

So I'm going to talk about the topic that's important to you if you want a kidney, and that's how you get one.

So just some numbers first. So there's 400,000 people or patients on dialysis in the US, and of those, about 1/3 are listed for transplant. 18 patients on the list die per day while waiting for a kidney. And everyday we add 110 patients to the wait list.

And we do about 19,000 transplants per year, of those over 7,000 living donors. And the rate of unrelated living donor transplants have tripled. So that's, of course, a huge source of potential donors for those who don't have family members. So there is an increasing need for living donors, because most of the cadaveric donors are old and not suitable for donation.

So these are as of yesterday the UNOS wait list data. So there's 95,000 patients on the kidney list, 113,000 total for all organs.

So the benefit of transplant is that you would have a longer life expectancy and obviously no more dialysis and fewer dietary restrictions. You can return to your lifestyle and work, and you can travel without having to make arrangements.

So the people that live 10 years later, most of them had a successful transplant. So fewer patients that remain on dialysis are alive 10 years later. And actually, National Kidney Foundation data suggests that only 30% of patients are alive at six years, which is the average wait time for a cadaveric kidney. So 70% of everyone who don't have a living donor cannot get a transplant because they are not alive.

So this graph shows the increase in life expectancy after a transplant. So the blue line is the normal population. Of course, the older you are, the less expected life you have left. The red line, though, are those patients on dialysis. And it's really depressing to see that even the young patients, 20-year-olds, only have a 15, 20-year-old lifespan ahead of them. And the green line shows the potential of increased life expectancy after a transplant.

So if you add this whole volume-- this doesn't work. So it's a lot of years that all these patients can enjoy after a transplant.

So the transplant process, it starts with having kidney disease. And then you get education about options, hopefully, from your nephrologist. Then you get a referral to your transplant center. If not from your nephrologist, you can self-refer to a transplant center. Then you get evaluated by us, and we evaluate everyone.

And then if you are approved, then you can get listed for transplant. Immediately then we start looking into living donor transplant, which is the better option. And then the best way is to list before you need dialysis, but then eventually you may need to start on hemodialysis or peritoneal dialysis. And during the wait time, you will undergo yearly reviews by our team. And we call it wait list management. And that's basically optimizing the health of patients and making sure they get all the consults and so we can identify contraindications to transplant.

And if we did a transplant missing some of these contraindications, then of course we could fail and the patients would do worse than having the transplant. And then if you didn't have the living donor transplant, eventually off the wait list you get hopefully then the cadaveric transplant if you're one of the 30% that are alive at six years.

So the cadaveric transplants are managed by UNOS. So it's basically an extension from the government. So it's a government contractor. It's a nonprofit organization, and the members are all stakeholders in transplants.

So the job is for UNOS is to balance the efficacy of a transplant to equity, that everyone should have access to a transplant, but of course we want to focus on those patients who are expected to have better outcomes. And we would like to not have any inequalities in the system. So it's tricky, and it's an ongoing process. So I'm going to discuss a little bit how this works.

So UNOS was formed after the 1984 National Organ Transplant Act. And part of this act is that we prohibit, or the government prohibit buying and selling of organs. They formed the OPTN, that licenses out UNOS how to manage the organ allocation. And it also established a scientific registry of transplant recipients, which is extremely important for us to track outcomes and optimize management and optimize care.

So OPTN and UNOS facilitates organ distribution, establish equitable policies, and maintains the national transplant wait list, monitors members for compliance. And I'm going to go through next slide who is a member. And they also collect, validate, or report transplant data, which is all available on their website. So there's a treasure trove of information available on these websites. And they also do a lot to promote organ availability.

So the members of UNOS are transplant centers, organ procurement organizations, and here we have core histocompatibility labs are members. And they do the cross matching and HLA typing. Public organizations, medical scientific organizations, and then individual members. I'm not really sure who these individual members are.

So the organ have to be matched with a recipient. So we have patients listed. They are entered in the matching system. And then for each potential donor, there's a list of recipients that is generated. And when those two meet, then we can call in the patient, we can get the organ to our center, and then do the transplant. So that's what I'm going to talk about next here.

So UNOS continuously develops and modifies and optimizes their policies. So they try to address different issues. So they get public comments, and they also get input from the transplant community. And then there are different committees within UNOS, they report to a board of directors, and then a policy is generated.

So it's a flexible process, but it can also be a very cumbersome, a very complex process. It took-- the last change in allocation took I think three to four years from start and comparing different policies and checking potential outcomes with computer simulations and everything. And it could be as fast as three months or as long as several years.

So at UPMC, this is the process, how you get from evaluation to the transplant. So we start with the evaluations. Then that includes a physical exam, routine labs. And then we do special testing. We check blood group, of course, and HLA antigens, so we can match it with appropriate donor. We check for antibodies. We also have to make sure that the patient has a good chance of succeeding by having adequate social support, psychological optimization, and dietitian and pharmacies also involved to make sure the patients are good candidates.

And then we need to get insurance input, very importantly. And then when all these pie charts are checked, then our committee as a whole then approves or declines a patient. So typically, if we decline the patient, that's because they would do worse with transplant and we would cause harm. So we try not to do that.

The medical evaluation includes establishing the primary cause of kidney failure. That can help us assess the risk of medical or recurrence or kidney disease. We also make sure that the cardiovascular system is optimized, and that's normally the most common reason why we decline patients, that their heart wouldn't tolerate a transplant. The risks are too high. They wouldn't survive the operation. We also need to assess cancer, and we also try to optimize obesity. We look for infections and other-- so anatomical issues.

Absolute contradictions is the top one, not expected to live long enough to make the transplant sort of successful, immune concerns. If you have an active malignancy, we could really make you worse-- sorry. With a transplant we could kill you, and we want to avoid that.

Active infections are no good, either. Psychiatric, behavioral, social issues. So we can do a perfect transplant, the patient can be all excited, but then they can't get to the transplant clinic. So we've had patients who get in real trouble because they simply can't get to us.

But the important thing here is that there's no one that should not come to evaluation. We will see anyone. Even if we have a BMI cutoff of 40, we would be happy to see patients of BMI of 55 so we can discuss the rationale for why they should try to lose weight, for example.

So our cardiovascular workup includes for those who have had diabetes for 20 years, we do left heart cath, because a stress test is often false negative and those patients. We do a left heart cath. We do an echo pretty much for everyone above a certain age, and with any changes on the EKG. And we do non-invasive stress tests on almost all patients over 50.

We do vascular assessments. We have to have targets to do the transplants. And if we have a young, healthy patient with good pulses, then that's all we need. Otherwise, if you're diabetic for a long time or have other issues with claudication, we may need a CT scan to make sure that we have targets to plug in the kidney.

So it's a multidimensional assessment. And we discussed the-- so the functional component is important. We hope that with a successful transplant, patients can improve the functional status. But if somebody is basically bedridden and with low potential to improve, then a transplant won't really help that patient.

So then living donors. So that's a key. So the donor, of course, should be willing. We cannot force anyone, and we shouldn't force anyone. That's illegal. So the donor has to be able to consent. That means they have to be over 18, and they typically have to be less than a certain age.

So this is a little bit a gray zone. So in the US, the oldest donor I know of was 84. Typically, they're limited because of medical problems. Their kidney function may not be good enough, or they have heart limitations. But we do not really have a fixed age limit. Any patient can have any donor of any gender or any race, blood group compatible and cross much negative for the actual donor, but if your donor is not, then we can do all these swap programs.

Related donors in our mind is a parent, sibling, or a child. Everyone else is an unrelated donor, and that's the group that has increased the most. And then of course, the donor needs to be healthy enough to undergo the surgery and we need to eliminate or address the risk factors that we know can cause them to have kidney failure in the future, like obesity or diabetes and things like that.

So after evaluation, we then review the patient and we list the patient. So then we notify UNOS and we give information to UNOS about HLA typing and blood typing and everything, and we notify the patient and their physician. And then that's start of the wait time. And wait time is on average, six years here. And of course with a living donor, you don't have to wait.

So things for patients to know that you're not on the list just by going to the evaluation appointment, like I've described-- you have to complete the testing, and then be reviewed and approved. And then we need to maintain your health, make sure you have all the necessary components to have a good outcome while on the wait list. And then patients can always call UNOS directly if they have any questions about their listing status. So a couple of years ago, UNOS changed how kidneys are allocated, and they tried to fix a couple of problems I'm going to detail next, but in the past, it was mostly driven by wait time.

So you got one point per year, and then you got some extra points if you had a good match. You got some extra points if you had antibodies previously formed-- so typically, patients can form antibodies from either previous transplant, pregnancy, or a blood transfusion, or exposure to allogeneic tissue, like heart valve or something like that. You got extra points if you were pediatric recipients or if you had previously donated a kidney. So there were problems with this-- so we lost effective years the kidneys could work in the recipient.

So we didn't optimize the matching, so young, good kidneys went to older donors because they had more points on the list, and that's unfair, because the kidney then lost a lot of functioning years-- so there was a mismatch, so we could fix that. And then it was unfair to those who were heavily sensitized in the past, so they didn't get enough points. By math, we could figure out that if you had 99% or 100% sensitization, you have to wait 212 years on the list, and few patients make that. Many kidneys were also discarded. And there was a poor use of marginal organs, because they weren't offered to the right patients.

And there were also lots of variances and payback systems within the organ procurement organizations, so it made it very cumbersome, and we lost quality because the kidneys had to be shipped around the nation unnecessarily. So these things were addressed. So this is just an example on the years lost. So we tried to have the kidneys that are expected to work a long time go to go to patients that are expected to live a long time, so that means that the best kidneys should go to very young recipients.

This is the donor quality. So this is more detail here. So we tried to more granularly describe the expected outcome of a kidney. So a kidney that has several strikes against it may work great for a patient who's 82, but that same kidney may not work great for a patient who is 11 because it's not expected to work a long time, so it's hard to see, but the graph to the lower right there, those curves-- the curves dip down, so the higher the KDPI number, which is the quality number, the less time is the kidney expected to function based on historical data from the previous three years.

So we know that the KDPI number, the donor variables, directly impacts the longevity of the transplant. So for example, donor age, race, ethnicity, hypertension of the donor, diabetes in the donor, serum creatinine at death of the donor, and then the stroke, or how the patient died has an impact. And then size of the donor, and whether it's brain-dead or a heart-dead donor matters, and whether the donor has hepatitis C or not. So all these 10 factors are weighed into this KDPI number, so then we try to optimize things.

So on this graph, you can see the-- let me go back. So the goal is to get off dialysis. So if a patient is old, or has been waiting a long time, then it may be worth to have a shorter wait time to get transplanted to get off the list, and so you have better survival with a marginal kidney than no kidney. So it's better to have creatinine of 2.5, that maybe you could have 1.5 with the best kidney, but it's better to have a creatinine of 2.5 and alive than not. All right-- so we remove patients on the wait list.

So we try to keep patients on the list until they're no longer transplantable, and they would be non-transplantable for reasons listed here. So for example, you could have a deceased donor transplant; you could have a living donor transplant; you could have deterioration of your medical condition, so you're no longer a candidate; or you could have died, then you're no longer on the list; and other reasons listed below there. So if you in the past had a PRA of 80% to 100%, meaning highly sensitized, it was basically flip of the coin whether you were going to get a cadaveric transplant or die on the wait list.

So to optimize the situation for those patients who, from no fault of their own, were sensitized, now we give a lot of extra points. So I mentioned the number 212 years, and now those patients get 212 extra years on the wait list. They get advantage to the point where, hopefully, they compete similarly to patients that are not sensitized. So there are different sequences then. So that starts with the kidney becoming available from a cadaveric donor, and then we'd look at the quality of that kidney. So the best 20% go to sequence A, and the worst 15% of kidneys go to the sequence D, and then in between sequence B and C.

And this is the details of those sequences-- so the best kidney here, sequence A, go firstly to highly sensitized patients; and then there's a big focus on recipient H-- so, local pediatric recipients and prior living donors are highly favored here, and those with good tissue typing, so the focus is on younger recipients. And for the sequence D, which is the worst kidney statistically, they are now focused on being offered to a national sort of audience quicker. The goal is to minimize the discard rate of those kidneys that could help someone.

In the past, they would percolate in our area for many hours, and then much later, they would be offered nationally, and then they would be too old, and nobody would want them, and then they would be discarded. So the changes seen by this change in allocation is that 8,000 additional life years gained per year, which is a big number. It also improved access for those candidates that are highly sensitized, as I described before, and also ethnic minorities were less disfavored with the new system, and that's mostly because the wait time before started with the listing-- now we can backtrack listing to when they started dialysis.

So ethnic minorities historically, and continue to, have later presentation to the transplant center, so they are more commonly listed after starting dialysis than majority ethnic groups. So early referral is key here, and the goal, of course, is to get listed before you start dialysis-- the outcomes are much better doing the transplant before listing, and the chances are much higher, of course, to get to that point is to have a living donor. So the transplant procedure here-- so the patient on the list can be called at any time.

If they're not in town, they need to contact our coordinator so we know if we need to call them earlier, or if we simply can't call them at all if they're too far away. And then we need the patients then to follow a post-transplant with our team and their referring nephrologist. So this is the unit. So UNOS manages the wait list, and when we are on call, we get organ offers. So this is what that looks like. So we get, on the computer, sort of a call that we have an organ offer, then we can log in and look at the details of the donor.

So this donor is in Pennsylvania. The donor is 67-year-old female, and the KDPI is 96% at this case. And then the computer system matches blood type, O here, with the recipient blood type O, and then this is the potential recipients. So here, we have crossed out the Red Cross to the right there some of these patients, and the list may go-- we may have to cross out many patients because unacceptable antigens. We do this cross match virtually with the HLA lab, so we can't offer the kidney to that recipient.

And then the list goes down, and down, and down. And to the left here, we have the sequence 20, 21, and it's not until-- let's see here. So basically this is what it looks like. So the list of patients-- and we evaluate each patient for each organ. We decide if this kidney is going to be good for these patients, and we talk to the patient. Are you interested in this kidney? And they may say no, and they do not lose any place on the wait list. Other things that go into the decision, of course, is to look at the details of the donor.

So we get culture results, we get CT scans, chest X-rays. We get laboratory values-- of course, creatinine is key for kidney transplants; and for pancreas transplants, we're interested in amylase, lipase as a marker for organ injury, and then we do provisional accepts for our patient, and then the donor team go to the operating room, and then it may fall apart because we may find a cancer in the donor, so then we have to cancel everything. All right. So organ donation is from deceased donors. Most common cause of death is stroke and trauma.

And brain death criteria are used thus define them by no brain stem reflexes. And diagnostically, we do that with a brain flow scan, angiogram, and an apnea test. And then malignancy would be an exclusion criterion for a donor. So it's sort of a complex dance here. So the prospective donor gets to the hospital with an EMS. They come to the hospital, they are recognized by the hospital staff as a potential donor, then they call CORE. And CORE then gets involved peripherally, and assesses the donor to see what happens.

And then the patient may or may not proceed to brain death, and then CORE takes over management of this patient because the patient is dead. Other donors are the DCD donors-- donation after cardiac death-- and that's a situation where the patient has no capacity of quality of life, even if they get out of the hospital. Then the family may honor the patient's living will and withdraw care from that patient, and then CORE also gets involved because we can use organs from those donors. So CORE manages the consent from-- if the patient had a first person consent, it should be in the driver license registry, and they have the right to go without a loan.

The family may protest, but legally they can proceed anyway-- but it's of course better to have the family understand why the donor made these wishes, and what happens from this point on. And then the organs are resuscitated, so CORE do a good job with managing the patients with fluids and blood pressure medications, and everything. Sometimes they're brought over to the CORE ICUs, which makes it easier for families and the transplant teams to do all these things. During the time the organs are placed, the surgical teams are called in, and it's a big organization that can take over 24 hours to do all these things.

And then after a successful organ recovery, then the kidney or heart or lungs are transported to the transplant center, and then we do the transplant. So what can be donated? So patients can donate heart, lungs, liver, kidneys, pancreas, and small intestine. Tissues can also be used-- for eyes, heart valves, pericardium for vascular surgery patches, long bones, connective tissue, and skin. So federal requirements demand hospitals work with OPOs, tissue, and eye banks, and they must report all imminent and completed deaths to the OPO, and the OPO decide suitability for donation.

And this is linked to hospital accreditation and Medicare reimbursement, so it's not voluntary at all. And then the OPO will audit all deaths in the area, and then the federal government also audits the OPO to have an expected utilization rate of organs. So if all of us decline organs for no good reason, then we'll all get investigated, so the government is a very active player trying to optimize the transplant care. So for organs, we look at blood type, size, location-- for timing issues, mostly-- organ quality, and how sick the recipient is. So all these things are entered into UNOS, and you saw what that looks like, how we review the data.

So brain death is determined by a total and irreversible cessation of the brain functions, including the brain stem. So we can do that clinically with the reflexes, or we can do it with confirmatory tests with EEG, angiogram, or blood flow studies. So this picture on the right shows absence of blood flow in the brain. Because of swelling, no blood can reach the brain. So this is Homer Simpson's brain. Dr. [INAUDIBLE] slide.

[INAUDIBLE] one of our fellow [INAUDIBLE].

Yeah. So the CORE team approaches the donor. So there is a watertight seal, basically, between the caring team for the patient and then the donor team. So we don't want to muddle the limit there, because there is a belief in some people that the hospitals are collaborating in producing organs, so of course that's not the case. So in the operating room, it's a crowded field, so there's outside surgeons. We have lung team and heart teams often fly in from afar. Normally the local team do the liver procurement and the kidney and pancreas procurement.

Sometimes distant teams come in, and then they procure all the organs, and we may get a kidney or pancreas from that team. But normally, in the OR, there is anesthesia, there's a nurse anesthetist, circulator, scrub nurse, and then the OPO coordinators and perfusionists, and then the liver team, abdominal team, are two people-- sometimes a different pancreas team is there with two people. Heart and lung teams usually have two people each, and then they also have their own [INAUDIBLE]. So there can be a lot of people, and it's typically at 2:00, 3:00 AM, and everybody's pushed to get back with a good organ to their home centers.

They have to time the cross-clamp of the donor with their teams, so it's a big, big process. So I'm going to go show too many pictures of the OR, but we dissect out the big vessels, and we cannulate the aorta, and then we cross-clamp the supraceliac aorta, so we then infuse called preservation fluid in the aorta. So that washes out blood from the organs we want to procure. So we cool them down and preserve them, and then we dissect out the vessels and the structures that are critical to each organ, so we start usually with the liver, and then the pancreas, and then the kidneys after that.

And the pancreas procurement is tricky because the anatomy is complex. Sometimes we cannot use the pancreas if the liver team needs vessels that maybe go straight through the pancreas. So this is what the pancreas looks like after it's out, and before transplant, we combine the two arteries that supply the pancreas to one. The kidney procurement is fairly straightforward. We grab both, and the ureters, and we hold them up, and then cut underneath to safely remove the vessels.

And we need to do this pretty fast, so from cross clamp to implantation, the heart and lungs only have four hours. Liver has about 18 hours effective time. [INAUDIBLE] 12 hours; pancreas, 16 hours; kidneys, up to 36 hours. But in general, for all teams, the shorter, the better. So there is a nice study from South Korea that looked at call times from cadaveric donor with only two hour-- so they were in basically adjoining operating rooms, so they had only two hours between cross clamp and transplant, and those results were as good as a living donor transplant.

So it's a delicate dance here. So the transplant team gets the offer, looks at the quality, contacts the patient, brings the patient in. We evaluate the patient, and then we wait for the recovery to happen, and then we go to the operating room, usually when the organ is at least on its way or here. And from the OPO perspective, they get an organ offer from the hospital, they go evaluate the donor, they optimize the donor, arrange for these multiple teams, and sometimes they have to call multiple teams because one team may provisionally accept, and then they decline because the recipient, after arrival to the hospital, was not deemed a candidate anymore.

Suddenly they have to start over, and their goal is to not waste an organ. So it's sort of a complex dance that's done basically several times a day. And that's it-- that's how you get your kidney. Any questions? Yeah?

Who watches the matches?

Who watches the matches? Well, so the donor--

Is there an actual person who is responsible for that, or how do you [INAUDIBLE]?

Well, much of that is automatic because when a potential recipient is entered into the system, we need to enter the blood type and unacceptable antigens. So for the antibodies. That predicts a positive cross match. So when there is a potential donor, all the recipients that are not compatible are excluded. So all donors only go to all recipients, and then only those recipients who have acceptable antigens remain. And then after that, they're ranked based on how many points they get, according to this formula.

But you're right-- sometimes we enter the wrong information into UNOS, and then we always catch that, because we do a cross match before we finally accept the organ. So sometimes, that happened recently where we didn't enter the correct unacceptable antigens, but we got a positive cross match, so we didn't do the transplant. Dr. Taylor had a question.

Martin, is there any way to figure out where your patient is on the list? That's a common question we get-- where am I on the list? Am I high level, am I low level, am I in the middle? Is there any way to figure that out?

Not to my knowledge. I think you can predict maybe a little bit based on how many years' wait time you have, but I don't think-- there's no effective answer because we may say you're on the top of the list, but you're not really, because there may be other patients that are listed the day before that get ahead of you, and there are so many factors, so you may not be a good candidate for this particular kidney, so I think that wait time is probably the best factor. So if you've been on the wait time for six years, it's about to become your time. Any other questions? Yes.

What sort of factors make you turn down an offer just based on an initial phone call? What sort of things [INAUDIBLE] right away?

Well, sometimes based on the history of the donor that they have-- most of the time it's unknowns that make us decline. For example, if somebody-- even if it's a great young patient, excellent organs, but they have a meningitis of unknown origin, then we cannot treat the recipient, and then we often decline, for example. But there are many things that make us decline. Sometimes, we don't decline until we have all the information-- the anatomy, and the biopsy of the donor kidney, and then also it depends when we decline.