BBGuy Essentials 052:
"Patient Blood Management; What are You Missing?" with Aryeh Shander
Released June 25, 2018

Joe Chaffin: Hi, everyone, and welcome back (or just "welcome" if this is your first time listening) to Blood Bank Guy Essentials, the podcast designed to help you learn the essentials of transfusion medicine. My name is Joe Chaffin, and I'm your host. Today's episode is a discussion on a part of Patient Blood Management that I believe is being ignored WAY too much. My guest is a true leader in the field: Dr. Aryeh Shander from Englewood Hospital and Medical Center in New Jersey. More on Dr. Shander and today's topic in just a second…

Before that, you should know that this episode is NOT eligible for continuing education credit. You can find other episodes where physicians and laboratorians can earn CE credits (for free!) at BBGuy.org/podcast (just look for episodes ending with the letters "CE"), or just visit wileyhealthlearning.com/TransfusionNews. The continuing education episodes are brought to you by TransfusionNews.com, and Transfusion News is brought to you by Bio-Rad (who has no editorial input for this podcast).

I don't think you can be involved in transfusion today and not have heard at least *something* about "Patient Blood Management (PBM)." Most everyone is aware that PBM programs involve things like improving physician blood ordering practices by "tightening up" approved thresholds for transfusing red cells and platelets, especially. Many have heard cute little phrases like, "Hey, why give 2 when 1 will do?" to describe current thoughts on transfusing one unit of red cells as a default instead of two units as a default. Some might also know that good PBM programs also emphasize reducing unnecessary blood draws and promote innovative methods of reducing blood loss during surgery. All that's great. What I'll bet many do NOT know, however, is the fact that you can do all of those things and you can still miss what may be, in my opinion, pretty close to the most important part of PBM: Detecting and managing pre-operative anemia before the patient is ever admitted! I call it the "forgotten pillar" of Patient Blood Management, and Dr. Aryeh Shander wants you to know just how important it is.

Dr. Aryeh Shander is a hugely important voice in PBM. He is an anesthesiologist, and is in fact the Emeritus Chair of the Department of Anesthesiology at Englewood Hospital and Medical Center. His publication list is longer than my arm (it's ridiculous!), and he lectures extensively and internationally on PBM topics. He's a giant in this field, and you should listen to him!

This episode is the second in my "friendly collaboration" with the Society for the Advancement of Blood Management (SABM.org), and I am very grateful to SABM for helping to arrange this interview. In fact, Dr. Shander is a past president of SABM. I highly recommend you check out their resources and web site.

And now, I'm really, really happy to present my interview with Dr. Aryeh Shander: Patient Blood Management: What are You Missing?

****

Joe: Aryeh, thank you so much for being with me on the podcast. Welcome!

Aryeh: Thank you, Joe.

Joe: It is just an incredible honor to have you here. I have read things that you have written, heard you speak on many occasions, and I am a big fan of your approach to Patient Blood Management and transfusion in general. And I wonder as we get started, Aryeh, if you wouldn't mind, before we get to the topic we're actually going to discuss today, I can't help myself but ask you, if you were in the position (and I'm guessing you don't get put in this position very often anymore, but put yourself maybe 10-15 years ago), when someone was saying to you, "Aryeh, this 'Patient Blood Management' thing? What the heck is that?" If you were explaining Patient Blood Management to someone who was just learning about it, and just trying to figure out what to do, how would you just thumbnail it, or give an overview of Patient Blood Management?

Aryeh: Well, thank you, Joe. First, I want to thank you for giving me the opportunity to be on this podcast. I think it's important for our listeners to understand all these issues that you just outlined. And to start with, I think that the answer to your question is not really that involved, because what has happened over the last century, in a way, has been that transfusion has taken this sort of a central role and has become a “default” treatment for all kinds of anemia in hospitalized patients. And I could actually spend a whole podcast just talking about transfusion, which is a therapeutic approach, without ever mentioning a disease that we're treating. This is how skewed things have become over the years.

The essence of Patient Blood Management is really going back to the medical model, identifying what is the disease. And clearly, we're talking about anemia, but keep in mind, anemia may have different etiologies. So if it's iron deficiency anemia, the therapy is going to be very different than if it's "inflammatory anemia" (or "anemia of chronic disease" as most people refer to it). In addition to that, the workup of a patient with these different anemias is again going to be very different. So, the issue is, we are looking at, from a Patient Blood Management point of view, we're looking at *disease management*: Putting the patient in the center, and therefore selecting the best therapeutic intervention for that particular underlying disease, under of the circumstances of the disease. Which means, as you know, when a disease first appears, it's very different than when it's been around for say, 15 years in the same individual, though the chronicity of the disease may also alter the therapy. So, essentially moving from just using a product (or as we call it, a "component") as a therapeutic agent, we're going back to the medical model, where we put the patient at the center, and look at what disease they have, make the right diagnosis, and then apply the correct therapy.

Joe: Just out of curiosity, Aryeh, is this approach and this feeling about considering the overall management of the patient and not defaulting necessarily for transfusion, is this

something that you've had your whole career, or is this something that developed over time for you?

Aryeh: No, I have to admit that I was swept with the same issue of transfusion medicine in early days, where we only thought of transfusion as the only intervention for patients who had anemia. We're also expanding this, in many ways, to look at coagulation abnormalities with the use of plasma, which is now today being critically looked at. And, of course, platelets, and there are now other derivatives of blood components such as Cryo. So, these are appropriate therapies, and what we need to do is, again, look to where the disease state is and what kind of defect it is that we need to treat. And, you know, sometimes blood components are the right thing. But in many cases, we're seeing that we could care for patients without issues without again resorting only to blood components.

Joe: So, I wanted to take the opportunity today to have a conversation with you about a topic that I know is very near and dear to your heart. I think when you look at Patient Blood Management, the part that we're going to look at today is really, for me (and this is my editorializing for a moment, Aryeh), when I consult with hospitals as I do from time to time about establishing or improving Patient Blood Management programs, they're very happy to talk about "making those doctors transfuse better" by knocking hemoglobin thresholds down to 7 and things like that. They're OK with talking about intraoperative methods, and sometimes OK with talking about decreasing the amount of blood drawn post-op. But one thing, for me (and I would love your feedback on this), one thing for me that I find a lot of resistance to is evaluating patients preoperatively for anemia with enough time to do something about it. Is my perspective skewed, Aryeh, or do you see that as well?

Aryeh: No. We see that. It is an issue in terms of interfering with what is currently the "production pressure." But, if you look at it from the point of view of the patient... Let's take a large joint replacement, let's say it's a hip or a knee joint replacement, or even a shoulder, it's an involved surgery. These patients go to surgery after years of having progressive debilitation, if you will, or pain over the years, until the surgeon feels that this is the time to do the joint replacement. Anemia may have been present for all those years in that patient, and essentially been ignored, because it could be easily treated with a transfusion. So, by saying to the surgeon three weeks or two weeks prior to surgery that, "Hey, you know this patient is anemic," and anemia has, as you already know, Joe, anemia does carry an increased risk of morbidity and mortality to surgical patients (and now we know it's not just the surgical patients but most likely ALL hospitalized patients), we need to step back and do the appropriate thing, which is make the right diagnosis, knowing what the anemia is caused by, and then making the appropriate therapy so that the patients risk, which is modifiable, which is anemia, can be addressed prior to surgery, improving outcomes. So, yes, there is resistance because of the production pressure, but there are ways of again educating our colleagues that this is the right thing to do. Now we would not take the patient if they had evolving cardiac symptoms. There is no reason to separate out

the hematologic versus the cardiologic system in terms of saying, "Well, we can ignore one and not the other," because both of them carry risks which potentially are modifiable.

Joe: And that brings me to my first question in delving into this. You and I both know, anemia, worldwide, certainly, is an incredibly common diagnosis. And that's certainly true here in the United States as well, perhaps not as much as in less developed countries, but it's obviously very common here. Do you feel that clinicians underestimate the impact of anemia in general?

Aryeh: Absolutely, and I think they have traditionally ignored it, because it's a silent disease until it becomes critical. So, as you mentioned, over two billion people around the globe have some level of anemia. So this is an epidemic, by all means. In addition to that, about half a billion of those are women in their childbearing years. And we do have data looking at both gross national product as well as contribution to economic efficiency, and we both know that, again, the data shows that anemic patients produce less in terms of the social responsibility. But in addition to that, they may also have, on a personal level, they may have difficulty in terms of their daily activities. But, otherwise, it's silent, because everybody probably feels a little tired, everybody feels a little foggy, everybody feels a little of this or that. So, again when you have a hemoglobin, say, of 10 or 11 g/dL, the physician is more apt to say, "You know what? It's not that bad. And since there are no acute symptoms, we're just going to ignore it."

Joe: And, just for clarity, just so everyone...obviously, people listening to this are going to be at varying levels of expertise...When we say "anemia," is there a standardized definition for that, Aryeh?

Aryeh: That's a great question, Joe. And we tend to look at hemoglobin, which is a concentration. In the United States, it's measured as grams per deciliter (g/dL). So it gives you an idea of the weight and the amount of volume. **And unfortunately, what we really need to look at is the number of active red cells in the circulation. We don't have a non-invasive (meaning a "simple") way of getting that number**. **So, we have to rely on what we call a "surrogate" measure, which is hemoglobin.** And the World Health Organization over 60 years ago looked at a distribution of hemoglobin concentration amongst multiple populations and came up with a gaussian distribution and arbitrarily cut off **males at 13 g or below, females at 12 g or below, and the pregnant woman at 11 g or below**. This is now being revisited, because there's a lot of disagreement, both in the hematologic literature but also amongst us, that the concentration probably should be the same, meaning 13 g/dL, but that the total blood volume and red cell volume may be different. But as I said, we don't measure it. So, I think we're going to see a change that for adults, it's going to end up at one number, which is 13.

Joe: OK. And that's actually a really interesting and important discussion, because one of the things that I have...I've had many discussions with people, when they're talking about

Patient Blood Management (and again, this is a slight sidebar, but I'd love to get your take on it), I'm long on record as stating that in "the old days," when people used to use a trigger of 10 g/dL of hemoglobin to transfuse people, that was silly. But now, I fear that the pendulum has swung the other way, and I hear people saying very strongly, "Any transfusion with a hemoglobin over 7 is obviously automatically inappropriate," and I think that's just as silly. So again, I know this is a sidebar, Aryeh, but I wonder if I could get your take on this? My position is, those are numbers and we're not treating numbers, we are treating patients, and I don't want to influence your answer (obviously I couldn't), but how do you feel about that argument?

Aryeh: Well, I feel exactly the same. I think hemoglobin is just one number, and to use hemoglobin as an indication for a transfusion clearly overlooks the fact that you may have different levels of hemoglobin with the same red cell mass, depending on your plasma volume, and that's what's really important for oxygen delivery. Everyone lives with this formula that's been created for oxygen delivery, which is the cardiac output times the carrying capacity of oxygen, where hemoglobin plays a major role, but that's a calculation, that is a formula. When you are actually doing the measurement, the response to the increase in the hemoglobin varies significantly when you're giving banked blood. So this becomes a real issue with people using a single number. You really have to take in the clinical aspects of the patient, clearly the surgical situation, and if you're looking at blood loss should be another consideration. But using a single number by itself may actually end up with an inappropriate therapy and an inappropriate amount of blood being given to the patient.

Joe: So, before we dive into, specifically, preoperative anemia screening and evaluation and treatment, I wonder if you could just briefly discuss for us, again, just speaking of anemia in general (you've mentioned some of this already), but do we have data and information on how specific organs or specific systems are impacted by anemia, again, just in general?

Aryeh: That's another very good question. So yes, we're generally talking about total body outcome when we're looking at population. But we do have data in terms of oxygen delivery and reserve rather than the impact of anemia. We know that each organ, including the heart and the brain, have significant amount of reserve. Now, when that reserve is consumed, what happens is we generally go into what we call "supply dependency" or "anaerobic metabolism," and we produce lactate. Now everybody worries about that, but in fact, if you look at it from a purist's point of view, anaerobic metabolism is just inefficient, meaning you don't have enough oxygen, so you're diverting the energy production through a different mechanism which is less efficient, and you produce lactate. Clearly, supply dependency of the worst kind, meaning when there is no reserve and is prolonged, may have some damage to the organ. And the organs that generally don't do well with supply dependency include the kidneys (which I would put as number one), but of course the heart and the brain are another. And there are probably some other endocrine organs that

also suffer. The lung, on the other hand, has varying responses depending on the amount of fluid the patient has on board.

So, again, to go back to this issue of the reserve of organs and the impact of anemia in organs, it takes quite a while before you actually get a significant impact because of two things. One is the compensatory mechanism of both the organ and the body to anemia in terms of trying to preserve oxygen delivery. But, today, we know that there is another element, which we were not aware of years ago, and that is the **genetic expression that occurs during reduction of hemoglobin and oxygen delivery**. And those of us who have what's called "**HIF-1**," it's "hypoxic inducing factor 1 and 2," what happens during the hypoxemia is there is a genetic change, immediate gene expression for the HIF, which again protects the organs from necrosis. They convert from necrosis to what's called "apoptosis," which is organized death, which preserves the organ, versus disorganized, chaotic death, which is necrosis, which does not preserve the organ. And those individuals who have the gene expression do very well with very, very low hemoglobin. I could tell you anecdotally that we've had patients with hemoglobins less than 2 g/dL that with aggressive treatment went home to normal life.

Joe: Wow! All right. I think we could talk a lot longer about about those points. There is a lot of interesting stuff in there, but I think we need to move along to our specific discussion today about preoperative anemia: Evaluation, screening, treatment, etc. I guess that the first and simplest question for you is: You talked about the fact that anemia is very common in the general population. Do we have any idea on whether or not anemia is more or less common in preoperative patients?

Aryeh: So, yes, the quick answer is "yes." We have data, and I will tell you that the data is now decades old. We've identified patients going for large joint replacement or arthroplasty now going on almost two decades ago, where we noticed that the range of anemia in that population can be **as low as 25% and as high as just over 40%**. So if you look at it, we can easily say that **one out of three patients has some level of anemia, which is a modifiable risk that needs to be attended to prior to elective surgery**. Now, the range of prevalence of anemia amongst the surgical population is different depending on the underlying surgical condition. So, for example, patients going for right hemicolectomy as an elective procedure for a rectal, or let's say for a colonic mass, can have anemia, iron deficiency anemia, the prevalence could be as high as 75%. So, again, keep in mind that there is some variability depending on the surgical procedure and the underlying medical condition. But, in addition to that, we also know that patients coming for cardiac surgery have a significant prevalence of anemia. And again, the production pressure has always been to get those patients into the operating room, where, in fact, we know today that there are many centers that delay surgery until modifiable risks including preoperative anemia are managed.

I think what the audience should also understand is that if you come in and you have anemia for your surgery, you're likelihood of being anemic on discharge and the degree of anemia is going to increase. So, on discharge, many patients are anemic. Cardiac surgery, there's some data suggesting up to 90% of patients leaving the hospital have some level of anemia, which again, is not always attended to as an individual medical condition.

Joe: Well, how do you respond to people, Aryeh, that say, "Well, OK, so I have a patient that has preop anemia. Well, *of course* they do! They're sick! They have whatever it is that they're having to be replaced. They're chronically ill because they need a new hip" (I'm just pulling something out of the top of my head). But how do you respond to people that just suggest that it's just due to whatever disease process is going on?

Aryeh: Well I'll divert to another disease situation, OK? How about diabetes? So, if you're a diabetic, and you're under stress, your blood sugar is going to be elevated, which again, is not a good thing for a diabetic patient. And we tend to say, "OK, hold off." The surgeon may call the internist or the endocrinologist or the diabetologist who is taking care of this patient to get things adjusted to reduce the risk, if it's modifiable. We do the same thing for cardiac surgery or cardiac conditions. If the patient now has some abnormality on their electrocardiogram, or they are symptomatic, we try to evaluate that and see what needs to be done prior to surgery, so that, again, we minimize the negative outcomes that can occur if the risk is not modified. So, I think the same principle as we mentioned earlier in the podcast of how we address all medical conditions really should apply to anemia. Now, the argument, and I think that's behind your question, is, well, many people say anemia is just an expression of the underlying disease and not a disease in itself. You know, all I could say to those individuals is that while you are arguing back and forth, I know what to do for this condition [inaudible] which requires a diagnosis and therapy just like any other disease. We could split hairs, but in the meantime, we've got a patient who needs care.

Joe: Absolutely. I could not agree more with that. That's an excellent point! Well, so let's talk about, then, if we have a patient who has pre-op anemia, whether it is diagnosed or not (and we'll talk more about when to screen and all that in just a moment), but what are the potential negative consequences of someone going into a surgery who is anemic? You already mentioned being discharged at a level of anemia, but are there other things that could happen, or are more likely to happen?

Aryeh: Very good question. So again, we have a couple of large data sets that we could look at. So the first data set that I'm going to refer to is large observational trials looking at outcomes in surgery of anemic patients. And, whether the data that's gotten from "NSQIP" [NOTE: National Surgical Quality Improvement Program. Risk calculator is available from the American College of Surgeons at https://riskcalculator/facs.org], the surgical risk tool that's out there that collects data on all surgical patients, or whether it's, again, European registries, **we all know that patients, if you just use anemia as your only measure in terms of risk, is an independent risk factor for increased morbidity**

and mortality. And that, by the way, extends not just to the adult population, but there is work being done and published from Boston showing that also in the pediatric population, it resonates with the same type of risk of morbidity and mortality.

The other data out there shows that **94% of transfusions are due to three areas that we know can be modified**. And the first one is anemia, the second one is blood loss, and the third is the "default" of treating patients with a transfusion who are hospitalized, whether they are surgical or not. I'm going to zero in on the first one showing that, again, one of the major risks of anemia coming into the hospital is the risk of allogeneic transfusion. Now that would be okay if an allogeneic transfusion only conferred benefit to the patient, was low cost, and did not cause any type of negative outcome. And we all know that that's not the case. So, again, large datasets show the risk associated with transfusion as well as the cost of transfusion alone without adding the cost of any complication. So is it avoidance of transfusion that we're looking for? The answer is, "No." What we're looking for is the appropriate management of the perioperative surgical patient who has a modifiable risk, this one being anemia.

Joe: I think that's very well put, and I think what you just said kind of answers the discussion, or at least the "accusation" (that's probably a better way to put it), of people that suggest that someone like Aryeh Shander is "anti-transfusion." I think that is an incorrect way to put it, when what you just said is that you're looking at it as not necessarily a "default," but potentially as part of a portfolio. Is that a better way to put it, Aryeh?

Aryeh: Yes.

Joe: OK, very simply, "Yes." [laughs] One thing before we leave that, you had mentioned that blood transfusion is not cheap, and one of my very favorite papers that you've ever been involved in (and I've read a lot of them), is something that you did, I believe it was in Blood in 2008, which was an analysis of how much blood transfusion really costs. Do I have that reference right, Aryeh?

Aryeh: Yes, it was actually in Transfusion, and it was the activity-based costing of red cell transfusions [NOTE: Shander A et al. Activity-based costs of blood transfusions in surgical patients at four hospitals. Transfusion 2010;50:753-765].

Joe: Got it. And just for those who haven't read that (and I will I will make sure I have that reference on the show page for everyone to see it), I mean, cost is part of this discussion, it's not the most major part, obviously, but I wonder if you could thumbnail what you described in that paper?

Aryeh: Actually, I'm going to tell you that that paper is a result of research of over about 10 years. What we did first, is we got together, and I'm not sure, I think it was around 20 both U.S. and European transfusion experts around the table. And the task that they were given

was to actually list all of the steps that are required an individual to attend to when we collect blood from vein and then transfuse a patient on the other vein, if you will. So, it was "vein to vein." And they had to agree that those steps were only steps that were taken for that activity, and they came up with a little over 90 steps. What we did was we published that, and looked for peer review comments, including rebuttal, which none came. And we waited the adequate time for response, and we got no letters to the editor. No one ever basically complained about it. So, we went ahead and used those 90 steps, clocked each one of them, and looked at four hospitals, two in the United States, two in Europe; two who were analog, and two were computerized blood bank; and two were community, two were academic centers. So, we felt we covered most of what we needed and then measured those steps in terms of what it costs to transfuse a unit of blood. So, the true title is the "cost of transfusion," not the "cost of blood." And what we did is use the cost of blood, meaning the hospitals buy blood from blood centers most of the time, unless they produce their own. And what we came up with sort of a rule of thumb is that **the cost of transfusing a unit of blood is anywhere from three and a half to four and a half times the cost of procuring that unit of blood**.

Joe: Wow. That's surprising to people, I'm sure, and I still run across people that say, "Isn't transfusion free?" I'm sure you do as well. [laughs]

Aryeh: In some countries, that's the way it is. The cost is absorbed by the health ministry, and not by the hospitals that transfuse. But, as you know, there's no free lunch when it comes to...SOMEONE'S paying!

Joe: Someone's paying, exactly! OK. So, thank you for taking that little sidebar with me, Aryeh. I want to get back to looking at preoperative surgery patients to screen them for preoperative anemia. So, let's just bottom line this: In your opinion, what is the optimum time to screen a patient prior to surgery for preoperative anemia? And how do you do so?

Aryeh: So that's another great question. So, the optimum time has been published over and over again, and it's anywhere from 28 to 30 days. Now why "28" is because, I guess there's some payment issues, but we're doing basically the workup as an outpatient, and can use codes for anemia with the proper diagnosis if revenue (or "reimbursement" as people call it) is an issue. But 30 days allows you for a few things. Number one, it allows you for even a slow laboratory to get the results done, so that you can make the right assessment in terms of the cause of the anemia. If the anemia now points to maybe another underlying disease, which I'll explain in a minute, then it also allows you to address that, and also gives you the opportunity to try and treat the patient for their anemia. Now when I say "opportunity," it's because there are some patients who may not respond to the therapy, but at least they've gotten the opportunity to be treated appropriately.

Now, there are a couple of scenarios. So, if, for example, this is a, let's say, a 63-year-old male going for a left knee replacement. And on the diagnostic panel for CBC, we suspect that the patient has iron deficiency. And we then do the iron panel, and lo and behold, we've diagnosed iron deficiency. That individual with iron deficiency is very different from a 22-year-old woman who has iron-deficiency anemia. This gentleman needs to have a G.I. workup, whereas the young woman most likely either has heavy menstrual bleeding (HMB), or again is just iron-deficient from blood loss, from menstrual blood loss. So, you see that it not only helps in terms of the anemia diagnosis, but we're also now picking up some other risks the patient may have and addressing them appropriately. There are other scenarios like that. But the algorithms that been published clearly address all of these side alleys.

Joe: Right and you have published that in modified form in several, at least two different papers that I've seen, and I will make sure that again those references are on the show page. One in particular has a very, very nice flowchart, essentially. I believe that's the one that you and Tim Goodnough published not too long ago that has a very nice flow chart.

Aryeh: Well, there's one that Tim published for orthopedic patients. Ours, I think, was in 2005 where we had internists involved, because we wanted the internal medicine community to recognize that they are going to be instrumental in treating these patients.

Just another thing, Joe, and that is, and you actually framed it well: "Ideally." Ideally, we're looking at a month, but we'll take ANY amount of time.

Joe: That makes sense. I mean, I guess the obvious question is, is there a point that's just too darn LITTLE time. I mean, obviously, the day before would be too darn little but...

Aryeh: I would say the minute the knife falls on the skin!

Joe: [Laughs] Okay! That's fair enough. I think what that brings me to, and the question that that raises in my mind is, when facilities are establishing this part of their Patient Blood Management program, it seems clear that it's important not just to get the data, but who's evaluating the data, and what you're doing with that data. Do you see that as kind of a "hole" in this sometimes?

Aryeh: I think it has to be sort of a stakeholder, a concert team approach. So, yes, we need to first of all be able to identify patients going for elective surgery. So, that could be a relationship between the surgeons and the booking office with whoever is going to be running the preoperative clinic, which is generally anesthesiologists. I usually say to my audience that there are only two diseases in anesthesiology: Malignant hyperthermia and pseudocholinesterase deficiency. We could easily adopt anemia for the protocols, as our disease to manage. Learning, it just increases your repertoire, and there are now tests that are available to where you don't have to interpret them an iron panel which sometimes can

be confusing. There is now something called "reticulocyte hemoglobin content," which is a single test that comes with your reticulocytes, and if the number is below 30 (or some places 28), the likelihood then is close to 100% of these patients are going to be iron deficient. So, you've made the diagnosis of iron deficiency without doing a complex iron panel. The interpretation, you know, there are so many references and resources out there on how to construct the pathway, the clinical pathway for anemia detection, diagnosis, and management. I'm not going to go into detail, but I think that it has to be a commitment first, and the commitment has to be from above as well as from below. And once you've committed, your own institutional culture will dictate who's going to be involved, and who's going to be in charge, and who's going to be the one who makes the diagnosis, and how treatment then is applied either through an infusion center or through a private doctor's office. However it is that gets the job done.

Joe: And that brings me to a "priority" question, Aryeh. And I think I know what your answer is going to be to this, but let's just put it out there in as simple a term as possible. Here's my question: What is more important: Keeping the surgery date intact, or fixing the anemia?

Aryeh: So my answer to that is my department's motto: "There is never the wrong time to do the right thing."

Joe: Nice, nice! I don't think anything more needs to be said. I completely agree with you. OK, so, Aryeh, we've talked a little bit about how we screen and when we screen (and again, for those listening, please be sure to check the show page for this episode. You can find it at BBGuy.org/podcast, and just look for this episode [NOTE: Or go directly to BBGuy.org/052]. I will have a ton of references there for you), but Aryeh, I wonder if you would take us through just a little bit about some of the facets that we need to be considering when we're talking about the evaluation (especially) and then the correction of preoperative anemia?

Aryeh: So, I think that the first thing, clearly, is to look at which surgical procedures should all have an evaluation for anemia. And, I would tell you that **any surgical procedure that has either a type and cross or a type and screen clearly has to have an anemia evaluation, with the idea that if it's elective surgery, something's going to need to be done**. So, that's sort of starting way at the starting line. Then, what we need to do is to address where the patient goes to get their preadmission testing, and that should include either a hemoglobin level or a CBC. Most places will just do a CBC. And, once you look at the CBC, if the patient has a low hemoglobin, lower than normal, then the investigation has to be made. Now, you could do a reticulocyte hemoglobin content, and if that's normal, the likelihood is that you're dealing with either a nutritional anemia (which would be maybe megaloblastic, such as B12 and folate deficiency), or you'd be looking at anemia of inflammation. Anemia of inflammation has two issues. One, of course, is that erythropoietin is blunted. And the other is that iron metabolism is also affected. Those patients who have

anemia of chronic disease or inflammatory anemia, we generally look at a creatinine, to make sure that they're not evolving into renal failure, which is the most common cause of this particular underlying disease. But arthritis and other and sundry diseases will give you inflammatory anemia. But, renal failure is a major risk, as you know, for patients going into surgery, especially if it's in the early stages, you want to do things to protect the patient.

So, once you've decided, let's say, that we have anemia that does not fit iron deficiency anemia, and we really don't think that this is anemia of chronic disease, but we do think that this is megaloblastic anemia, you could look at the size of the red cells and the RDW (which is, again, the range of the different sizes of red cells), and if they're all large, you could then... Some places will just treat with iron and folate. Some places will do level to confirm. Because it's so inexpensive and easy to treat, some places don't want to expend any energy or money on doing that test. So, that takes care of the iron and the other nutritional anemia.

For anemia of chronic disease or inflammatory anemia, the only therapy that we have is exogenous erythropoietin. And there are label recommendations for erythropoietin in orthopedic patients, and, of course, if you're dealing with a non-surgical patient, since you're treating the patient outside the hospital, outside surgery, you may want to use, again, the current anemia diagnostic codes and therapy course to treat the patient. But, erythropoietin will become the mainstay of that therapy. Now, what happens when you give patients erythropoietin is that they produce red cells and release them from the bone marrow very early. Iron gets incorporated into the red cells late in the production. So, what happens is that if you don't have iron available for these patients, they will be microcytic. Again, they're going to be making ineffective red cells, to be as blunt as possible. So, we always, as routine, always add small amounts of intravenous iron to patients who are receiving erythropoetin, or every other day oral iron if the patient is an outpatient for three weeks prior to surgery while they're getting the therapy.

Joe: Well, let me just address the elephant in the room for just a second with the erythropoietic stimulating agents. There are people that are concerned about the use of those due to the, primarily, concern about thromboembolism.

Aryeh: So, let me just say this: Clearly, increase in thrombosis is part of the side effects of erythropoietin, exogenous erythropoietin. Now, let's compare that with the risk of thrombosis from a single allogeneic red cell transfusion: Not much different. In addition, by the way, iron deficiency has been associated with "sticky" red cells and possibly "sticky" platelets, so again, another risk factor. What we do know is that from prospective randomized control trials done in critically ill patients, that when you use erythropoietin, what happens is that your risk of thrombosis increases from 3%, which is the general population, to 6%. And if you use prophylaxis, you go back down to 3%. So, if you're concerned, and most of these patients are going to be on prophylaxis anyway, but if there is a concern, just treat that concern. There are clearly other concerns in terms of cardiac,

and those, I think, have been misplaced and mostly due to very poor structure of the trials that were done. In one of them, which actually was used to again denounce the use of erythropoietin in cancer patients, the primary author in that particular article had written an editorial where he didn't recount the data that they had, but what he did was say that he himself believes that that's not a concern. So, I think we're seeing a lot of change. You know, it's been over 14 years since the restriction on erythropoietin was placed because of an aggressive marketing issue, and the FDA as well as CMS responded because of the cost of the drug and the possible risks associated with it. But, I think we're starting to see more rational loosening of all those, because the data clearly supports the fact that on-label use of erythropoietin, the benefit is great, and the risk is very low.

Joe: Awesome. Well, you mentioned one other form of therapy that I'm guessing that some people out there may have given them a momentary pause, and you mentioned intravenous iron. And those of us that have been around for a while, I think, recall that there have been some concerns in the past with IV iron (in particular with certain formulations) and severe allergic reactions. I wonder if you would address that and what we know about that now?

Aryeh: So that's another very good question, and we do have another one of those consensus statements about the myths about use of iron [NOTE: See SABM.org for this resource]. So let me categorically say that **iron deficiency in the pre-surgical patient, oral iron really has no place**.

Joe: Wow, that's a strong statement, Aryeh!

Aryeh: I'm making a strong statement, and let me explain to you why. We now know that when you actually prescribe oral iron on a daily basis, what happens is that when you ingest oral iron, the hormone that controls iron absorption and iron transport is called "hepcidin," and it is an acute-phase reactant, meaning that if you're inflamed, what happens is that hepcidin levels rise and block the entrance of iron through the gut. And interestingly, without any inflammation, if you give oral iron, hepcidin rises and blocks the absorption of iron. Now, you wanted to treat the patient for iron deficiency prior to surgery. You're not going to get the result you need.

Now if you give intravenous iron, hepcidin also rises, but not to the same level, and does not interfere in the transport of iron or absorption of iron. And that's why I say, categorically, oral iron should not be given to patients who have iron deficiency who are going for surgery, and iron deficiency anemia going to surgery, or even iron deficiency (which is a whole other area we haven't addressed).

So, going back to that, there are different preparations available. The one preparation that has had the most reaction is the high molecular weight iron dextran, and many hospitals have taken that off formulary. As far as reaction from IV iron, there are some reactions in

terms of joint pain, back pain, etc. Anaphylaxis is rare. Let's put it this way: **If you're concerned about anaphylaxis, the class of drugs you want to be concerned with is not intravenous iron, but antibiotics**. So, let's put the concern where it really should be. But it's not to minimize the fact that these patients, there is a requirement for having test dose in some of the preparations, and there's also a requirement for monitoring of these patients. So we take all that seriously. But most reactions to IV iron are fleeting and not anaphylactic.

Joe: Have we developed any research, any data on what you just said: Intravenous iron, and/or, if you'd like to discuss the use of erythropoiesis stimulating agents as well in terms of the data. Again, we don't have time for you to go into enormous detail, but do we have information that suggests that those strategies work well?

Aryeh: Yes, and I think that we just had one of those with Manuel Munoz accepted for publication in Anesthesia. It goes really through the whole myths of IV iron in the perioperative period.

Joe: Well, Aryeh, before I let you go, I wonder if I could just toss a couple of things at you that people have thrown out as objections to everything that we just (well out necessarily everything) we've just talked about, but just the overall process of preoperative anemia screening in general. And I would love to get your take on these. I have heard these personally, so I'm speaking from personal experience objections that people have had. The first one that I hear quite often is, people say, "Well, Joe, we're putting in our Patient Blood Management program, we're addressing intraop stuff, we're addressing post-op conservation, and especially appropriate transfusions. So, do we really need to worry about correcting pre-op anemia? Isn't this just overkill?" How do you respond to that?

Aryeh: So, if you're looking at appropriate transfusions as one of your goals, I'm going to replace it with a different question for you: **The real question is not whether a transfusion was appropriate. The real question is whether a transfusion was AVOIDABLE**. If you're ignoring the underlying condition for which you're going to be transfusing, you will never get to the appropriateness of the care of the patient. You will justify the appropriateness based upon hemoglobin level. But really, the culprit is going to be the fact that anemia was not managed. So, not overkill, nor is it a waste of time. It is clearly...if one of your goals is to make sure that your care is appropriate, and as I mentioned, it's not the appropriateness of the transfusion, it's the avoidance. Would you want to avoid chemotherapy, or would you say chemotherapy is appropriate because you ignored the cancer?

Joe: [Laughs] Well put. Absolutely. OK. One more, Aryeh, if you can hang with me for one more minute. What I hear a lot from smaller facilities that are considering how best to do this is what I would call a "myth," and I think you would as well, but people that say that specifically establishing a preop anemia clinic is not cost-efficient. It costs too much, it

delays things too much. And again, you've kind of already answered that, but but just specifically for people that hear those objections, how would you respond to that quickly?

Aryeh: Well, you know, again, I think that central to Patient Blood Management is the patient and their disease they come in with, and trying to again modify the risk. So, I think a stand-alone anemia clinic is not something that I want people to walk away from this podcast thinking that that's what we're promoting. I think what we're promoting is the full gamut of preoperative preparation of the patient by looking at all modifiable risks, and again, manage them appropriately. Now if you do that, yes, there is going to be an investment. There's no question. But that part of medicine where investments are needed is always, again, countered by the return on investment. And the return on investment today is pretty broad, because, number one, you want to reduce disease. That's what we're here for. And reduce the burden of disease, that's the other reason we're here for. But now, we also have this whole issue of satisfaction, and some of us think probably satisfaction in terms of hotel management. But, I think the satisfaction is that we really attended to all of the patient's needs, not just one, which is the surgery itself. I think that if we can express that to the patient that we're doing that, that's another added return on investment. It may not be monetary but could be translated into money at some point as well.

Joe: Aryeh, this has been an excellent experience for me! It's such an honor that you were willing to talk to me and that you were willing to share your incredible expertise. Thank you so very much. I know my listeners will get great benefit from this.

Aryeh: Well, thank you, Joe.

****

Joe: I can't help but feel like I've just been in the presence of greatness! In my experience, finding anesthesiologists who are as passionate about making transfusion part of an overall strategy rather than a default method to correct anemia is uncommon. Aryeh's expertise and opinions were fantastic for me to hear, and I know you learned something, too. I thank Dr. Shander for joining me, I thank the Society for the Advancement of Blood Management (especially Dr. Carolyn Burns) for helping arrange this interview, and I thank each and every one of you for listening. I never take it for granted, and I deeply appreciate your support of this podcast over the past two years. Please take a minute to rate the podcast at iTunes so more people can learn about the essentials.

So, the next episode WILL be eligible for free continuing education. I had a terrific discussion with Dr. Chris Tormey from Yale on what we've learned about why people make those darn red blood cell antibodies that torment blood bankers so much (to say nothing of our patients!). Chris has published multiple articles about this very issue, and I think you will find his viewpoints interesting (and maybe a little bit surprising!). That episode is coming very soon. I'm excited for you to hear it!

But until then, as always, I hope that you smile, and have fun, and above all, never, EVER stop learning! See you next time on the podcast!