

**BBGuy Essentials 071:
New Therapeutic Apheresis Guidelines with Nancy Dunbar
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Nancy: Hi! This is Nancy Dunbar, and this is Blood Bank Guy Essentials Podcast.

Joe: Hey everyone, welcome back to Blood Bank Guy Essentials, the podcast that's made to help you learn the essentials of transfusion medicine. My name is Joe Chaffin, and I am your host. Today's episode is a discussion with one of the co-editors of the "hot off the press" Guidelines for the use of Therapeutic Apheresis, and her name is Dr. Nancy Dunbar.

But first, you should know that this is NOT a continuing education episode. You can find other episodes where physicians and laboratorians can get those free continuing education credits at BBGuy.org/podcast. I have over a dozen episodes there and all of them end with the letters "CE." It's not a really hard code to break, right? You can also find those continuing education episodes at wileyhealthlearning.com/transfusionnews. The continuing education episodes at Wiley Health Learning are brought to you by transfusionnews.com and transfusion news is brought to you by Bio-Rad, who has no editorial input into this podcast.

I've recorded several episodes of this podcast discussing therapeutic apheresis and all of those have been with the great Dr. Jeff Winters from Mayo Clinic (and you can check those out in episodes [025](#), [026](#), and [049](#), as a matter of fact). And in those interviews, Jeff and I have talked about the "Guidelines on the use of Therapeutic Apheresis in Clinical Practice." And that's a document that's pretty much the standard on how best to use procedures like therapeutic plasma exchange, therapeutic cytapheeresis, red cell exchange transfusion, and even things like extracorporeal photopheresis (that kind of make your mind explode when you say them even!). It's a hugely important document and it's put out by the American Society for Apheresis, or "ASFA," and a brand new version just became available in the June 2019 edition of the Journal of Clinical Apheresis.

Now if you go to the show page for this episode, which is BBGuy.org/071, I'll give you the link to directly go to where that document is available. But I wanted to have one of the co-editors of this new version, the 2019 version of the guidelines for this episode to just discuss what you should know about and I'm really lucky to be able to speak once again to the marvelously talented Dr. Nancy Dunbar from Dartmouth. So Nancy and her co-editor, Dr. Anand Padmanabhan (from Versiti and the Medical College of Wisconsin) and their entire team of additional experts have put together a tremendous document that you really need to have as part of your arsenal of references.

And to that end, I want to answer the question that I know beyond a shadow of a doubt some of you are asking right now, which is, "So what Joe? I don't do apheresis in my facility." Well you know what? Maybe you don't. But chances are SOMEONE is doing it and you might have to get involved if, for example, just as an example, someone has a diagnosis of Thrombotic Thrombocytopenic Purpura,

TTP, and they're using a TON of your plasma resources. Or if someone has another disease that the guidelines say you shouldn't use plasma and yet they're trying to use plasma as a replacement fluid. So it's practical, it's helpful from that perspective. But further, if you're a learner, especially in pathology or transfusion medicine, well you know you better know something about therapeutic apheresis because you are going to get tested on it.

You've met Nancy Dunbar on this podcast before, but in case you're new or haven't heard one of her previous episodes, let me introduce her again. Nancy is medical director of the blood bank at Dartmouth-Hitchcock Medical Center in New Hampshire. She's an associate professor of pathology and lab medicine at Dartmouth and she's the associate program director for both the pathology residency program and the transfusion medicine fellowship. Nancy has done extensive research, has published over 50 articles and reviews in transfusion medicine journals, and she's authored several chapters in standard textbooks including the "AABB Technical Manual."

Now finally I have to mention the American Society for Apheresis, or "ASFA," as we call it. This is a terrific organization (and no one is paying me to say that!), and their sole purpose is to advance the practice of apheresis medicine. You can find more about them at apheresis.org (I love that address), and you can also find access to the guidelines that Nancy and I are going to discuss. And you can get those if you're either a member of ASFA, or if your institution subscribes to the Journal of Clinical Apheresis.

So no more waiting! Here is my interview with Dr. Nancy Dunbar on the brand-new ASFA Guidelines for the use of Therapeutic Apheresis.

Joe: Nancy, this is getting to be a habit! Welcome back to the Blood Bank Guy Essentials Podcast.

Nancy: Thank you so much, glad to be here.

Joe: This is a great opportunity for us, I think. I've already mentioned that Nancy has been heavily involved, and I'll let her tell you her role in just a second, in the development of the 2019 (or "8th Special Issue," as it's called), the "American Society for Apheresis Guidelines on the Use of Therapeutic Apheresis in Clinical Practice." And Nancy, I wonder if as we get started on this, if we can just set the stage a little bit and talk a little bit about first, what IS the American Society for Apheresis?

Nancy: Yeah, that's an easy question. So it's a society of professionals that are actively involved in apheresis medicine. So that could be transfusion medicine positions like myself that do clinical work in an apheresis clinic. It can also include other subspecialties that provide apheresis care. And that typically could be nephrologists, hematologists, those are the two big ones I think of but quite a number of subspecialties here in the United States do involve themselves in

clinical apheresis. So it's a society for those folks that are interested in that particular treatment modality.

- Joe:** So you mentioned a couple of phrases there. Let's start with talking a little bit about therapeutic apheresis, and can you tell me a little bit about what role therapeutic apheresis plays in your particular daily practice there at Dartmouth?
- Nancy:** Yeah, so here at Dartmouth, our apheresis program is overseen by the pathology department, so the transfusion medicine physicians do rotate clinical service duties in the apheresis clinic. So a pretty large part of my on-service time is spent providing direct care in apheresis clinic, supervising residents that are learning about apheresis in their routine transfusion medicine rotation, and doing clinical consultation for patients in the hospital who may need apheresis treatment.
- Joe:** And has that always been the case for you Nancy? Have you always practiced in places where the transfusion medicine department or pathology department is responsible for TA?
- Nancy:** Yeah, actually no. I trained in a program where apheresis was ... both actually my fellowship and my residency, I didn't actually have any direct exposure to apheresis, amazingly, and yet I still went into transfusion medicine. In my residency program, it was a centralized service that would come with mobile apheresis and treat the patients. And the stem cell collections were done by the hematology service, so I really didn't get any exposure to apheresis other than theoretical exposure as resident. And the same was actually true in fellowship. There was a mobile apheresis service that covered the whole city where I trained. I had the opportunity to spend a week with those physicians, kind of learning about what they do, but I didn't really do any direct clinical care in apheresis until I landed in my first position here at Dartmouth. And it was a pretty big learning curve, you know, to just basically show up and be a "real doctor" and have real patients and real clinical notes I had to write every day and learn all about that. So it's not the same at every institution.
- Joe:** I think that brings us to really maybe one of the most important questions I'm going to ask you today, which is simply this: As you mentioned (and my experience was similar to yours, by the way, when I was in training, I had essentially no exposure to therapeutic apheresis, I've just been exposed to it in different places that I've practiced over the years), but what if someone works in a facility, either as a pathologist or even as a clinician that doesn't do therapeutic apheresis, or a lot of laboratorians listen to this, what if you work in a place where TA is something that's done by someone else? Is there any value at all for any of these folks to have knowledge about therapeutic apheresis?
- Nancy:** Well certainly if you're a trainee in pathology, you are expected to understand clinical apheresis. It's definitely going to be on your boards, it's a big portion of that. So those people are very motivated, I think, to learn about apheresis, even if they don't actually have the opportunity to directly engage in it. And I would say if you're working in a blood bank, oftentimes you're supporting apheresis patients,

and it's useful to understand the "why" and the "how that works," because you may be thawing, like in the case of TTP you made, you may be thawing 15 units of plasma every day for a patient, and it's so different from normal transfusion practice that I think it's useful to understand like, "Who are these patients, and what are they doing with all this plasma, and where's it going and why do they need so much?" And having to manage that...It affects blood banks in other ways as well, you know, doing red cell exchange in sickle cell patients, or having to get units ready for that. It does really impact the whole field of transfusion medicine, and I think that's why in many places transfusion medicine does oversee the apheresis care.

Joe: Exactly, but as we've said, in a lot of places they don't, so I think that for me personally, Nancy, and I'll just share my story a little bit, as I mentioned, I didn't have any exposure to this in training and in the early years of clinical practice, I didn't have a lot of exposure either. And then I found myself at Cedars-Sinai a number of years ago thrown into the fire, if you will, where in a scenario where I was part of a great team there overseeing residents and fellows that were doing heavy-duty therapeutic apheresis, that actually brings me to my personal experience with the American Society for Apheresis Special Issue, which is, as we've said, the guidelines for how therapeutic apheresis is used in clinical practice. So for me, it was invaluable to have these fact sheets, these guidelines. So before we talk about the history, which I'm really fascinated to hear you discuss, let's talk a little bit about what these guidelines are meant to accomplish, and what the fact sheets are meant to do. How are they useful as a tool to learners and to people in daily practice?

Nancy: Yeah, I mean I use them nearly every day. They are actually in PDF version on my phone so when I take calls, I can refer to them. I mean it's a very distinct description of each disease that may have therapeutic apheresis as a treatment modality and it's kind of a quick reference if you ... in my context, I'm often getting consultation for apheresis and maybe in situations that I have very little clinical experience. You know, we treat a diverse number of diseases in all different subspecialty areas like nephrology and rheumatology and hematology, so getting calls from specialists all over the hospital who may or may not be familiar with the up-to-date evidence about therapeutic apheresis to say whatever particular disease indication.

And so we're trying to very quickly make a determination, "Is there a role for apheresis or not?" And the guidelines are really helpful to very quickly hone right in on that disease. Is this a category I thing, which is straightforward, absolutely first-line therapy? Or are we more in a category III, where it's not really clear if this is going to help the patient? And so it's a quick resource, it definitely helps you use evidence-based guidelines to decide whether or not to do apheresis in a particular patient.

And so they're on my phone, they're in a binder in the apheresis clinic. We use them every day, and in fact when residents rotate through, that's the first question when they come to me with a consult: "What's the ASFA category and

recommendation? Do you know where does this fall in that spectrum of should we treat, should we not treat using apheresis?"

- Joe:** So Nancy, there is a great reason that we're talking about this right now. We're having this conversation in early June and this month, in fact by the time this podcast is released, the brand new, as I mentioned, 8th edition of the "Special Issue," the ASFA "Guidelines on the Use of Therapeutic Apheresis in Clinical Practice," should be available in the Journal of Clinical Apheresis. Everyone that will be linked on the show page, people that are members of the American Society for Apheresis will get printed copies of that, I believe. And everyone else, well actually I don't know, Nancy, I assume that people can get it with their institutional access to that journal, is that correct?
- Nancy:** Yeah, absolutely. So it'll be on PubMed as previous editions have been. And if your institution subscribes to Journal of Clinical Apheresis, you know, in their multitude of journals that they can access, then that should be available to download in PDF form. But yeah, if you're a member of ASFA, you actually get the print copy and there is something nice about having that on your desk that you can just grab and flip through and stuff to quickly find the information that you need.
- Joe:** Oh Nancy, we're betraying our age. I'm way older than you but we're betraying our age. We like that printed stuff.
- Nancy:** I have the PDF on my phone and I use it, but if I have the choice, the book is much faster to quickly get to the page I want. It's a good document, so I can't wait to see it in print because we have been working the committee on this for the past three years. It's really been just an enormous amount of work and it's almost like a baby. I just can't wait to see it!
- Joe:** Well, let's talk about that for a second, Nancy. I totally get that, with you guys have been working really, really hard on this. So why don't you tell us a little bit about what your role has been and the committee's role in putting together the new guidelines.
- Nancy:** Yeah, so I have the great fortune to be selected to co-edit this edition with Anand Padmanabhan, who I worked with on that previous edition in 2016, I was a committee member. And so Anand and I were selected by the ASFA board to sort of lead the charge for the 2019 issue. We did get some help from Yossi Schwartz, who stayed on as a guest editor to sort of mentor us in the process and help us in this enormous work that starts three years in advance by assembling the committee. And it's a committee that people actually have to apply for, and we have to try to put together the best committee to be diverse and in the types of practice and also geographically diverse.
- And then once the committee's assembled, really divide up all of these fact sheets, of which there are more than 80, and review the latest evidence. For for some diseases, there are many, many publications in the intervening time period that you have to look at and really do a critical assessment to see if the role of

apheresis has changed in that disease, or if there are other new treatment modalities that need to be considered. And then the actual writing part, the actual shepherding a document written by 13 different people and trying to make it cohesive at the end and catch all the little typos...And I read this document so many times, I can't even remember which fact sheets I wrote personally and which were written by others. Honestly, I've read it so many times on so many airplanes. It's a great thing to do when you're flying across the country. So yeah, it's been a tremendous amount of work for all of us involved and it's really exciting to see this coming to fruition.

Joe: I can't wait to see it myself, and congratulations to you and the whole team for your really, really hard work. Nancy I think before we talk about the "baby," as you put it, and what you guys did with the 2019 edition, let's talk a little bit about the history. And I wonder if you could just take us on maybe a little bit of a whirlwind tour through what's happened with these guidelines over the years? When did we start and what kind of things have been the highlights of the issues over the years?

Nancy: Yeah, sure. So this started back in the 1980's, in fact, in 1986 was the first special issue. And those folks got together to really try to consolidate what was going on in apheresis. When was it acceptable therapy? Was there data to support whether you should use apheresis or not, whether it's beneficial compared to conventional therapy? So they produced the first guidelines in 86, it was very different than the fact sheet format you see today. It was really more like a review article that really just in purely text format kind of described the treatments, the indications for apheresis, and kind of whether it helped or not. It was really the beginning of the guidelines as we know them today.

And initially, they were only updating the guidelines every seven years. It was probably a ton of work to start, but the next one came around in 93, and then that's when we first started to see the division of the indications by related disorders in terms of maybe subspecialties. So that's when you start to see like instead of one document, there were actually five separate documents, lumping the indications together into indications in the realm of hematology and oncology or neurology or renal. That was dividing up a little bit from just one long review paper.

And in 1993 was really the first time they applied "category definitions," which were very, if you practiced apheresis, you really think in terms of categories. So category I, no question that you're going to do apheresis. It's standard, it's acceptable, it's the primary therapy. That's kind of something like TTP where it's life-saving, and there would never be a question about withholding apheresis. And then it goes all the way down to category IV, where it's really been proven to not help and actually potentially even harm patients. And that's where you would definitely say "No, we cannot do apheresis here." Like apheresis for schizophrenia, for example. It doesn't help and you wouldn't want to expose patients to the risk.

And then in the middle are the "II's" and the "III's." II is sort of second-line therapy, if what the first-line therapy you would normally do fails, then you would consider

apheresis. And then category III, where most of the indications actually are right now, is that we just don't really know. There's not enough evidence really to establish efficacy. More work is needed. That is where you really have to do some clinical decision-making based on what you understand to be the pathogenesis of what's going on in the disease and whether you can postulate some plausible reason that apheresis might help remove some harmful factor or replace something that is missing.

So yeah, so in 1993 they first sort of broke it down into those four category descriptions. And they weren't exactly the same as they are today in terms of the specific wording, but they were beginning to go in that direction. Seven years later, they updated it again but really not anything earth-shattering with that update. Just a few minor changes. But in 2007, that's when we first started to see the fact sheet format. And I think that was really a tremendous improvement on the previous guidelines because it allowed you, and again this is where we show our age, it allowed you to make a photocopy and carry said photocopy...

Joe: Wait, what's that? A "photocopy?" [laughs]

Nancy: [Patiently] It's like a scanned document but it's an actual paper [laughs].

Joe: Oh okay, now I've got it...

Nancy: It lets you take that photocopy, and actually put it in the patient's chart, so the other teams that may be caring for the patient who may not be as familiar with what therapeutic apheresis is have some access to something that's really easily digestible, that you can take a quick look at and understand what it is that we're doing and why are we doing it? So I think the fact sheet has been something that I have personally really liked. Even in this age of PDF's, I still think it's very important to have it be just one page, because I think that we in medicine, the amount of knowledge we need to know is overwhelming and if you can really just distill something down into something that's really just one page, then there's references at the end if they want to learn more about it.

So that's 2007 is where we first started to see the fact sheets sort of look like what we're used to seeing today. Very structured and organized and you know what section to find what information you need. In 2007 they also started to really look more objectively at the quality of the evidence supporting apheresis. So this is where you differentiate things like well-designed, randomized control trials from case series and case reports, you know the strength of those other ones really is different and needs to be weighted differentially. So in 2007 they had the strength of evidence that eventually resolved into the GRADE system, which is used today and was adopted in 2010.

Yeah, it's been a little bit of a whirlwind. Around 2007 is when they started to update it every three years and I think that is just because so many publications on apheresis are coming out and if you only do it every seven years, it's a

tremendous amount of literature to review. So switching to every three years kind of keeps it fresher, more up to date and also probably decreases the workload.

So yeah since 2010 it's been every three years. A couple minor changes to the category definitions and the grading system has continued, the fact sheet format has continued. And really it's just been since 2010 adding fact sheets, eliminating fact sheets, reorganizing, renaming things, kind of seeing more I think cosmetic tweaks, really to the foundation, which is the fact sheet format.

Joe: I wanted to just follow up with that, Nancy, before we get to what you guys did in the 2019 special issue, and the guidelines. There are a couple things that jumped out to me as you were talking about that and the first is that I am aware just because of having been around this a little bit, that over the years, category III has kind of been a little bit of an issue, perhaps in some of the wording that was used previously and reimbursements and things like that. Do you have any perspective on how the wording of category III has changed and maybe been optimized in recent years?

Nancy: Yeah, I do. Let me go back to 1993. So in 1993, when category III was first defined, it was worded something along the lines of "reported evidence is insufficient to establish efficacy of therapeutic apheresis and/or favorable benefit not clearly documented." And I think insurers kind of misunderstood that as something that doesn't support apheresis. And I think what they were trying to say is you don't really have enough evidence to make that decision one way or the other. So I think there were some issues with getting insurance coverage for category III, so over the years they tried to tweak that. So it went through several iterations until it got to, I think in 2010, more like what we see today, which is that the optimum role of apheresis is not established and decision making should be individualized. Which is what I think where we are at with most of the category III indications. It's not that it's a "hard no," it's just that there's not a lot of evidence to guide us and so we have to do clinical decision-making based on the patient.

Joe: And that brings me to my next question which is you made a statement that to those that do therapeutic apheresis is probably not surprising, those that do it consistently. But for the rest of the folks that may not see this on a daily basis, my guess is people heard what you said earlier and it might've raised their eyebrows a little bit. And you said that when you look at the numbers, there's more of these diseases in category III than any other category. How can that be? How can we be in 2019 in this situation where we still don't know the optimum role for apheresis for so many of these diseases?

Nancy: Yeah, well there's a number of factors that play into that. Some of the category III are indications that are really rare, things that don't happen very often, so it's hard to accumulate even case series. And I think about things like Wilson's disease and catastrophic antiphospholipid syndrome, these are things that many of us don't see on a routine basis in our practice. I might see that once or twice in my own practice. So things that are rare, where it's just hard to assemble even a case series about doing apheresis. And I think another factor is doing randomized

control trials in apheresis is difficult. It's expensive, it's not like a drug, necessarily where you're going to make a lot of money. So there's not a lot of work being done to really boost evidence that might help tip things into a category II or category I in that way. So we're left with a lot of diseases that apheresis is reported in things like case series or retrospective data analysis of patients previously treated and trying to make conclusions, and evidence isn't as strong. So a lot of times we're not really sure where to put things so it winds up in a category III usually if there's some plausible pathogenesis, like you can make sense of why apheresis may help, but you can't really prove that it's helpful or should be first-line therapy or even second-line therapy.

Joe: Okay so Nancy, when I have talked to residents before and they pull up one of these fact sheets that you've described so well, when you look at the top of this fact sheet, you'll have a particular disease or condition listed and there will be a procedure, for example, with the thrombotic thrombocytopenic purpura fact sheet, it'll say the procedure is therapeutic plasma exchange, TPE, and it gives a recommendation. It'll say the grade of that recommendation, and the category. So one thing that residents tend to in my experience get a little confused on is those recommendations. And as people look through, they don't see a whole lot of "1A" recommendations. First, can you just tell us what the steps are in as you mentioned before, the GRADE system, and what do you do with that info on the fact sheet?

Nancy: Yeah, absolutely, that is actually a great question because I can see how it would be quite confusing if you weren't familiar with the system. So the recommendation with the GRADE level is really looking at the quality of evidence supporting apheresis in that particular indication, and the quality of evidence has to do with the type of studies that were done to support apheresis. So the highest quality that the things would be a grade 1, A, B, or C would be randomized control trials, or really a lot of observational studies of case series that really seemed to support apheresis in that particular indication. But we know that it's hard to do randomized control trials and certainly apheresis it is hard to do "sham procedures" so a lot of the evidence comes into this grade 2, which doesn't mean the evidence is bad, but it's generally more evidence from case series, case reports, and so the grade doesn't actually determine whether or not you do apheresis as much as the category recommendation.

And it's funny that they're not in this particular order. I would look at the category first. The category is sort of what ballpark are we in? Is this a clear first-line therapy, category I thing? Or am I...what you're more commonly going to be in this situation of a category III, where it's not clear about the role of apheresis and you really need to use individualized decision-making. So once you know kind of what ballpark you're in, then you can look at the grade to say "Okay, what is the evidence that's informing this category recommendation?"

Joe: Got it. Okay, I think that helps us put it into context a little bit. I know we could spend a whole lot more time on that but let's jump ahead and get to what you guys did with the 2019 special issue. And you've already kind of talked a little bit about

your work with Anand as co-editors of this particular project. I think we should start with, again, I think you've already kind of alluded to this, but this is multidisciplinary, right? This is not just a transfusion medicine thing?

Nancy: Correct. And in fact we try to assemble our committee of authors to reflect the actual practice of apheresis medicine internationally. So we have nephrologists, we have hematologists on the committee, we really try to get input from all the subspecialties that are involved in apheresis medicine, because we want to make sure we're all on the same page about our guideline recommendations and what the evidence supports. And I think that's really the value of the guidelines is that there are so many different diseases and so many different subspecialties that it would be really hard any one person to be an expert on apheresis without the ability to look at a few guidelines. It's not information you can carry around in your head.

Joe: Right, absolutely. I'm just going to open up the floor to you. Why don't you take us through in whatever way you want to what changes we should expect in the upcoming 2019 special issue?

Nancy: Yeah, so I mean one of the luxuries of joining something like this that's already sort of established, you don't have to reinvent the wheel. So going into this, I think we knew that we really liked the fact sheet format. We were committed to maintain that one page fact sheet, even though we may not be actually making photocopies anymore. You could potentially either electronic medical record link the document so that people could read an electronic version.

So we didn't really have to change a lot in terms of the overall structure or the intent of the document, but we wanted to, again, really reflect the current evidence and the current knowledge in the field. And as you know, medicine is changing constantly. There are new drugs being brought on board that may be able to replace apheresis as first-line or second-line therapy. And so we really had to go through each particular fact sheet and reassess the evidence and then make an assessment on whether there were any changes in the category recommendations in terms of category I-IV, or the grades in the recommendations. The quality of the evidence might change, certainly if new randomized control trials have been published.

So that was our biggest goal, just to get the fact sheets up to date, to make sure that the recommendations were valid. That took a lot of effort on each committee member in terms of just reviewing whatever body of literature, in each particular disease indication had been published since the fact sheet was last reviewed.

So that was the main work, and then we did a little bit of cosmetic things like renaming or reorganizing things, merging some fact sheets that maybe on their own were kind of scanty and could be lumped together. I'm definitely a lumpier, not a splitter, so I try to put things together if they go together. So we did some more cosmetic things. We retired fact sheets that didn't really have any new evidence. So those were kind of the biggest changes. But I think you know if you're looking

at the fact sheets what you're going to see is not anything that's dramatically different than the 2016 issue, but there are going to be many more updated references, newer publications. We tried to include review articles where we could, so that if someone was interested in learning more about the disease, they could go right to that reference and see something fairly recent to give an overview of what's going on in that particular disease.

There are some big changes that we made but not a lot. The field of apheresis hasn't honestly changed that much except for a few things that we did change that you and I can discuss maybe more in depth.

Joe: Sure, why don't you give us the highlights? Absolutely.

Nancy: Yeah, so I think the biggest change is I think there was one indication that was upgraded from a category II, which is second line therapy, to a category I. So that to me is kind of the biggest upgrade, that you get category I status. And that was using therapeutic plasma exchange for catastrophic antiphospholipid syndrome. This is an antibody-mediated disease and you can imagine that therapeutic plasma exchange certainly could remove antibody. And I think the reason it had been category II previously is it's a very rare disease and there weren't a lot of large case series looking at using plasma exchange in catastrophic antiphospholipid syndrome. And really what changed between 2016 and 2019 was there's a registry collecting data on patients with catastrophic antiphospholipid syndrome, and looking at those patients in aggregate and looking at the patients who received plasma exchange. In recent publications based on that registry data, there was new evidence supporting improved outcomes in these patients who received apheresis. And that really prompted us to move it up from second line therapy, category II, which it was in 2016, up to first-line therapy, which is category I.

So I think that was one of the bigger changes. There were a few indications that were upgraded from category III, which is that kind of "we're not really sure, so individualized decision making is best," to category II, which I think is clearly second line therapy if whatever the first-line therapy fails, then definitely think about apheresis. So those include lipoprotein apheresis for focal segmental glomerulosclerosis, or FSGS, which is a renal disorder. Lipoprotein apheresis did get FDA approval recently for the use in FSGS. So that definitely supported moving it into more of a mainstream kind of category II indication. As well as looking at plasma exchange for thyroid storms, some new evidence there showing that was beneficial as a second line treatment and red cell exchange in sickle cell disease particularly in pregnancy and in recurrent vaso-occlusive pain crises, those both moved from category III to category II based on new evidence that have been published.

There was also a downgrade, or two downgrades, in fact. And so that's kind of big too where you get "demoted." The biggest one I think is using therapeutic plasma exchange in progressive multifocal leukoencephalopathy, or PML, associated with the drug natalizumab. The drug natalizumab is a target that can be removed with

therapeutic plasma exchange and initially this is a catastrophic disease seen in patients primarily with MS who receive natalizumab as a therapeutic. They can develop this leukoencephalopathy. And I think initially, in 2016, it was thought that if you could get the drug out sooner, you might improve outcomes, and it was given a category I recommendation. But there was a newer publication of an observational study, a retrospective study looking at patients who received therapeutic plasma exchange to remove natalizumab and it didn't actually show that there was any decreased morbidity or mortality by using plasma exchange, even though you clearly removed the drug. Maybe the damage is already done. So based on that, that really changed the way we think about it. And now we've moved that down to category III, which doesn't mean, "don't do it." But you have to look at that patient in the context of what's going on with that patient, how severe is the disease, and really do individualized decision making.

So I think that was the other sort of really big change in this particular issue.

Joe: And I think, to be fair, there's one additional, well what I view as a big change anyway, and correct me if I'm wrong, Nancy, but didn't you guys for the first time add some criteria for how you're going to decide about new fact sheets in the future?

Nancy: Yeah. Actually that's a really good point. So in spite of the fact that we developed new criteria, we didn't actually end up adding any new fact sheets this year. And that I think, again this gets to me being sort of a lumpers and a splitter. I think in the 2016 edition we had quite a number of new fact sheets, but when we looked at the number of publications that those fact sheets were based on, some of them had very few publications, very few patients, and I think we wanted to be a little bit more critical about how we decided that there may be enough evidence to support apheresis or the creation of the fact sheet. Because naming it in a fact sheet really does imply that apheresis can be considered, so I think we need to be careful and not base that on just one or two case reports.

So we as a committee decided that we ideally would like to see a minimum of 10 cases describing apheresis in that particular indication, and ideally they would be published in peer-reviewed journals and by more than one group. So if one person believes that apheresis is helpful in a particular disease and publishes a lot, we want to see other groups publishing that as well. And we have restricted it to 10 years because we thought if this is something that has a large bucket of evidence prior to 10 years ago, it should have already have a fact sheet, so it should be something new, something that apheresis is being applied to in a new way.

And so with those considerations, we've reviewed over 10 possible considerations, many of the considerations had one or two case reports but not enough really to meet those criteria. So those are sort of standing by as indications that we're going to revisit in 2022. It'll just be whether there have been new case reports enough evidence to really create a fact sheet.

There was one though, Alzheimer's disease, which was also presented at ASFA. And they have recently concluded, a randomized control trial using a kind of modified plasma exchange, albumin replacement therapy for Alzheimer's disease, and that one has potential to be a game changer. I think we're just waiting for that study to be published in a peer-reviewed journal before we can really assess that. So I think that one is the one that probably has the best chance at the moment of being a new fact sheet in the next edition. Just because they did a randomized control trial and it's about to be published probably in this calendar year or next, so...

Joe: I'm glad you mentioned that, Nancy because I too found that presentation really fascinating at the annual meeting. So I'm glad you brought that up. So we're left at this point with a brand new Special Edition and everyone by the way, to make it clear again, this is the June 2019 edition of the Journal of Clinical Apheresis. I will have a link to at least where you can get access to that if you're either a American Society for Apheresis member or as Nancy mentioned, if your institution has subscribed to the journal. You'll have that on the show page for this episode, which will be at BBGuy.org/071. I'm really excited for everyone to get their hands on this, Nancy, as I know you are, so why don't you just, if you don't mind, close us out with what you and the committee hope that people will get from this new set of guidelines.

Nancy: Like I said, it's not that much different from the previous guidelines with the exception that it does include the newer evidence that's come out in the past three to four years. So I think if you're looking for an up to date, concise resource that will help you kind of wrap your head around the use of apheresis in a particular indication, it's incredibly helpful. If you're a resident, it's helpful just kind of organizing your thoughts about a particular disease, indication. It can be used definitely to learn more about a particular indication if you're putting together a presentation or something. You know, for me, I used it every day. It's really helpful. It's nice to know that it's current and it's up to date and it's not that the recommendations aren't obsolete because there's a new drug on the market or ...

With that being said, I have some sadness in the sense that once it's published, it's already outdated, right? So even in the interval as we've been preparing it for press and reviewing the proofs and doing all that work, more studies have been published. So it just makes me excited to think about 2022 and what we're going to do to carry the work forward, and I have to confess I already see things in this print version that I'm like "Oh, next time we're going to do that differently. I don't like the way the table's structured. I want it to look this way or that way." So it is an ongoing sort of living document that we are going to use for the next three years until 2022 comes.

Joe: Nancy, you might've just given yourself away as a perfectionist. I could be wrong, but you might've just showed that you are a perfect blood banker, because you're a perfectionist.

Nancy: I am a blood banker and a pathologist, so there you go.

Joe: That's awesome. Well Nancy, with all that said, I think that you've given us a great overview of this entire situation with the special issue and the exciting stuff that's coming out both in this 2019 edition, and as you've previewed in the 2022 edition coming forward. Thank you so much for taking the time to be with us and explain this. I really appreciate it.

Nancy: Yeah, thanks so much for the opportunity to be here and just a shout out to the other people on the committee. They made this possible, this was a work of many, so it's my pleasure to talk about it but the credit really goes to them.

Joe: Hey, so before you go, you should check out the show page for this episode at BBGuy.org/071. I've included a link to the guidelines that Nancy and I discussed, and as I said, even if you don't personally do therapeutic apheresis in your facility, you will benefit from having a copy of these guidelines just available there for your reference. And again, learners, pathology residents, clinical laboratory students, SBB students, et cetera, you really need to know a decent amount about therapeutic apheresis, so be sure to check those out.

So you can hear future and previous episodes of this podcast directly on the website BBGuy.org, or you can go to [Apple Podcasts](#) or [Google Play](#) or [Stitcher Radio](#), or Spotify, or even "Ask Alexa" on your Amazon device to play the blood bank guy essentials podcast. I appreciate all of you who have given this podcast a rating, especially on Apple podcasts and all of you that have subscribed. I do read all those ratings and I appreciate the kind words, and Apple also uses them to suggest the podcast to other learners so thanks for your help and for those ratings.

The next episode, which will be available next week, will be a continuing education eligible interview with a very, very smart neonatologist, her name is Martha Sola-Visner from Boston Children's Hospital. And Martha and I will discuss how we might have been making all the wrong assumptions when it comes to neonatal platelet transfusion, giving platelet transfusions to little tiny babies, over the last few decades.

I'm really excited for you to hear that episode, 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 will catch you next time on the Blood Bank Guy Essentials Podcast.