8th Annual Transfusion Medicine Symposium
Videoteleconference: Transfusion in the Female Population
Questions and Answers (morning session)

Management of the Postpartum Hemorrhage and Use of RhIG in Pregnancy

Presented by Dr. Elianna Saidenberg

Q: How long after Rh immunoglobulin administration can you expect to detect a positive antibody screen?

A: (ES) The answer in textbooks is 4 weeks, but unless I know that the patient received Rh immunoglobulin, I don't rely on the testing to determine if that is the cause of the positive antibody screen. Patient history is your most important tool for determining whether a patient has received Rh immunoglobulin

(JB)The half-life of IgG is 3 weeks, so depending on the dose, could go up to 6 weeks.

Q: What about the administration of whole blood in massive transfusion?

A: (ES) Whole blood is not available from CBS, so it is not an option. I agree that when someone is bleeding out whole blood, it would be very useful to return whole blood. But really massive hemorrhage is the only setting in which whole blood transfusion is indicated and since it is impossible to predict when you are going to get a massive transfusion it would really be a waste of the donation if we didn't divide it into component products.

Q: Question in regards to the use of cell saver technology, in terms of filtering out the amniotic fluid debris, so that it does not go back into maternal circulation?

A: (ES) In cases where you have massive vaginal hemorrhaging, I have yet to see really good guidelines for how to use a cell saver in that setting. The situation where it can be very useful in minimizing transfusions is if you have a high risk C-section or if you're going to take this patient for a hysterectomy postpartum, this may be a good time to set up your cell saver. That's my experience. There are some published papers on how to use a cell saver in vaginal hemorrhage, but I've not seen it successfully done. Part of the reason is that you don't have them set up in labour and delivery. There is so much other debris in vaginal bleeding that I'm not really clear on how safe that is at this time.

Q: We are a small community hospital, you mentioned that you have a 24 hour support line for massive transfusion, I was wondering if you could give us that number, so that it could be in our Emerg?

A: (ES) Your hospital may have a transfusion specialist or you may be associated with a larger hospital with a transfusion specialist to assist with any questions. You should contact the nearest large teaching hospital in your area to ask if they would be able to provide that for you.

Use of Tranexamic Acid and Management of Iron Deficiency in Women with Menorrhagia
Presented by Dr. Janis Bormanis

Q: As they are encouraging blood donation in high schools, do you take into consideration the rate of growth and development of kids at that age?

A: (PL-CBS) This is one of the things that CBS is looking at right now, in terms of how to best manage those donors. There are obviously conflicting priorities in terms of making sure that we always look after the donors, never causing them harm, but on the other hand, for all the recipients who are in desperate need of blood products, we have to balance those two issues. Blood collection agencies around the world are looking at what the best age to start donating should be. Some countries have moved to even younger than Canada (ie. 16). In Canada it's 17. We also have the added issue for female donors, with respect to their metabolism of iron. There have been no final decisions made, in regards to potentially reducing the frequency of donation of either female or younger donors.

(JB) Clearly the frequency of donation is linked to iron, if you are iron deficient you can't donate. So is it reasonable for anyone who donates more than twice a year, to have them take iron? That's a more complicated question that should be considered.

Q: Are there any contraindications to Tranexamic Acid with menorrhagia?

A: (JB) Nausea can be pretty significant in bigger doses. But I am not aware of any contraindications, apart from some people showing an intolerance.

Q: Tranexamic acid, does it have any prothrombotic effects?

A: (JB) It has been studied well in joint surgery and cardiac surgery. Even in joint surgery there haven't been any risks with thrombosis. There are no clinical studies in post-surgical areas that indicate there is a thrombotic risk.

Blood Products – How Fast Can I Get Them?
Presented by Melanie Tokessy

Q: Is it worth it to keep platelets at smaller remote sites?

A: (MT) I don't think that it is recommended to keep platelets at remote, smaller sites. Platelets are only good for 5 days and very often you get them on day 3 of their lifespan, so you are probably just keeping them for 2 days on the shelf. So it is not good for inventory management.

(ES) Within most regions there is a large hospital, with a cancer center, that does stock platelets. For instance in Northern Ontario, Sudbury stocks platelets and if another smaller hospital nearby needs them for an urgent case, they could be asked to redistribute them. The need for platelets in an urgent situation is infrequent therefore it would result in very high discard rates if smaller sites stocked platelets.

(JB) Chances are more likely that if your patient needs platelets urgently, you are going to transfer the patient to a larger hospital and they will receive the platelets there. For routine requests, there would be time to order from CBS.

Q: Is the temperature still a consideration when blood is returned back into inventory after 30 minutes?

A: It is. Every red cell unit that comes back, that wasn't transported in a cold box, we do take the temperature and it must be less than 10 degrees.

Q: If you are working in a dialysis unit and time is of the essence, is it okay to transfuse the red cell at a faster rate?

(ES) In a patient who has underlying renal or cardiac disease may not tolerate increases in volume well. If transfusion and dialysis are being undertaken concurrently, there is no reason to slow the rate as the excess fluid will be removed during dialysis. But in a patient that is being transfused separately, I would not want to increase the rate.

Follow-up Questions: We actually have very few patients on dialysis that get transfused anymore, but those that do, typically they are transfused while they are being dialyzed and we recommend that they transfuse slowly for the first few minutes or so, but after that they can transfuse a little quicker typically, two hours. Can you comment on this?

(JB) I agree with the rate of infusion, however, the latest study in the States show that with the back-off of use of ESA (**erythropoiesis-stimulating agents**) in renal patients, that the rate of transfusion has gone up significantly in dialysis patients. I don't know if that has caught on in Canada, but as you know the ESA use in renal patients has dropped with cardiovascular risk issues and they are running their patients at lower hemoglobin, so I predict that you will have an increased risk of transfusion.

In regards to rate, if you have a non- critical patient, you can transfuse that patient more slowly. You can split the unit with one half over three hours and the other half over three hours. For any non-urgent transfusions, take your time to decrease the risk of complications.

Q: Does Tranexamic acid have any effect on platelet distribution in spleen?

A: (JB & ES) No.

<u>Interesting Case Studies from the Emergency Room</u>
Presented by Dr. Tonja Stothart

Q: In case study #1, how many units would you consider transfusing?

A: (TS) For the first case, because things are happening relatively quickly and the cross match will be available in 30-45 minutes; I would start with 2 units then a bolus of crystalloid and then see what happens. The history is extremely important.

(ES) As you are treating for symptoms, you can cross match for 2 units, however you can try giving only 1 unit and if the patient is feeling better, you can potentially avoid that second unit. Also, think about what can be done to decrease the bleeding. For example, is she going to go for a D&C in an hour and all this will be dealt with. In this case, you could avoid transfusion altogether. (TS) I agree.

(JB) One of the important things with these patients who are bleeding, you need to look at the MCV. Without it, you don't know if there was iron deficiency pre bleeding. If the MCV is 90 you know they bled, if it is 60, you know that they bled from a low level. That also helps in your decision.

Q: Right now there seems to be a little controversy about giving crystalloid for hemorrhage. What's your attitude towards starch in some of these cases? (In regards to volume control, specifically trauma, Physicians are using less and less crystalloid)

A: (TS) In the department, we have starch available. You are not dealing with a lot of risk and it can buy you a little bit of time, but as long as you are considering transfusion, you can consider a multi-directional approach. Crystalloid is the first thing you pick, but I do use a fair amount of starch.

<u>General Question Period</u>

Q: Do all pregnant women need iron supplement? How much iron does the fetus require in utero?

A: (JB) There's lots of studies on this. The baby is essentially a parasite and takes from the mother. Generally speaking, it is recommended that you use prenatal iron with folate. The baby will take from the mother first, the mother becomes anemic. Actually, when you look at mortality, in the mother and the baby it is higher if the mother's hemoglobin is higher.

(ES) The amount of iron in a pre-natal vitamin is not sufficient to treat iron deficiency anemia. Additionally, many of the vitamins will also have calcium in the tablets which could impair iron absorption so that prenatal vitamins are not an appropriate treatment for iron deficiency. Iron deficiency anemia in pregnancy should be treated seriously because there is evidence that these women will have difficulty lactating. Having a newborn is a very fatiguing time in your life and having the additional fatigue associated with anemia increases your risk of post partum mood disorders as well. Also, there is some indication that women who suffer from anemia are at increased risk for bleeding in the postpartum period, which will further worsen their anemia. If the patient is referred later in pregnancy, that would be another time where I will consider IV iron. You will get the iron up a lot faster than with oral iron supplementation.

Q: Do you need to give vitamin C with the iron supplementation for better absorption?

A: (JB) Yes. When you look at iron absorption, if you take food iron, you need acid. If you take pills you don't need acid and the iron goes across the pancreas quite easily. People who can't tolerate a full dose may increase their absorption with vitamin C. You can prescribe Proferrin, the hemoglobin based iron, that is better absorbed but it costs approximately $90 a month and is not covered by insurance. If they are intolerant, I tend to prescribe Ferrosol first, smaller amounts, it goes up nicely. I'll go to Proferrin next and again, intravenous iron is interesting, but the policy is different across every institution in Ontario. In Ottawa we give IV iron in medical daycare, but a lot of smaller hospitals don't.

Q: Do you know the rate of thromboembolic events in obstetrical population who have been treated with Tranexamic acid for postpartum hemorrhage?

A: (ES) There is no increased rate of thromboembolic complications in people treated with Tranexamic acid. I would not treat someone who has had venous thromboembolism in the last 4 weeks with

Tranexamic acid or somebody with bleeding that could be from the ureters (Further clarification: In cases of hematuria due to bleeding from the ureter, Tranexamic acid is not used because, failure to dissolve a clot in the ureter can result in hydronephrosis). Otherwise, there are no other situations in which one should not to use this therapy. It is also used extensively in joint replacement and cardiac surgery, which are both high risk for thrombosis settings and there are not increased rates of thrombosis in these patients in the post-operative period.

Q: When a patient is given oxygen and transfused units, how does that negatively affect their short term and long term reproduction of red cells?

A: (JB) This is a rather complicated question. When you transfuse blood you don't get immediate, substantial increased oxygen carrying capacity because of the decreased 2,3 DPG in the donor blood. It's pretty well back to normal within 24 hours. If your lungs are normal, adding more oxygen does not increase your oxygen saturation. It is only useful if you are a chronic smoker or bronchitis, etc. If you donate blood, you get iron released and that would increase oxygen carrying capacity, but if you receive a transfusion, you can actually blunt the erythropoietic response. You get an immediate increase in hemoglobin with the transfusion, oxygen carrying capacity should be back to normal within 24 hours, that may suppress the erythropoietic response a little bit, but that probably doesn't make that much of a difference.

Q: Is there a role for Tranexamic acid in the case studies that were presented?

A: Yes.

Q: Should smaller hospitals, that have obstetrical units, carry Tranexamic acid? In what order of priority should it be given?

A: (ES) The drug has very few side effects, if any and no significant known complications. There's mounting publications indicating evidence for its benefits. There are great studies for its benefits in trauma and postpartum. It's not expensive. I can see no reason why any pharmacy committee would say no to stocking it.

Q: What type of stock does a small hospital carry in regards to blood grouping?

A: (TC-ORBCoN) For a small community hospital, outside of the Ottawa area and dependant on their average daily transfusion rate, smaller sites stock 4-6 O pos, 4 O neg and maybe some A pos, A neg red cells. Some hospitals carry some frozen plasma, usually 4 units of frozen plasma (one adult dose). Some hospitals that have an obstetrical unit carry cryoprecipitate (Note: this should be reviewed and approved by the physician responsible for the transfusion laboratory).

Q: Could you provide more information regarding redistribution of outdating products?

A: (MT) The Ottawa Hospital is very proud of our redistribution program that we implemented with ORBCoN. At The Ottawa Hospital, General Campus, we will accept any blood product from a smaller hospital that is near to outdating, within reason. This has really reduced the amount of wastage for our region and allowed smaller hospitals to stock more product. Products that are outdating in 5-7 days can be redistributed to the larger hospital. Smaller hospitals also may redistribute products amongst themselves.

(JB) In regards to the age of blood issue, we know that "old blood" is considered older than two weeks; "young blood" is less than one week. The ARIPI trial in newborns showed that old blood was no worse than fresh blood, in fact, it appeared that fresh blood was not as beneficial. The ABLE study is currently going on and has not been stopped, so you know that there is likely no difference in patient outcome. If you have a choice, you might consider not giving old blood that's 21-22 days old to someone that is acutely bleeding. The age of blood is an issue that is currently under study and who you give older units to may be an important decision.

Questions asked post-symposium, via e-mail or question form:

Q: Is there any reason why a fetal Hgb screen cannot be performed before WinRho is given? (The process at our hospital is: 1. When cord blood type is found to be positive, in an Rh-negative mother, the blood bank issues the Rh immune globulin (RhIG) and the Fetal Hgb screen is ordered. 2. The RhIG is given and the following day, the Fetal Hgb screen is done and if positive, additional RhIG is given as needed. We are prompted to enter the test when RhIG is issued, because those moms are the only ones who need a Fetal Hgb screen. I think we could be doing things more effectively. Save mom an extra needle potentially, and do things in a logical manner by assessing the required dose before giving any RhIG.)

A: (ES) The key reason to give at least one 300 mcg dose of RhIG before testing is complete is to ensure that mom gets a dose before she leaves hospital. Remember that blood bank operates all night (which is when babies seem to be born!), but the lab that performs quantitative fetal hbg test (Kleihauer testing) may only perform that test during Monday to Friday 0800-1600 hrs. I do not advocate changing your practice as it may result in missing RhIG administration in women who need it. You may want to audit your practice to see how often your process results in moms needing additional injections.

Q: At what temperature and/or unit number do you consider using a blood warming device?

A: (ES) A blood warmer should be used in any setting where massive transfusions occur or are anticipated. Its use is best instituted before the patient's temperature drops.

(JB) Temperature preservation is important and should be proactive. A patient temperature of 35°C or below translates to poor patient outcome.

Q: Would recombinant Factor VIIa be considered in a post partum hemorrhage or massive bleed?

A: (ES) There is no evidence for the benefit of this agent for off label use (ie. in any setting except hemophilia with inhibitors and bleeding) but there is evidence indicating that rFVIIa increases the incidence of arterial thrombosis when used for these off-label indications. Hence, I do not recommend its use in management of massive haemorrhage.

Q: What is the percentage of venous thrombotic events **(VTE) events among obstetrical patients treated with Tranexamic acid for PPH?**

A: (ES) There are no reports of increased rates of VTE among obstetrical patients treated with Tranexamic acid. The drug is also routinely used in joint replacement surgery and cardiac surgery, which are also high risk for thrombosis setting and its use has not been associated with increased rates of thrombosis.

Q: In cases of miscarriage early in pregnancy (20-25 wks or less) is a fetal bleed screen (or rosette test) required in addition to administration of RhIG for Rh negative mother? Or is the one dose of 300ug sufficient to cover bleed at this gestation?

A: (ES) As there is usually not significant fetal-maternal hemorrhage at that early stage of pregnancy, 300ug of RhIG is usually sufficient.