a very important study where he tried to define the relationship between thrombocytopenia and clinical bleeding in the context of acute leukemia. And actually he was not able to find a well-defined threshold, although he did clearly show that the lower your platelet count, the greater your risk of bleeding.

So what he showed really was the platelet counts less than 20,000, 10,000, they were associated with increased risk of bleeding, and the risk of bleeding fell off dramatically once the platelet count increased. Now, it was very interesting that Gaydos never actually gave a number in his paper. And he actually said that he could not see any well-defined threshold. But if you look carefully at his data, you could probably surmise that a platelet count, which is very low, less than 10,000, if you look at his data from that paper, had an increased risk of bleeding.

So then we fast forward to the 1960s into the 1970s and 80s. And what we have really are retrospective observational studies, and most of these largely showed that the risk of bleeding increased when the platelet count fell low, indeed, EVERY low, typically less than 10,000 and indeed, that most of the bleeding events were less than 5,000. So this gave rise to the randomized control trials that were done in the 1990s and the early part of the current century, where patients were randomized to receive platelets with platelet counts of less than 10,000 or platelet counts of less than 20,000, that was the randomization. And to summarize, virtually all those studies showed that a platelet threshold of less than 10,000 was as good as a platelet threshold of less than 20,000, and was associated with fewer platelet transfusions. So that brings us pretty close to our current way of thinking, which is that if the platelet count is basically a single digit, and I don't mean 10,000, I mean actually less than 10,000 platelets, which is a single digit, (and this point was emphasized in the recent ASCO guidelines, of course), that the risk of bleeding seems to be at a point that the judicious use of platelet transfusions would be helpful.

So you actually sort of really asked me two separate questions. I think it's important to address them. One is at what point is risk substantially increased? And what is the role of platelet transfusion? So if we define the risk of bleeding as prophylaxis for spontaneous bleeding, if we define that in hematological patients, certainly with acute myeloid leukemia

undergoing induction therapy or autologous transplants or allogeneic transplants, if the risk is less than 10,000, then that would be the threshold at which we would administer a platelet transfusion prophylactically. So that becomes really enshrined as what might be regarded as current practice, certainly until maybe three to four to five years ago.

And there's been a slight variation, a slight wrinkle thrown into this recently from the work of [Inaudible] in Germany and more recently a paper by Simon Stanworth from Oxford in the New England Journal that showed that actually not all thrombocytopenic patients are created equally. So that if you look at patients with undergoing autologous transplant, you know, after conditioning therapy, when they become thrombocytopenic typically a few days after conditioning therapy until maybe day 12 or 14 or so, when the platelets begin to return, the current thinking is that those patients should only be given what's called "therapeutic-only transfusions." Our current practice is not to transfuse those patients anymore if their platelet count is between 5 and 10,000, providing that they do not have evidence of an inflammatory process (a clinical measure of that is typically a fever, of course). And so, our current thinking is just not to transfuse those patients, but other kinds of patients, we do transfuse when the platelet count drops below 10,000. So we're mostly talking about acute myeloid leukemia patients undergoing induction therapy, patients undergoing allogeneic bone marrow transplant who have had conditioning therapy and therefore are thrombocytopenic until they engraft, the threshold typically is less than 10,000. And then for autologous transplants we like to transfuse at less than 5,000, and certainly if they're between 5 and 10, if they exhibit febrile evidence of an inflammatory process.

But I also think it's probably worth noting, Joe, that there are two important exceptions that we should put into the equation. Again, going back to the early studies in the 50s and 60s, the relationship between clinical bleeding and thrombocytopenia brought a third factor into interplay, which is the the presence of inflammation. And the old observation that many of the so-called "spontaneous bleeds," getting back to our earlier conversation, occur in the context of evidence of an inflammatory process. So I tend to call those "unstable thrombocytopenics," and my current practice and suggestion is I tend to transfuse them if the platelet count is less than 15,000. So that's one difference that's important.

And then there is one other important consideration: When patients are undergoing induction chemotherapy or even conditioning for a transplant, the platelet count begins to drop. And the rate at which the platelet count drops is, I think, somewhat relevant. So for example, if your patient's dropping their platelet count from, you know, 90,000, the next day it's 50,000, the next day it's 31,000. The next day it's 16,000; that's the patient I probably would transfuse with a platelet count of 16,000 rather than waiting for the platelet count to fall below the "magical threshold" of 10,000. So there are the two exceptions, patients who are exhibiting

evidence of an inflammatory process, I use a higher threshold of 15,000 typically (some people perhaps use the threshold of 20,000), but I think we should consider a higher threshold than 10,000. And then those patients who have a rapid decline in the platelet count. I worry about those patients when the platelet count is diminishing very, very quickly. I think that we need to be careful not to apply the same criteria as we would apply say the "standard" criteria.

So I think that sort of summarizes a lot of where we are with platelet transfusion therapy as prophylaxis against spontaneous bleeding. But there are some other one or two important clinical situations that are probably worthy of comment as well.

**Joe C**: Well, fire away, Joe! What are those? What are those... No, don't let me stop you. You're on a roll! Go for it.

**Joe S**: You know, sometimes we have patients who are on an outpatient basis. Now I'm talking about patients with myelodysplasia or patients with aplastic anemia. where really, we're at the end of the line. We're just kind of managing them with supportive care, and these patients come into clinic intermittently, and they often have platelet counts of less than 10,000. And it has become a practice to sort of routinely transfuse these patients. And I've been trying to push back a little bit about this, because really, if you follow these patients for long periods of time, they tend to do okay in terms of clinical bleeding, and just simply transfusing the patient with platelets every time they arrive in clinic with a single digit thrombocytopenia, I think can give rise to an overuse of platelets. Now, of course, I know it's difficult to get our hematology and oncology colleagues to get on board on this, but I've been trying to push that as much as possible.

The second situation, I think related to this, and we haven't talked about dosage, Joe, but there's an excellent article in this month's, July issue of Vox Sanguinis, which addressed the question of dosing. So, you know, some of my colleagues in the past, they wanted to give these patients "double doses" before long weekends. They're worried about, you know, "maybe they'll bleed over a long weekend." And I think we need to push back on that. So there's two separate issues. One is, should we give a platelet transfusion at all? That's a "yes or no" decision. And then if we do give a transfusion, what dose should we give? And we're talking now in the context of an outpatient because we know a lot better about dosage for inpatients from the PLADO study.

**Joe C**: So let's move on and talk about, perhaps a bit more controversial and I think you would agree an area that's not as well defined, at least in the available literature that we have, and that's the second category, as you mentioned, prophylaxis for "provoked bleeding." So there are many, many, many different clinical scenarios that we could talk about. And again, we're

going to try and stay as as high level as possible with this, but I know one of the things that you have talked about before is the use of platelet transfusion in liver biopsy. So I wonder if we could just use that maybe as an example, and we'll hit some of these other ones more briefly, but would you like to expand on what's available in terms of the data for platelet transfusion and liver biopsies?

**Joe S**: Okay. Well I think again, probably when we get into that it's probably worth discussing, what is the risk of bleeding in patients who are undergoing a liver biopsy? And actually we have some data on that, particularly from the "HALT-C study" [NOTE: The recording sounds like Dr. Sweeney says "HALT-T," but "HALT-C" is correct] you know, the interferon-alpha study in patients with hepatitis prior to development of these antiviral drugs. And what, what do we learn from the HALT-C study? Well, we know that the risk of bleeding increases in patients undergoing liver biopsy. It's when the platelet count is very low. And to give a number, it's typically around either 50, from the HALT-C study, 60, let's not worry about a threshold of 50 or 60,000. So I think you could find evidence to support the contention that patients with, let's call it "severe thrombocytopenia" undergoing liver biopsy have an increased risk of bleeding.

But is that really the case or not? Or does it vary between the type, the liver pathology, and does it vary by the method of biopsy? That's when it gets a little bit more tricky. So let's take the first question, for example: Does the risk of bleeding vary by the underlying cause for the liver biopsy? And so if you're doing a liver biopsy, for example, for patients with, you know, where you're trying to evaluate cirrhotic changes due to hepatitis, that's one clinical situation. The risk of bleeding there seems to be fairly low, in the region of about less than 1% overall, maybe a fraction of 1%. And then if you're doing a liver biopsy for a patient with a suspect mass, perhaps a malignancy, then that risk of bleeding tends to be much higher.

Now, as I've examined the literature on death from bleeding in patients undergoing liver biopsy, it very disproportionately contains individuals who are having liver biopsy for malignancies. I think patients who have a liver biopsy for a suspect mass in the liver, that's a whole different situation than a patient having a liver biopsy for, for example, evaluation of hepatitis, or the presence or absence of cirrhosis or other causes. I think the indication's important.

But here's a very important point: If we accept that the risk of bleeding increases in patients with thrombocytopenia, and I'm not disputing that, that does not necessarily mean, Joe, that a prophylactic administration of platelets actually would mitigate or decrease the risk of bleeding. Do you follow the different ways of thinking?

**Joe C**: I do!

**Joe S**: You cannot assume one or the other. And you might say, "Well how is it that patients with severe thrombocytopenia bleed?" And the reason may be not related to platelets at all! It may be that those patients have underlying liver, distorted liver pathology, which predisposes to bleeding, rather than the thrombocytopenia, per se. So thrombocytopenia may only be a surrogate marker for severe liver disease, and it's the severe liver disease that caused the bleeding. Now, if that argument is correct, then it follows that platelet transfusion would not be expected to mitigate, because there's never been a study that shows that platelet transfusions actually mitigate the risk of bleeding in thrombocytopenic patients, despite the assumption that many people seem to have, that, in fact, that's a logical extrapolation.

So I think liver biopsy is very interesting. I think that is important to make those caveats. And then the third point is, the question is whether are you doing a percutaneous liver biopsy or whether you're doing a transjugular liver biopsy. And the interventional radiologists, you know, they don't like to do the transjugulars because it takes a lot more time and effort. And I don't know if they get reimbursed as well for their efforts, but it's pretty clear to me that transjugular is the way to go if you're trying to diagnose, um, a, a pathology in the liver in severe thrombocytopenics.

And there's an important paper by Wallace, an interventional radiologist, in that respect. It was in the Journal of Vascular and Interventional Radiology in 2003, where he actually did a series of 51 transjugular liver biopsies in patients with severe thrombocytopenia and hematological malignancies and he used a threshold of 30,000 to administer platelets. So all of them got platelet transfusions because all the platelet counts less than 30,000. Well, it was very interesting. Wallace, he got no bleeding whatsoever when he did transjugular biopsy. So that was obviously a very desirable outcome. But more interestingly enough, only half the patients actually achieved a platelet count greater than 30,000 and half, obviously, did not. And there was no evidence that the half of the patients who did not achieve a platelet count of 30,000 did not show any more bleeding. So it raised a very interesting question: What IS the threshold for bleeding in transjugular biopsy, and what is the value of platelet transfusion in that context?

So as you pointed out in your introduction, we don't really... you're quite kind in saying that "we don't have a lot of good data." In fact, I think we have very little good data at all. We don't have any randomized controlled trials, all we are dealing with retrospective, observational studies. So, you know, what's happened in this area is that people, whenever we don't have enough information to make a reasonable, solid scientific judgment, we tend to default to what we might call "historical precedent." You know, we continue to do what we've always done. And historical precedent has been to set a threshold of 50,000 for invasive procedures. And unfortunately that threshold of 50,000 has absolutely no empiric

justification whatsoever. It's a very important area for us to challenge, I think, with our clinical colleagues, particularly the interventional radiologists, and for example, in our own institution, we're now using a threshold to 30,000 for a lumbar puncture. You'll find in the literature of many people advocate 40 or 50,000. The Germans are quite happy to do it at 20,000 or so. And I think that's a very interesting procedure next to liver biopsy because there's always a concern with lumbar puncture with regard to, you know, perispinal hematomas.

**Joe C**: Before we move on from liver biopsy and use that to kind of illustrate some of the other, provoked bleeding prevention things that we're going to talk about, one of the things that happens in hospitals that I work with, and I'm sure you've had this as well, Joe, is the call from, for example, interventional radiology. I don't want to beat up on my radiology friends, but the call that comes that says, "Okay, this patient needs to have a threshold count of 50,000 before I do this solid organ biopsy," (or whatever procedure we're talking about), "The patient has a platelet count of 47,000 and we definitely want to transfuse to get it above 50." How do you respond to scenarios like that?

**Joe S**: So my initial response when I see it is, I generally will talk directly with the operator. Now it's not always, Joe, an interventional radiologist. So let me just mention a few other scenarios. It could be a pulmonary doctor doing a fiberoptic bronchoscopy or it could be a gastroenterologist doing an endoscopy, so there's a couple of different cast of characters in this field. I always say the same sort of thing to them, and that is, "There is actually no difference between a platelet count of 48,000 and 50,000. And there's no data that the platelet transfusion will mitigate bleeding in this particular context." And I point out to them, "You're subjecting to patients to a risk of the platelet transfusion, which is not to be dismissed when there's no evidence of efficacy." So if you put it to them that there's no evidence of efficacy, and there is evidence of risk, then they sometimes will at least look at you in a sort of semi thoughtful manner.

The comeback is nearly always the same, Joe. The comeback is the same: "Yes, I understand everything you say, but the guidelines, the GUIDELINES tell me that I should do this." And I tell them, "Well, guidelines are only guidelines and even if they're produced by you know, eminent authorities such as the SIRS [NOTE: Society for Interventional Radiology] folks, and unfortunately they haven't changed their tune in the last 10 years or so, as you pointed out. You know, this is very unfortunate.

So what I try and do in practice is, you know, you refer to the individual situation of an individual patient with an individual platelet count undergoing an invasive procedure. Now some of those I "win" and some of them I "lose." So my personal opinion: It's a waste of time giving platelet transfusions to the patient you mentioned. That's my personal opinion. Okay. But I prefer to approach it slightly differently. So I try and talk to the

interventional radiologists as a group, and then I try and talk to the endoscopists, or even the pulmonary docs, and whoever else is doing procedures, you know, and talk to them as a group and say, "Look, let's just get some SENSE into this!" And so when I've done that, for example, for lumbar puncture, now, they've agreed to 30,000, for fiberoptic bronchoscopy, we use a threshold of 20,000, for central venous tunneled catheters, we now agree to a threshold of 20 to 25,000, and for endoscopy, I use a threshold of 25,000. And then occasionally, I'll cut them some slack if it's 26 or 27, you know, in that range. But once the platelet count gets above 30,000, I begin to get very uncomfortable in acquiescing to the demand for a platelet transfusion.

So it's not actually the 47 that you mentioned, Joe. I get very uncomfortable with the platelet count of 35,000, etc., etc. When you're dealing with the individual interventional radiologist, the individual pulmonary doctor, or the individual endoscopist, there's a lot, Joe, that depends on the personality of the individual and the culture of their department. And I think you need to put that on the table because we know the biggest cause of, you know, why blood transfusion varies from institution to institution, it's related to institutional culture. So if you have a culture that says, "Transfusion is good for you, it'll mitigate bleeding," and all that kinds of good stuff, then you'll give platelets. If you have a culture that is more transfusion-averse, more recognizing dangers of transfusion and lack of evidence for efficacy, you tend to avoid transfusion.

I think it's really important as we try to manage all blood components to shift transfusion culture, and part of that is talking to our colleagues, not the morning of the procedure when it becomes a bit of an emergency, but actually long in advance of that, you know, weeks or months in advance to go to their meetings and to talk to them about these issues and that helps a lot. It may not solve every problem, but it helps in many, many situations.

**Joe C**: There are many situations, Joe, as I'm sure you'll agree, where you're not actually necessarily talking to the person that's going to be the operator for that procedure, but you're talking to the hospitalist or the general medicine folks taking care of the patient who have been told, "Before you send this patient to get this procedure, by gosh, you're going to have this count at such and such a value." That complicates matters even further I guess, doesn't it?

**Joe S**: It does. And it's not just a hospitalist, it could be an intern, for example, who was afraid to make a decision. So what I actually do is, in that situation, Joe, is I ask the hospital who exactly is going to do the procedure, you know, and if they don't know the name of the interventionalist or the pulmonary doc or the endoscopist, if they don't know their name, I'll call the department and find out who exactly is going to do the procedure. And then I talk directly with the operator. If I'm actually in the institution, I tend to go down to the interventional radiology

suite or the endoscopy suite and talk directly one-on-one. And, I find that can sometimes be very, very, very helpful. So I usually don't try and reason with the hospitalist or the intern, because honestly, there's no point in doing that because they're being told what to do.

You know, they say that there are pros and cons of being in a particular institution for a long period of time. One of the negatives is you tend to perhaps, you know, "slack off" over the years, perhaps, you might get a little bit sleepy in your approach. That's always a danger. But there is an advantage in that you come to know the medical staff, and if they trust you, if they believe there's value in your opinion, you can work with them a lot better than if they don't know your face.

**Joe C**: Joe, I can't tell you how many times I've had that exact conversation with residents that I've worked with over the years. And, I could not agree more with what you just said. There is so much value in being seen as the "helpful person" (and actually BEING helpful of course), rather than being seen as the gatekeeper of the blood bank with your flaming sword saying you can't have this blood or redraw that sample. What you just said is a HUGE lesson to young blood bankers everywhere. Great point, I love that.

**Joe S**: And, just to finish off the point, Joe, and to amplify what you said, you know, all of us are involved, as you know, in blood management and actually this is one particular area of appropriate blood management. So I think the point is that we are not OPPOSED to blood transfusion. The objective is not to render blood transfusion to the lowest numbers possible. T he central issue is to engage in appropriate good transfusion practice. And sometimes we're advocating the use of components in different situations as well.

**Joe C**: Preach it, my friend! That's awesome. Completely agree. We talked extensively, obviously, about liver biopsy and you've mentioned some of the others. I wonder if we could just take a real quick tour through what maybe what your practice is and whatever limited data there might be on some of the other things that come up in routine practice. And some of these, I know you mentioned a few minutes ago, but again, let's hit them real quickly. What about bone marrow biopsy? Is there any data on that or any thoughts?

**Joe S**: Yeah, so I mean, it depends on the individual involved. I mean, certainly if the platelet count count is less than 10,000 we tend to give platelets or are happy enough to give platelets, but we might be giving platelets regardless anyway. And I sometimes see a threshold of 20,000 for a bone marrow aspirate and biopsy. Again, there's no data to support that. To the best of my ability, I try and talk hematologist-oncologists out of platelet transfusions if the platelet count is greater than 10,000. So that's really my position with regard to that, because, first of all, it's unlikely you're going to get life threatening bleed from a bone marrow aspiration biopsy. And we

have a very interesting hemostatic agent in our hand called "the finger." If properly applied for a reasonable period of time. I think that can actually do the trick.

**Joe C**: I know you've mentioned this one already, but, insertion and or removal of tunneled or non-tunneled central venous catheters.

**Joe S**: Yeah, we have actually some data on from the radiology literature as you know, with large bore tunneled catheters, and the threshold we use there is 25,000. Some people say 20,000 from the recent ASCO guidelines. I don't push it too far, but if the platelet count is greater than 25,000, we do not give platelet transfusions prophylactically.

**Joe C**: Another one that comes up, I don't think it comes up as often as it used to in my practice, anyway, I'd love your perspective, but paracentesis and/or thoracentesis.

**Joe S**: Yeah, they're messy ones, you know, I really don't like giving platelet transfusions if the platelet count is greater than 20,000. So that's really where we are. If it's less than 20,000, I'll cut them some slack and perhaps give a platelet transfusion prophylactically. But if it's greater than 20K, I actively discourage it to the extent that's possible.

**Joe C**: Another one that's often controversial, and again, I know you've mentioned this already briefly, but lumbar puncture.

**Joe S**: Yeah, well, I mean if you look at recent ASCO guidelines, they actually don't give a threshold. They actually say between 40 and 50,000; you know, the historical threshold was 50,000, Joe. I think our current threshold is 30,000 and that's where we are right now. I mean, I don't know if I'd like to go lower or not, but I'm moderately happy with the 30,000 threshold. The Germans, as you know, use a 20,000 threshold. So the UK, I think it's 40 to 50, but you have my opinion versus what you might find in the literature, but certainly not great...certainly not greater than 50,000, Joe. So, I mean, I think I like our threshold of 30,000, but that's where we are right now.

**Joe C**: And interestingly, the AABB guideline from the 2015 paper suggested 50,000, but it was a weak recommendation with low quality evidence. The British guideline is actually, I believe 40, it is, it's 40, and you'll like this, Joe, if you haven't seen it, the Society for Interventional Radiology one that I just mentioned actually says 20, shockingly enough!

**Joe S**: They must have woken up a little bit then. Delighted to hear that, Joe, definitely. Thank you.

**Joe C**: Ah, yes, no problem. What about, and this is one that I've seen people get really emotional about: Placement of epidural catheters.

**Joe S**: Very difficult situation, epidural anesthesia, that sort of thing. So you know, the traditional number there is, as you know, 70 to 80,000, the British have a 70,000 threshold, and in the US, it's more common to use an 80,000 threshold. And actually, there's two parts of that, Joe: There's the insertion of the catheter and the removal of the catheter. And so for example, sometimes these catheters are left in postoperatively for a few days for pain control, you know. So it's really difficult. I mean, the problem with it is you have these formal recommendations. You've got this huge concern on the part of the anesthesiologists about a epidural perispinal hematoma and the consequences of that. So I think that if the platelet count certainly is less than, you know, 40, 50,000, I don't tend to push it. And I realize that it's not the most common cause of provoked platelet transfusion. So I don't worry. I don't push it too hard. It's the same as a neurosurgical intervention as well, you know, where people arbitrarily use a threshold of 100,000, which there isn't evidence for that as well.

**Joe C**: Let's talk about other surgeries. The patient who is going to have a surgery tomorrow, say a colectomy or some sort of surgery that is considered a "major surgery," what kind of thresholds are we looking for there?

**Joe S**: We don't obviously have any good data to indicate what, you know, what would or would not mitigate bleeding. And, you know, surgical... Therapeutic interventions such as surgery are much more complicated, because, you know, the mechanisms of bleeding, could be variable. I mean, the surgeon could have a very vascular organ that could bleed regardless of the platelet count, or there could be inadvertent transection of blood vessels here or there in the abdomen. So I think really the surgical situation is very complicated. We really have no idea what the number is. So I default unfortunately to the historical precedent. In other words, I try to discourage platelet transfusions if the platelet count is greater than 50,000. If the platelet count's greater than 50,000, what I tell the surgeon and the anesthesiologist is, "Look, go ahead and do your procedure. And if you encounter intraoperative oozing that concerns you, we'll administer platelets." And many of them do fine in that context.

I've had surgeons who have agreed to do a major surgery such as bariatric surgery with platelet counts of 35 and 40,000. And they report back to me that they do not observe any excessive microvascular oozing. So I think that's an area that's open for at least some retrospective observational studies. It would be difficult to do a randomized controlled trial, I would think. But I would say I use a threshold of around 50,000 without any good data to support it one way or the other.

**Joe C**: I feel like before we leave the prophylactic platelet transfusions to prevent provoked bleeding, and actually before we leave prophylactic platelet transfusions in general, I wonder if you could just take a few minutes to talk about, and we'll get to therapeutic platelet transfusions in patients who

have acquired function defects such as due to drugs or renal failure or whatever, but let's talk quickly about prophylactic transfusions to those patients. Someone who you know their platelets aren't working well, again, either for pharmaceutical reason or for an acquired defect like renal failure or even a congenital issue. How do you feel about prophylactic transfusions in those scenarios?

**Joe S**: Okay, so there's various different situations. So we're talking about patients by and large with normal platelet counts. I mean, you mentioned some patients with hereditary platelet disorders; some of those actually have slightly low platelet counts. But let's talk about the patient who has a normal platelet count and who is on antiplatelet therapy, and let's say is undergoing a surgical procedure. So what in general we'll recommend, if it's an elective procedure, I often recommend discontinuing some of the antiplatelet drugs. So we don't routinely recommend stopping aspirin, that's number one, and then with regard to the thienopyridines or the anti-P2Y12 drugs such as ticagrelor or Brilinta, we recommend for elective procedures discontinuing the drug for a very brief period of time. So for clopidogrel, which is Plavix, we use a five-day window, for prasugrel, which is Effient, we use a seven-day window, and for ticagrelor, which is Brilinta, we typically use a three to five-day window.

But I also, of course, we do tests for the P2Y12 receptor. There are a number of tests that can be done. And our cardiac surgeons and other surgeons widely use these tests and go ahead and do the procedure. So here's what I generally recommend. If it's an elective procedure, consider if possible discontinuing the anti-platelet agent, not aspirin, but the other agents I mentioned. If it's an emergency procedure, which is not...which is a situation we find ourselves in from time to time, what I recommend is we do a test to assess whether the drug effect is present. If the drug effect is present, I still give the same advice. Go ahead and do the procedure. And if you notice significant compromise, hemostasis and oozing intraperatively, we have platelets available for you. And in the vast majority of cases we don't give them, I'll tell you from my experience.

**Joe C**: Joe, thank you for taking the time to go through all of those issues regarding prophylaxis for provoked bleeding, and I think those are the areas that tend to be more controversial. So I wanted to make sure we hit that fairly closely, but I want to close, in the time we have left, with just a quick discussion on therapeutic platelet transfusion, the scenarios where someone is bleeding and is thrombocytopenic. How do you make decisions and how you evaluate those patients in those settings?

**Joe S**: So a couple of things I think relevant to this particular clinical indication. I think first and foremost, we really don't have any good data, in fact we don't really have data of any real material value. What we have is observational studies and we have preconceived ideas, and unfortunately, that's not the best way to establish good clinical practice. Okay, important

to say that. But, so what do I do? Because that's the question you asked me, and it is a situation we see from time to time. We don't use a lot of our platelets in the context of therapeutic platelet transfusions. But it is an interesting, important indication.

So I don't know the answer to this question in terms of defining a platelet threshold at which we should or should not administer platelet transfusion. So in the absence of being able to do so, I default to what we consider to be "historical precedent," which of course is not based on good science, and I use a threshold of around 50,000. But I also like to look at what the clinical situation is. So let's say we have a patient bleeding from the gastrointestinal tract, let's say the patient has got alcoholic cirrhosis, a common enough situation, would I/would I not not give a platelet transfusion? And my general sense is that if the patient has exhibited a small-volume bleed, and let's say the platelet count is 35 or 40,000, and the endoscopist is going to go ahead and perhaps fix the problem in the gastrointestinal tract, whether it's varices or an acute gastric ulcer or something of that nature, then I try to avoid platelet transfusion.

If there's evidence of ongoing bleeding you know, the patient continues to bleed and require red blood cells, and I know I'm going to dilute out the platelet count, under those circumstances, I'm more inclined to give a platelet transfusion. But just arbitrarily, I use a threshold of 50,000 without necessarily having any data to support or refute that threshold.

But what's more important I think is to look at the totality of the situation. Is the patient currently bleeding? Have they stopped bleeding? Have they lost a small volume of blood? You know, one or two units and they're hemodynamically stable or are they hemodynamically unstable and they've lost eight, nine units of blood? So all those things I put into consideration in terms of giving a single dose of platelets or indeed even more than one dose depending on the clinical course of the patient. It's a very, very difficult situation I think to try and be, you know, "yes or no" about any given threshold. So just getting a number really is relatively meaningless stuff based on science.

Another interesting clinical situation occurs with patients with intracranial bleeding in thrombocytopenia. And I think that that probably is again, another very difficult area. There is one good retrospective observational study from MD Anderson published maybe 10 years ago or more, which looked at a moderately large series of patients with thrombocytopenia, intracranial bleeding, thrombocytopenia from hematological reasons. And, they used an arbitrary target of 50,000. So if the platelet count was less than 50, they would give platelets and try to attain a target of greater than 50. And what they observed was that there was no evidence that those patients who got large volumes of platelets, multiple dosing in order to achieve an arbitrary threshold of 50,000, did any better than those who did not. And, similarly, patients who failed to meet the threshold of 50,000 did

not have a worse clinical outcome than those who were successful in achieving a platelet count of 50,000.

So again, I think it was a useful contribution to the literature because it cast into doubt the whole question about, you know, what is the platelet threshold in this particular clinical situation? Neurosurgeons commonly use numbers like 50, some of them use numbers like 80,000, and sometimes they're totally unrealistic and unachievable. And I think that's where we are with it, it's a very confused area.

So my general approach is to try and be as reasonable as possible. So for example, let's say I have a patient with a subdural hematoma, comes in minimally symptomatic, they're worried about him and the platelet count is 40,000. I'll push and I'll give a dose or two of platelets for the first 24 hours or so. And then if I find that after a repeat CT scan shows that the hematoma is stable, I'll ask the physicians taking care of the patient to bring down the threshold. So we'll only give platelets now if the platelet count is less than 30,000, and then if the patient does not show any evidence of progression of the hematoma, it seems to be stabilized, et cetera, et cetera, I might drop it lower to 20,000. So I handle each indication, you know, on a case by case basis, because we don't really have a good guidance on the subject based in science, and that's true for all therapeutic platelet transfusions.

**Joe C**: We're still talking about therapeutic platelet transfusion, but let's throw a little bit of a kicker on that. Let's talk about intracranial bleeding. And you've already mentioned that a little bit, but let's talk about what data we have and in fact kind of a, maybe an alarming or somewhat earth-shattering study that that came out called the "PATCH study" in Lancet 2016 (I'll have that reference on the show page). What do you think we have learned from the PATCH study and how has that impacted your practice, Joe?

**Joe S**: Well, the PATCH study I think, was a very useful piece of information, because first and foremost, it was a randomized controlled trial and it involved a fairly large group of patients, approximately 200 with about 100 randomized I think to each of two arms. So these were patients who presented with primary intracerebral bleeding and who were currently on antiplatelet therapy. Now, it's a European study, it's a multisite European study, so the Europeans might have different antiplatelet agents, so you have to be careful about that. But nearly all the patients were on aspirin, some of them were on anti P2Y12 receptor inhibitors such as clopidogrel as well. So these patients were randomized to receive either platelet transfusions or not receive platelet transfusions. And then they were followed up at several months later with a neurological evaluation and overall survival.

And, it was quite interesting that the patients who received the platelets actually did appear to do worse, and they did worse in the sense of the neurological evaluation, I believe at three months using what the neurologist used, which I believe is a score called the "Rankin" score (and they modified it slightly), but regardless, it was evidence that neurological function was better in the patients who did not get platelet transfusions. At six months, there was no difference, and overall survival difference. So, the important take-home message is that there is no evidence that platelet transfusions improve clinical outcome in primary intracerebral bleeding in patients on antiplatelet agents. I think that's an interesting observation, and it almost is counter-intuitive.

So how does that influence what I do? Well, when I quote this study to my colleagues in the emergency room, for example, or my hematology colleagues, they look at me with a strange look on their face and say, "how could that be?" You know, the data are the data, right, Joe? And the question is, we can't dispute data. We can dispute the interpretation of data, but we cannot dispute data. so I thought it was a very interesting eye-opener about the value or otherwise a platelet transfusion therapy.

Now, can we extrapolate? It's a very interesting question. Can we extrapolate from intracranial bleeding, where the use of platelet transfusions therapeutically in patients on antiplatelet therapy did not improve clinical outcome, can we extrapolate that to other clinical situations, such as, for example, abdominal surgery in a patient or urgent hip fracture surgery in a patient on antiplatelet agents? Because if you've got a little bit of time, you can actually stop the antiplatelet agent for a few days and you can kind of surmount the problem. But we're talking about the patients who are actively bleeding. And I think that's, it's a complicated issue.

So my general approach is to try and avoid platelet transfusion, discourage platelet transfusion in patients with normal platelet counts who are on antiplatelet therapy. If I get pushed by the surgeons or by the anesthesiologists, I'll try and recommend interventions that are not platelet therapy. So for example, with aspirin, if they're worried about that (and I don't know why they should be), I'll often recommend use of DDAVP prophylactically and sometimes that keeps them happy and they they go ahead and deal with the situation. There is some evidence that DDAVP might be helpful as well in patients on P2Y12 receptors, much less data on that, more in vitro, not good clinical data. For gastrointestinal bleeding in patients or actively bleeding on antiplatelet therapy, I sometimes will recommend use of tranexamic acid, since there is a lot of fibrinolytic activity in the gastrointestinal tract.

So I try to handle each case as I see it. I try to recommend against just transfusing on the assumption that there's going to be efficacy from the transfusion. So it's more a discouragement practice.

**Joe C**: And really what that means, Joe, it sounds to me is like you practice medicine, right? I think that's one of the take-home messages for me in these scenarios is that we as transfusion medicine physicians and providers need to not just focus, and you made this point at the beginning, don't just focus on an individual number. Consider the whole patient, consider the whole process as you're making your decisions and your recommendations.

**Joe S**: I think so if we had better quality information, Joe, I think we could make decisions based on, you know, a single variable, you know, a single number. But I think it's generally a bad idea to make decisions about patients based on numbers and a very bad, very bad practice of medicine to treat numbers. We should treat the entire patient. And transfusion medicine is no exception in that regard.

**Joe C**: I can't think of a better place to leave it, Joe. So, that is fantastic. I am so honored that you were willing to spend this time with me and with my audience. I just really, really appreciate your time. Thank you so much.

**Joe S**: Thank you very much indeed.

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**Joe C**: Hi, it's Joe with just a couple of quick closing thoughts. I want to thank, of course, Dr. Sweeney again for joining me today. I hope you walk away from this understanding that platelet transfusions need to be carefully evaluated, and they are not always simple!

I do want to mention again, this is a continuing education activity, so if you are a physician or a laboratorian, don't forget to visit wileyhealthlearning.com/transfusionnews, to get your hour of totally free continuing education credit. My thanks for that, as always, to Transfusion News, to Bio-Rad who brings you Transfusion News, and to Wiley Health Learning. My thanks also to Transfusion News assistant editor Dr. Daniela Hermelin from St. Louis University for her help with the continuing education materials.

So, we've got a few episodes coming before 2019 ends. I keep promising an interview with one of the inventors of pathogen reduction technology, Dr. Ray Goodrich, and that episode, I promise, will be coming shortly. You will also hear from Dr. Mindy Goldman from Canadian Blood Services about choices that she and CBS have made in Canada regarding donor and patient safety. That episode will actually be available in early December and it will be the last continuing education opportunity for 2019.

But until that day, 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.