

Advantages of Bloodless Medicine - An Interview with Patricia A. Ford, MD

Host: Patients may choose bloodless medicine for medical or ethical reasons. How safe and effective are bloodless procedures compared to more traditional approaches? Joining us to discuss bloodless stem cell transplant is Dr. Patricia Ford, Clinical Professor of Medicine, Medical Director of the Center for Bloodless Medicine and Surgery and Director of the Peripheral Stem Cell Program at Penn Medicine. Thanks for being with us Dr. Ford.

Patricia Ford, MD: Thank you. My pleasure to share this information with you.

Host: I'm excited to hear about this. Perhaps we can start right at the beginning. What is bloodless medicine and what is the history of this?

Dr. Ford: Well, the history really dates back to care of the Jehovah's Witnesses, and they're certainly a population that based on religious convictions will not allow a transfusion of certain blood products. So, caring for Jehovah's Witnesses, doctors were challenged to think about some alternatives that might be appropriate to allow them to go through any time of medical illness or any type of surgical procedure, simply doing it exactly the same without the use of blood products. So the history really was based on the care of Jehovah's Witnesses, but as time went on, we've learned that there may be as many as 30% of blood transfusions in the United States that are given that may be unnecessary. So we really feel that some of these alternatives that we use and some very, very simple strategies we'll go into will help all of our patients, if not eliminate. Certainly reduce unnecessary transfusions.

Host: Very interesting. So this is kind of a term that applies to transfusion medicine and would be applicable in oncology situations, hematology, I imagine perioperative type of circumstances? Is that correct?

Dr. Ford: You're absolutely right and we've kind of expanded it now to using more the terminology of best patient blood management, so that it really gives the

connotation that you can use this in every patient, and we're really hoping to promote best usage of blood products.

Host: And obviously you mentioned the Jehovah's Witnesses—are there other patients who choose this approach for particular reasons?

Dr Ford: Maybe not totally eliminate blood transfusions, but reduce the risk of infections or other complications by looking at some of the alternatives. So there are some patients that actually will never take a blood transfusion even if it's deemed life-threatening, but there's many other patients who are much more educated and want to look at some of the alternatives that could reduce their exposure to blood products.

Host: Do we have things for all elements of the blood—packed cells, white cells, platelets—what are our optionsHere?

Dr. Ford: A lot of our blood transfusions are done in the surgical patients, so I'll start there with that patient population—and what we're finding for our elective procedures is that many of our patients going in for the more common procedures, which have a large blood loss potential, are orthopedic patients, cardiovascular patients, some oncologic patients. Those are the big ones. What we're finding is that a large number of this patient population is older, coming in anemic—having some anemia renal insufficiency, or anemic chronic disease. For women, it's a little different, the big procedures done there are hysterectomy, and some women caesarian sections, where you can lose a large amount of blood. Those women coming in anemic are very different. They're mostly iron deficient.

So one thing we found was trying to identify early those patients for elective procedures that have anemia that we might be able to correct ahead of time. So a very important strategy is identifying preoperative anemia and diagnosing it and if

possible correcting it before entering surgery because one the biggest risk factors for needing a perioperative transfusion is your pre-op hemoglobin.

Host: I should probably remember this, but what is the timeframe that you need if you're going to be giving someone iron to see a meaningful increase in their hemoglobin and hematocrit?

Dr. Ford: You can start to see an increase in reticulocytes and even the hemoglobin in about three to five days. On average, what I'm finding is that we can increase the hemoglobin about one gram per week, so we tend to have a target in our mind—for instance, if you're going into surgery, you'd like to have a normal hemoglobin, which is around 12 for women, a little higher for men. So we want to at least target a normal hemoglobin going in. So, if someone has a hemoglobin of 9.9, I know that I may need three weeks to hit my target of 12, by giving intravenous iron or sometimes the erythropoietic stimulating agents.

Host: So this is certainly something that can be employed pre-operatively and have a meaningful response.

Dr. Ford: Absolutely. That's a very simple strategy, and I think in re-education of the surgeons and the referring physicians to really — just like they prepare their patients for surgery by evaluating cardio and pulmonary function, to really look at the blood work and make sure that you're not sending an anemic patient into a large blood loss-potential surgery.

Host: And are there products that help with either white cells or with platelets or clotting factors?

Dr. Ford: So for the clotting factors, some simple things I've found to avoid any excess bleeding is to make sure that people have adequate vitamins, especially vitamin K, which as you know is one of the most important, in terms of the coagulation cascade, but, very importantly, what we've found is that nowadays, people are taking

an awful lot of alternative supplements, whether it's vitamins or fish oil or ginkgo, and what we do is we have a little education process. Everyone knows before surgery to avoid aspirin and maybe you have to come off of your Plavix and some of your other antiplatelet drugs to avoid bleeding, but what they may not know is that 1) alcohol use—and you have to be very careful to specify that this includes all alcoholic beverages—and you want to have them stop all alcohol seven to ten days before their surgery because that also interferes with platelet function—as do some of these supplements. Fish oil, ginkgo, etc. So we go through everything with them, and we strongly recommend that they come off of all unnecessary medications, certainly all supplements, all alcohol seven to ten days ahead to make sure they're entering with healthy platelets and lessen the chance of bleeding.

Host: Very smart simple things to do that I can see would really make a big difference.

Dr Ford: Very simple. And in the hospitalized patient, just thinking about another very simple strategy—what we find in a hospitalized patient is that they can literally lose anywhere from 300 to 400 milliliters, even on a general medical floor, with repetitive blood draws. So if you think about the hospitalized patients getting daily blood draws, the first thing that happens when the sun comes up is in goes the phlebotomy team and draws a lot of blood, and in a very stable medical patient or any patient you may not need to check a CBC and chemistry without an abnormality and change every single day. That can save an awful lot of iatrogenic blood loss.

The phlebotomy teams will often say they overdraw into the tubes because they know it's not infrequent that later on the house staff will call to ask for additional testing to be added on and they don't want to have to come back and re-stick the person. So what we find is that we really have to educate our phlebotomy teams to draw very small volumes, and just when they need it—they may only need to draw one to two milliliters instead of 10 ml tube, and to re-educate our house staff to not

order unnecessary testing. Frequently I see routine chemistry and CBC and they're normal every single day for a patients that's in for a medical issue—or on the day of discharge. There you go—blood had been ordered again on the day of discharge.

Host: Dr. Ford, those are all excellent points, very practical. Tell us a little bit about this interesting thing, a bloodless stem cell transplant.

Dr. Ford: I'm a general hematologist-oncologist and I also direct an autologous stem cell transplant unit and what I found as I was caring for Jehovah's Witnesses and becoming more adept at some of the alternatives and how to deal with profound anemia and thrombocytopenia, I was faced with the challenge of a Jehovah's Witness who had a relapse of lymphoma in our practice a number of years ago. And really at that point, no one had felt comfortable performing an autologous transplant because of the inability to provide red cell and platelet transfusion during their two to three week period of pancytopenia after the high dose chemotherapy.

So at that point, I felt very comfortable in dealign with low blood counts, and I really said I have enough strategies that I think someone can survive this by just doing some of the simple strategies already discussed, preparing these patients entering into transplant by getting their hemoglobin up as high as I possibly can, limiting the unnecessary blood volume draws, using some of the hemostatic agents in lieu of platelet transfusion. Normally in a transplant patient, once the platelet count is under 10,000, we would give a single-donor platelet transfusion.

In a Jehovah's Witness, we can't do that—that's one of the prohibited products. So what I do when the platelet count starts getting low is try to enhance hemostasis by utilizing simple things like vitamin K, aminocaproic acid, which is an antifibrinolytic, and I've actually found in the 100 patients that we've transplanted, I've had only one major bleeding complication in these profound thrombocytopenic patients by the simple use of these other hemostatic agents.

Host: That's incredible. And I know out blood supply is relatively safe, but have you applied this in patients who are non-Jehovah Witnesses?

Dr. Ford: I have, and I'm at the point right now in those patients who **will** accept transfusions that we're only transfusing about one out of three of our transplant patients. And prior to my gaining some expertise in this, I was transfusing upwards to 90% of patients going through transplant, so a pretty profound reduction in the **non**-bloodless patients, also, which I think is a good thing if they're unnecessary transfusions.

Host: And you just have a lower threshold in these non-Jehovah Witness patients for red cell transfusions?

Dr. Ford: That is an absolute fourth strategy that is very simple, and we call it tolerance of anemia. To really not transfuse someone based on a number. So, I know even for myself, I was trained in transplant that any time the hemoglobin was under 8 to give two units of blood. So the two mistakes I learned there was number 1: not every person with a hemoglobin under 8 is clinically in need of a blood transfusion; red cells are designed to provide tissue oxygenation, not to be used as volume. So we keep our patients very euvolemic, we keep them on oxygen and we decide when we feel they need a blood transfusion. And for some of these, they may have hemoglobins of six or five before there's any sign of tachycardia or some sign telling us that we needed to give a transfusion. We also don't knee-jerk give two units.

Again, it was one thing I was trained to give two units: every time you need a transfusion, give two. If you need to get it, you must give two. And we find that that's unnecessary. So we will give one unit of red cells and then reassess: do we clinically have a reason to administer a second unit? So these two very simple things rapidly reduced the transfusions I was giving: not transfusion upon any basic number and giving one unit instead of two.

Host: And you mention the tachycardia. Are there other specific things that you would look for that indicate “Hey, now’s the time to give that unit of packed cells?”

Dr. Ford: Right. All the things we learned in terms of assessing tissue oxygenation—because as you know there’s not a good correlation necessarily between the pulse ox and how you’re actually oxygenating tissues—so looking at the things we were taught so well as medical students, going back on your clinical skills, assessing mentation, looking at using output and of course looking at blood pressure and tachycardia and the patient’s symptomatic complaints, potentially, whether it’s on exertion or at rest. We also keep them monitored—continuous cardiac monitoring—also, so that we’re not missing some asymptomatic arrhythmias or some other signs there.

Host: Prognostically, I imagine there’s no big difference down the road for people who have a bloodless stem cell transplant versus traditional?

Dr. Ford: Well, there’s not difference in their response to their tumor—the efficacy of the transplant—because they all get the same dose of drugs. So they’re not attenuating—they all get high dose chemotherapy, as would be recommended for any relapsed lymphoma or myeloma patient. So they’re all getting the same standard treatment, so as expected you’d imagine that their response rates for survival of disease would be the same—and it is.

The difference with the Jehovah Witness population—and I’m very up front with them in this—I would say in the United States right now the safety of an autotransplant should be about one percent, maybe two percent mortality in most centers directly related to transplant. What we find is that our mortality is slightly higher. In our hundred patients, we’ve actually had four deaths. So there is a slight increased risk of mortality with they patient population, but the alternative for many

of these patients—this is their only curative potential—or maybe their best potential—so they find this slight increased risk acceptable.

Host: Is there any difference in terms of complication rate, or hospital stay, infection or other things?

Dr. Ford: We see no difference—and we've actually looked at this—so we've evaluated infectious complications, and they actually were somewhat lower. One thing that has been noted with blood transfusions in other patient populations—there's a leading article that was out in the NEJM a couple of years ago from Dr. Colleen Pock on her cardiac patients looking at older vs newer blood products being given and she did find a difference—so it seems like A) patients who are transfused have an increased infectious risk—we think it may be part of a whole immunosuppressive aspect of getting this product—if you think about it these are live cells so it is an organ transplant at some level.

These are live cells and even though we try to reduce our blood products, you do get some contaminating donor leukocytes, which are live and viable and account for things other than infectious risk in red cell products. They account for your transfusion-related acute lung injury, potentially, and we think may also alter the recipient's immune system and make them somewhat more accessible to infection.

We have also seen in this population a slight increase in infectious complications. In terms of cardiac complications, we have had an increased risk and they were all manageable and what I mean by that, there was a little bit more hypertension requiring more fluids and more cardiac monitoring, but we've had no significant events such as thrombosis or myocardial infarction. So it's been mostly a little bit more need to monitor them carefully interns of volume, cardiac monitoring and assessment of arrhythmias. We've had a couple incidences of arrhythmias.