Clinical Chemistry

Uterus Transplantation—Current Evaluation, Monitoring, and Emerging Diagnostics

Article:
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Clin Chem 2026; 72(1): 18–26. https://doi.org/10.1093/clinchem/hvaf143

Guests: Dr. Liza Johannesson is the Director of Uterus Transplant at Annette C. and Harold C. Simmons Transplant Institute at Baylor University Medical Center and Associate Professor at Texas A&M, TCU, and Rush. Dr. Massimo Mangiola is a Clinical Associate Professor at NYU Grossman School of Medicine and NYU Langone Immunogenetics Laboratory Director.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett.

For women with absolute uterine factor infertility, uterine transplant offers the opportunity for pregnancy and childbirth that would be unavailable through other means. With the first live birth following uterine transplant documented in 2014, this number has increased rapidly to more than 100 successful transplants and 50 live births in subsequent years. Within the spectrum of solid organ transplants, uterine transplant offers unique considerations and challenges. For one, the graft is not intended to be permanent. Additionally, clinical teams must weigh the needs of both the expectant mother and developing fetus when making care decisions.

The field now finds itself at a transition point, moving from largely experimental to clinical reality for an ever-growing number of patients. To ensure the success of this transition, a standardized approach to clinical laboratory support is essential. At each stage in the transplant process from preoperative evaluation of donor and recipient, assessment after surgery, maintenance of immunosuppression, monitoring of maternal and fetal health during pregnancy, and follow-up care of mother and infant after delivery, the clinical laboratory has many vital roles to play.

A new special report in the January 2026 issue of *Clinical Chemistry* provides a look at the complex field of uterine transplantation. Today, we're joined by two of the authors. Dr. Liza Johannesson is the Director of Uterus Transplant at Annette C. and Harold C. Simmons Transplant Institute at Baylor University Medical Center and associate professor at Texas A&M, TCU, and Rush. She has been working in the field of uterus transplantation for more than 15 years and her pioneering Swedish team delivered the first baby in the world after uterus transplant in 2014. Dr. Massimo Mangiola is a clinical associate professor at NYU Grossman School of Medicine and NYU Langone Immunogenetics Laboratory director with more than 20 years of experience in transplant immunology. And Dr. Johannesson, let's begin with you.

Let's just get with the basics here. Explain what is uterus transplantation and why is it important?

Liza Johannesson: Yeah. So uterus transplantation is a very new type of transplantation, of organ transplantation. In reality, it is a transplantation for fertility purposes, where we take a healthy uterus and transplant it into an individual who lacks a functioning uterus or doesn't have a uterus at all. It's meant for females with what we call absolute uterine factor infertility, which means that they are unable to carry a pregnancy because they don't have a uterus or they have a uterus that is not functioning in terms of pregnancy. And historically, this type of infertility was called the last hurdle of infertility because we didn't have any treatment available for these women and they actually had to look for adoption or gestational surrogacy if they wanted to achieve parenthood.

That all changed in 2014 in Sweden when the first baby was delivered to a mother that had received a uterus transplantation. With that, that last hurdle of infertility was actually treatable and was no longer a hurdle. From a scientific perspective, it represents a major advance in both reproductive medicine, but also transplant surgery because it's the first organ transplantation that is actually temporary. It's only meant to stay with the recipient for the time of pregnancy and childbirth, and possibly several pregnancies and childbirth, and it's also non-life saving organ transportation with only quality of life purposes. So, the field is very novel both in terms of reproductive medicine and transplant surgery.

Bob Barrett: That is fascinating. Now you started answering this. I'd like you to delve a little deeper into it—who is a good candidate for a transplant?

Liza Johannesson: Yeah. So a good candidate for uterus transplant is typically someone who was born without a uterus or has undergone previous hysterectomy due to disease or postpartum bleeding or tumors of the uterus, but apart from that, that is otherwise healthy, has healthy ovaries, and wants to carry a pregnancy and give birth. The candidates must be not only wanting thing this, but they must be medically fit for major surgery, and they should also be medically fit for having immunosuppression therapy, because immunosuppression, you have from the time you get transplanted until you remove the uterus, and that means that there is risks to their general health.

Another important thing with these candidates, that we evaluate them in a psychological way. So they need to be prepared and they need to have a good support system before they go through this transplant.

Bob Barrett: Who are the donors? Where the uteri come from?

Liza Johannesson: So it's an interesting transplant because you can use uteri from both living donors and from deceased donors. So when you look at the living donation first, you can either have what's called a directed donation and that often comes from a relative or a friend of the recipient, but you can also, and we've had that more commonly here at Baylor, something called non-directed living donation, where an individual volunteers to donate her uterus without having a prior relationship with the recipient. And it's been interesting here at Baylor, because when we opened the program, we all of a sudden had all these women from all over the US calling us and wanting to donate their uterus and to date, we have more than 2,000 women that wants to give up their uterus.

So it's quite remarkable what people are willing to do for someone else to become pregnant and carry a child. All the living donors of course undergo extensive medical evaluation and also a psychological evaluation much similar to that of the recipient, but they go through importantly, and that's very important, is that we make sure that this living donor herself are done with her family formation, so she doesn't want any more children.

When you look at the deceased donor uteri, those are retrieved from organ donors after death and that is often done at the same time as other organs are retrieved from that donor. Of course, that is an easier process in terms of that it's limiting the surgical risk to a donor and potentially expands availability of donors although we have, note, this many living donors that are willing to give up their uterus.

In terms of outcomes, successful pregnancies have been reported both using living and deceased donor uteri. We are now focusing on comparing the outcomes, but so far, it looks like they are the same.

Bob Barrett: As we mentioned in the beginning of this podcast, you've been a part of this field for many years. How has the field changed over time?

Liza Johannesson: Well, I think that's the most interesting part of this because this field that was so novel and so science fiction, has evolved remarkably. So in the early days, we focused a lot on the animal models and to prove that this was even doable, the surgical feasibility. Whereas today, we have all these successful pregnancies and live births, so now, we have perfected the surgical techniques. We have better immunosuppression protocols that are tailored to the patients and we are much better at patient selection as well. So the focus had shifted from proving that this is actually feasible to understanding how to make this safer, more efficient, and

more accessible. It's actually just today that we are starting to see trends, because now, we have the right amount of numbers so we can guide patients in terms of the outcomes and the risks associated with this.

Bob Barrett: Well finally Dr. Johannesson, what would you say is the greatest challenge for the field of uterus transplantation today?

Liza Johannesson: Yeah. I think the greatest challenge has been and will always be the balancing of the risk and benefit in this because it is a non-life-saving surgery and it involves a huge complex surgery and also immunosuppression that carries great risks for both the living donor and the recipient, also the child. So the challenge has always been to reduce surgical morbidity and to minimize that immunosuppressive exposure, and you have to remember that we have to think about three parties in uterus transplant, at least, because you have the donor, the recipient, and then the child or the children in this, and those are of course, their safety are key priorities.

The other thing that we are focusing on now, and it's a challenge, is because insurance rarely covers this procedure. It's mostly today available through very, very few specialized centers and that makes it very hard for patients to access. So the whole field is not focused on not just improving the procedure itself but also gathering evidence that we need and numbers that we need to make uterus transplant more widely accepted and approved in more settings, more countries, and eventually if we can show that it's a real benefit, to make it covered by insurance, at least in part.

Bob Barrett: Well, thank you for that. That is really fascinating. Dr. Mangiola, let's turn to you now. Can you explain in simple terms what molecular HLA compatibility is and why this is important?

Massimo Mangiola: Thank you. Yeah, simply put, the current method is superficial and insufficient for matching patient donors because it doesn't address the differences between the patient and the donor of what is relevant for the immune system and what the immune system uses to generate and start a rejection response.

Currently, when we compare a patient and a donor, we look at the nomenclature number of the HLA, those tissue antigens, and we compare the patient tissue antigens with the donor tissue antigens by their number. However, this number doesn't tell us anything about what is different in the donor, in the organ, and especially those differences that are what the immune system of the patient looks at for determining whether or not to reject the organ. So, the current method is really not a true measure of the risk for

rejection post-transplant. This molecular HLA compatibility can do that. It is a method by which we can identify and quantify this difference. We call it amino acid differences, and those amino acid are really important because when the immune system detects a sequence of amino acids that is non-self, it reacts to it and it causes rejection.

Let me give an easy example. I live in New York City and of course, just have to make a sport example. Let's assume I want to go to a game and I want to go buy an Aaron Judge Yankees shirt. So I want to go the sport store, and there is no Judge, there is no jersey for Judge. What is my next option? Should I just get any jersey, perhaps one from the Red Sox instead? I don't think so unless I want to get arrested in New York City, right? My next best option is something that is very similar to what I want. So the closest thing that I should get for me is any other Yankee jersey because the only difference between what I want and what I'm getting is perhaps just two things, the number and the name in the back of the shirt. If I get anything else, which is what we do these days, the difference might be anywhere between 3 and 200. Those differences are really important to the immune system. So these things, we are trying to understand how we can implement this mechanism of identification of those difference in the allocation of organs, which of course is not something that is easy and/or achievable in a short amount of time.

Bob Barrett: And finally, just how important is early detection of transplant rejection and are there better, safer, more reliable ways to monitor for that?

Massimo Mangiola: Thank you. That's a very good question. So also, this is something like, it's a kind of a big miss in the field because the way we usually monitor for post-transplant problems, so rejection, is by detection of antibody—they are directed against the organ, the target, right? However, when an antibody is detectable is when the immune system has had the opportunity to be activated against this non-self entity, the organ, and is perhaps a little bit too late. So what happens to physicians like Dr. Johannesson and her team is that they are running on catching up, right? There is already an immunological event. There is physical evidence of the activation of the immune system and the organ is under attack, and what they need to do is try to reverse this immunological response, and sometimes it is possible, sometimes it's not. It depends on large number of factors. So the key here for poor transplant monitoring case, to have biomarker that will allow you to tell you that an immune response is happening.

So, at a time where there is no clinical evidence of the response and there is a very large number of biomarkers,

some of which we already know and we use, and some that are under investigation. The early detection of the activation of the immune system will allow physicians to intervene in a much lighter way with just small changes in the post-transplant monitoring and the post-transplant treatment and prevent the generation of the antibody and the generation of T-cell rejection. One of the most used these days is this biomarker we call cell-free DNA. So when there is a damage in the organ, any organ, the cells of the organ are under attack from the immune system and they are killed, and when this happens, the DNA of these cells goes in the blood. So with a simple blood collection, we can detect and identify the presence of donor-derived DNA, which is indicative of an attack to the organ that might occur even when we still do not have clinical indication or rejection.

Other biomarker, they are under investigation, are all the activation of genes that guide the immune system in to respond against an organ and there is a very large number of T-cells and B-cells genes that are telling you that the immune system is being activated. And usually what happens is that you can detect these changes one to two weeks before any clinical indication of rejection. So the key and here, the importance of these is two folds. One is that the way in which we can better define rejection these days, especially subclinical rejection, is by doing an invasive biopsy, and every time you do a biopsy, there is a risk to cause additional harm to the organ and to the patient, and it's also late, right? So finding those biomarkers, they allow physicians like Dr. Johannesson to have the information that something has changed and she must intervene to prevent the rejection, is incredibly important.

Bob Barrett: That was Dr. Massimo Mangiola from NYU Grossman School of Medicine in New York City. He was joined by Dr. Liza Johannesson from Baylor University Medical Center in Dallas, Texas. They wrote a special report in the January 2026 issue of *Clinical Chemistry,* describing current and future diagnostic tools to support uterine transplant. They've been our guests in this podcast on that topic. I'm Bob Barrett. Thanks for listening.