

**SPEAKER 1:** --the living donor graphed-- what's the amount of time of ischemia that might be incurred with the traditional adult-to-adult living donor transplant? Chris mentioned how important it is to minimize it. What's the expectation there?

**BENJAMIN SAMSTEIN:** So basically, we routinely time the operations ideally so that they're-- the donor and recipient-- are occurring simultaneously. And essentially the recipient liver comes out, the donor liver portion comes out and is walked over to the recipient room, prepared rapidly, and the amount of ischemic time in what we call "cold ischemic"-- the standard bag of ice-- is under an hour.

**SPEAKER 1:** Great.

**BENJAMIN SAMSTEIN:** And I think that that can help if we-- as ischemia/reperfusion, and the injury associated with it-- while we often see function in deceased donors, even out to 12 or 14 hours-- the shorter we keep that ischemic time, the better in general. And that's why these issues of trying to minimize ischemia/reperfusion injury. But in living donation, we try to keep it as short as possible, and usually under an hour.

**SPEAKER 1:** David, did you have--

**SPEAKER 2:** So, Ben-- I have a question, maybe for the audience. You talked about which recipients would be good for a living donor, but I think-- what is your criteria, or who do you think of as a potential living donor? You know at Penn, we have our criteria like age, medical history-- because I think you know what you're thinking about you're talking to your patient, and they say, well who could be a donor? What is your criteria-- Columbian, sort of? As for people here in Michigan, what might be what you think about as a potential donor?

**BENJAMIN SAMSTEIN:** So we've developed a protocol together. But in general, I would say that living donors have to be healthy people. Basically, we've chosen people who are 20 to 55. They can't have diabetes. They can't have morbid obesity, so their BMI has to be under 35. They can't have other serious co-morbidities and that.

But at the same time, what we've tried to do is encourage people to consider it. So as long as they don't have diabetes-- as long as they are healthy, and in that age group-- we've encouraged people to-- for example, sometimes people get confused as to what we think co-morbidities are.

So if I have hypothyroidism and I had to have my thyroid out, or I have to take Synthroid, is that a serious condition? Well that would not be a serious condition for excluding someone from living donation even though someone might say, well it's a chronic condition and I have to take medicine the rest of my life. That's an example. Or I had a history of a breast biopsy and I have to undergo screening-- that might be another example in which we feel that's an appropriate candidate for a living donation.

**SPEAKER 1:** There's another question for both of you. How many living donor centers are there in the United States? And you told us a little bit about the learning curve. What is that about?

**BENJAMIN SAMSTEIN:** So there are-- so I think it's important to understand the context of how many hospitals do liver transplants. So there are about 6,000 hospitals in the United States. Or Somewhere around 135-- 100 do liver transplants. So a very small percentage of the hospitals in the United States do liver transplants. And then living donor is done at about 35 to 40 centers, with about 10 centers having a significant portion of their transplants. So it's a relatively small percentage of the transplant programs, but transplant programs are an even smaller percentage of hospitals in general.

**SPEAKER 1:** And, Chris-- you mentioned that there's this study going on. What do you tell a patient about there's this new technology? Is it proven from that European data? Is it just a formality that we have to wait for? What do you tell patients?

**CHRISTOPHER SONNENDAY:** I think-- I mean-- so, this is an investigational study. So patients that agree to participate are consenting to a research study, and there is some uncertainty in that. I do think that this is a kind of a phase two / three study in that all of the organs that would be transplanted out of this study-- whether you're randomized to cold storage, or you're randomized to the preservation device-- are organs that we would otherwise take.

So we're not picking donors that we don't want to use, see how they perform on the machine, and then deciding after that whether or not to transplant them. That study that I just described is actually going on in the UK right now. And as you can imagine, there's more risk in that type of study because those are organs that we're not used to using.

But in the US trial we're essentially comparing standard organs-- or at least organs we would currently utilize-- with a different preservation technique. So I think from a safety perspective, there are certainly unknown risks. The European trial was very successful in terms of no surprises or device failures or things like that. But it is a research study, and patients need to realize that.

I will tell you that just totally anecdotally that this is the type of thing that our patients are very enthusiastic about. They see this as the potential for a way to expand-- eventually-- the field and contribute to the growth of the field.

You know, I think the liver transplant population is interesting. In kidney transplantation and Ben alluded to this a little bit-- in kidney disease, people do have this alternative. It's not a great alternative, but there is an alternative of dialysis. So kidney patients are often willing to wait, so to speak, for the ideal transplant, if possible-- particularly younger patients that tolerate dialysis OK.

In liver disease, it's different. Our listed patients are thinking, talking about, worried about their mortality every minute of every day. Our nurses and social workers that are here in the audience can tell you those are what their conversations are about. And so the willingness of patients to consider living donation-- which is a growing part of our field, but new-- an experimental trial like this is kind of greater than average because they realize what they're up against. I mean, that gap between the patients we currently transplant and the number of patients that need an organ is profound and scary to people.

**BENJAMIN SAMSTEIN:** Can I make a comment? One of the things in liver transplant is talking to patients a lot about risk. So Chris mentioned that the organs were transplanted last year were up substantially. Again-- basically the reason they were up was due to the heroin epidemic in the United States. And if you take that to a logical thought process, that means that donors are overdosing on heroin and becoming donors.

So the conversation that you're having with recipients is that the donor died of a heroin overdose. There's risk. And most heroin is injected through your veins with risk of disease transmission. And even though we test donors for HIV and hepatitis C and hepatitis B, there's still a window period. There's risk inherent in donors.

I like to tell my recipients if you think that the donor liver was made in a factory, or is going to be taken from a 21-year-old nun walking out of the nunnery who just happened to get a bullet in the head-- I'm sorry, that's a terrible thought-- I understand. But people want this idea that it's totally clean-- that there's no risk involved. That's not who our donors are. Our donors-- they drive too fast, they eat, they drink, they do drugs-- that's who donors are. And so, in that context, having a discussion with them about this-- I think is-- because you're talking about risk. You're not talking about that factory that had that contamination issue. You're talking about risk all along the discussion.

**SPEAKER 1:** One other question for Ben is-- on a practical basis, you said the donors have to be completely healthy. They're in the prime time of their working years and making money-- maybe have families, et cetera. What do you tell them how long it's going to be before they can go back to work-- before they can drive a car-- before they can exercise-- what are the sort of practical things? And maybe you could tell us how that differs from donating a kidney, just to get perspective.

**BENJAMIN SAMSTEIN:** So let me start with a kidney. Most donors for a kidney will stay in the hospital one to two days. They will usually feel comfortable returning to work in about three or four weeks. And they're usually off of pain medicine and therefore can drive, somewhere in the middle range between one to two days and three to four weeks.

So most of the time, we tell them you should probably shouldn't drive for your first post-op visit, but after that you're probably OK to drive. And that you can return to work in three to four weeks. Of course, it really depends on what your job is. For your-- if you're a police officer or a very physical job, you know, where you have a lot of lifting to do, or you're crane operator, whatever it is that's very physical, then you should take longer time off of work.

For a liver donation, we basically tell people it's about twice to three times that of a kidney. So we tell people what your hospitalization will usually be five to seven days. You should plan to be on pain medicine for about two weeks. And you should plan to be out of work-- I have this whole formula where I basically tell people for every 10 years-- so our average donor is 40-- for every 10 years you are under 40 you get to subtract a week. For every 10 years you are over 40 you get to add a week. And then people usually say but I'm in great shape, and I'm like, all our donors are in great shape, that's why they're donors.

So compare yourself to when you were 20 if you're 50-- you're probably not as fast as you were when you were 20. And so your recovery is related to your age. So our 50-year-old donor should anticipate that their recovery will take more in the 8-12 week range and my 24-year-old donor from last month went back to work three or four weeks after donation. In general, we say about twice to three times that of a kidney.

**SPEAKER 1:** And Chris, what do you think about that? Is that a reason why a lot of people don't donate? We know economic times, and so on-- two to three months can be quite a bit, or your job is gone. What can you do? Is there any legislation, insurance?

**CHRISTOPHER SONNENDAY:** So it's a great point. In fact, there's data to support that kind of conjecture that you just made. In fact, if you look at the financial crisis that we just went through in 2008-2010 range, living donation actually decreased during that period. And it was thought to certainly be because people felt less comfortable leaving their jobs or less financially secure taking time off work.

You know, I think there are-- as I think Ben laid out, particularly in living liver donation-- the majority of time there is a close emotional connection between the donor and recipient, and they're watching their potential recipient literally waste away in front of their eyes, so the decision-making in that way is a little more urgent and easier from that standpoint.

But there are certainly people who-- financially and otherwise-- just can't afford that time off of work. There is a program called the National Living Donor Assistance Center that provides grants to living donors that meet certain financial criteria-- that helps mitigate the cost of being off of work.

Just so people understand the financial arrangement, the health care costs incurred by the donor are paid for by the recipient's insurance. But there is no subsidy given for time off work and things like that. That's been hotly debated in national circles but that does not exist. That would be considered paying for donation, which is currently illegal. So it is a financial hardship for many donors, but there are some resources that can be brought to bear in certain cases.

**BENJAMIN SAMSTEIN:** So I just wanted to follow up on that. So, a couple of things-- one is the most common job that donors have is probably related to this issue. So teaching-- so a couple of things we know about living donors. So women are more likely to donate than men, they're are a higher proportion--

**CHRISTOPHER SONNENDAY:** Every woman in the room is like, yep.

[LAUGHING]

**SPEAKER 1:** And at this time, this is liver, is that right?

**BENJAMIN SAMSTEIN:** That is true of both liver--

**CHRISTOPHER SONNENDAY:** That's true in kidney.

**BENJAMIN SAMSTEIN:** --and kidney. And one of the largest professions in the United States is teaching-- which usually, in many places, has both disability benefits and ability to take time off. And if the operation can often be coordinated, can be coordinated around periods of time where the donor might have less job responsibilities.

The second most common profession is nursing.

**SPEAKER 1:** A lot of people shaking their head.

**BENJAMIN SAMSTEIN:** I will tell you that physicians are much less likely to donate. They're kind of like gave-at-the-office type of people. But again, related to how many people are in a particular field, many nurses have benefits that enable them to-- one, have disability, so you can go out on short-term disability and recoup a lot of your income related to that. A lot of employers recognize that nurses can go out for a period of time and they can, therefore, have security about their job.

And then there are also a number of states, including, for example, New York state, where donors are allowed to take a tax deduction due to lost wages. So in New York state, if you lose up to \$10,000 you're allowed to deduct that from your taxes-- so enabling, actually, a refund. And there are a number of states that have-- so you know one of the things that we talk about with donors is the process of minimizing the financial impact of donation because it can be a substantial financial impact, but it can be often minimized.

**SPEAKER 1:** David? Yeah.

**SPEAKER 2:** So I guess one point and one comment. Just the point is-- the letter of the law is you can't financially gain. So we tell our donors the recipient-- if they have the means-- can reimburse lost wages, and many donors will set up GoFundMe pages. And if that amount that they get is not exceeding their wages that also is legal.

**BENJAMIN SAMSTEIN:** Allowable.

**SPEAKER 2:** Yeah. My disclosure is that also Ben actually took a piece of my friend's liver to help save her niece, so I obviously am supportive of living donation. But Ben, what do you tell your donors? So a kidney donor-- for the rest of their life-- they have one kidney. For that liver donor, how do you tell them it will affect their long term health-- their ability to have kids-- things like that, because I know those questions come up, especially with-- young women ask me that question a lot.

**BENJAMIN SAMSTEIN:** Yeah. So I try to be as transparent as possible about what we know and don't know. So the first adult to adult-- the first living donor in the world for liver was 1989. That person-- basically the very first transplant in the United States-- she is 25 or 26 now. She's a social worker at the University of Chicago. The recipient-- her mom-- was the donor. And it's relative-- in contrast to kidney donation, which was 70 years ago, we have less long-term follow up. And I explain that the procedure itself is relatively new when we're talking about a lifetime of follow-up-- we have a procedure that's 25 years old-- 27 years old.

But I will say that we have followed-- as part of the University of Michigan and New York Presbyterian Columbia-- we're part of a multi-centered consortium along with the University of Pennsylvania, in which we've followed donors for up to 11 years. And we did not see the development of liver failure in an expedited or accelerated way for donors in any way. And in fact, what we know is that the liver regenerates in a way that is different than kidney.

We know that the average liver volume for donors at one year is-- so you have a liver that-- let's say-- weighed 1,000 grams. We remove 600 grams for donation, so now you're left with 40% of your liver volume. By a year you're usually around 93%, so you're up to 930 grams and you're at 93% and there's no diminution from there.

So at least as far as I-- and anecdotally, we see lots of donors resume all sorts of normal activities, including pregnancy. It's our recommendation, in fact, people actually try to avoid pregnancy for 6 to 12 months. They sometimes do. It's our recommendation. They don't always listen to it.