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| TPWKY |  | This is Exactly Right. |
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| Carol Offen |  | I'm Carol Offen and 14.5 years ago I donated a kidney to my son, Paul. He was in college when he was diagnosed with kidney disease and it came totally out of left field. He was not someone with risk factors, he didn't have high blood pressure, diabetes, he wasn't obese, he was a skinny college kid and he was otherwise healthy. What he had was a lingering strep infection. But he was otherwise healthy and they said, well, we'll monitor it but it could be years, it could be 20 years before it ever got to kidney failure and by that time, you know, there's gonna be a cure or some great treatment, you know, so let's just watch it and put it on the back burner. Which we did, and a couple months after college graduation he went for his normal lab work and found out that his kidneys were failing and that within a few months he was gonna need dialysis but ultimately a transplant. |
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|  |  | And we were just blindsided. Everyone in the family said they wanted to be tested but my husband had had kidney stones, they eliminated him, our daughter was barely 15 at the time and they wouldn't even consider her. I was the only one who was healthy enough and the right blood type but anyone who knows me knows that I was not an obvious choice, I'm a wimp. I faint at flu shots, I've been known to pass out thinking about a blood test. So the idea of voluntarily giving up a bodily organ was not something that anybody thought that I would ever do. |
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|  |  | But when your kid's kidneys are failing and there's something you can do to change it, I think any parent would want to. And so we started the testing. And you name it, they did lots of lab work, chest X-ray, and EKG, and a lung function test and stress test and sent me home with a big receptacle for 24 hour urine collection. So it was incredibly thorough, I mean most of the tests are to make sure that you're healthy enough for yourself and that it's not gonna jeopardize your health. The testing went on for months and so I kind of went through all the phases of you know, do I really wanna do this, yes I do, no I don't, but by the time we went through advanced testing I was pretty sure. And I kinda wondered, you know, would I secretly be relieved if I found out that I couldn't? I mean, hey I tried, I did everything I could. And Paul, my son wouldn't think ill of me if it couldn't be. And I don't know when but at a certain point I realized no, I wanted to do this. |
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|  |  | Fact is he had no other options and he'd been on dialysis, he was on dialysis for 20 months and it was hell for him. He was depressed, it dominated his life, it was really rough and we watched him going through this feeling like there was no light at the end of the tunnel. And he was on the list for a deceased donor but the wait for a deceased donor was then and I think still is in our state 5-7 years. And the thought that this could go on and on longer was just unthinkable. And so yeah, if I could turn things around for him, you bet I wanted to. And I did. And June 27th, 2006 is still the proudest day of my life. And it was not only easier than I expected, it's major surgery of course but it's laparoscopic, I was walking the next day, I bounced back quicker and it was even more gratifying than I expected. |
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|  |  | I mean, I knew I'd be relieved and I knew I'd be thrilled because of the difference it was gonna make for my son but I had no idea what an incredible high it was gonna be, that it's just an indescribable feeling to know that you have made such a incredible difference in somebody's life, whether it's a loved one or not, just anybody, another human being. And I wanted to shout it from the rooftops. I'm an editor and writer by profession but I was intimidated by the subject and it was years before I wrote anything about it and years before I became an advocate, but I wanted to spread the word and tell anybody who'll listen and reached out to Betsy. |
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|  |  | Betsy and I know each other from when our girls were in Girl Scouts, I knew that not only had she had a transplant but she was kind enough to come talk to our son when he was on dialysis and give him some sense of how much better his life was gonna be when it finally happened. And I reached out to her, 'I remember you mentioning years ago that you were thinking of someday writing about donation and I kind of want to too. Wanna talk?' And she did and that was over six years ago. |
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|  |  | The title is The Insider's Guide to Living Kidney Donation: Everything You Need to Know if You Give or Get the Greatest Gift. And it should be out in late spring, we hope. And anyway, but that also led to my wanting to widen - while we were working on the book - my impact and created a website and started advocating more and more not just through writing but through involvement with the National Kidney Foundation and Donate Life and UNOS. And wanting to make people aware not just of donation but of kidney disease and basically I want people to understand what happened to our family can happen to any family." |
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| Betsy Crais |  | My name is Elizabeth Crais, most my friends and family call me Betsy, and I am a professor at the University of North Carolina Chapel Hill. And like Carol have a linked kidney story and that is that I needed a kidney some years ago, I needed a kidney in 2003. I have family history of polycystic kidney disease, so my kidneys began to get bigger and bigger and bigger. By the time I had my transplant both kidneys were about 5 lbs each, so just imagine two bags of sugar, carrying it around. So people frequently asked me when my baby was due. And if they were strangers and I didn't know them, I would just make a guess, 'Oh July' or something like that. Some people wanted to touch my belly, it was very strange. |
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|  |  | At the time, you know back then in 2003/2004, there just wasn't much information about kidneys. And I went to the library cause that's what you did, we didn't have the internet, and all the things that I read were just technical texts and not really personal or practical things. And now it seems like with the internet we have lots of things and it's really hard to kind of read between the lines or know what to read or what to follow. So that's really what Carol and I put this book together for, to help both donors and recipients kind of know the steps. From my own family, I mentioned the polycystic kidney disease, the best thing is that I have two sisters that had polycystic kidney disease in addition to my mother and so we really were our own support group. And so when I had my transplant, one of my sisters had already had a transplant, she came, helped me through the transplant process and was invaluable in terms of her own experience. |
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|  |  | So again, I think it motivated us to think about putting this book together for people. My own donor is a colleague and we still work together, her name is Linda Watson, she was very concerned and didn't know that she could be a donor because she wasn't a family member. And so that was one of the things she found out early on in the donor process. The other thing that's important to know is that even if we hadn't been a match for each other, now there are programs, kidney pairing programs, where if you're not a match for your donor or donee, you can get in a computer system and sign up for this matching process and they can find other people who can be a donor or a donee. |
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|  |  | And so this donation happened, I had both my kidneys taken out in 2003 because they were so big, and in 2004 my friend, good friend Linda Watson stepped up and went through donor testing and became a donor. And she did great too. Within a few days she was up walking around, I think she took off a couple of weeks from work, but she said that even that was not necessary. I had felt like I didn't know how I was gonna express my gratitude, I mean who can thank someone enough for giving a kidney? That's incredible that someone would be willing to do it. And yet at the time, afterwards, I was kinda struggling with this responsibility and I had this other person's kidney and what if I didn't take care of it? And what if I didn't eat well or something? |
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|  |  | And it was really great that the transplant staff really helped me come to realize that I was a good patient, that I was following the rules, I took my meds, I did all the right things, and they were saying, 'You are a great person to receive a kidney, you're gonna be very careful and take care of it.' Linda also wrote me a note afterwards when I was trying to express my gratitude to her and wrote me this beautiful note, I probably grew a bit teary, and said that her giving to me was sort of a coming back to a whole for her and making her feel whole, that she had done this extraordinary thing for someone else. And really changed my life. |
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|  |  | So I've had her kidney for almost 17 years, next month it'll be 17 years, so it's been quite a while. But unfortunately kidneys last about 14-15 years, but here are people who have had their kidneys 20-30 years. And so a couple of years ago, her kidney began to have less kidney function, I'm back on dialysis, and I'm also gonna need a kidney and a liver. So I'm listed for a kidney and a liver transplant. But yeah, I'm having a good life. I work full-time, I'm happy, I'm healthy, and feeling really good about it. |
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| TPWKY |  | (This Podcast Will Kill You intro theme) |
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| Erin Welsh |  | Thank you so much Carol and Betsy, it was so great to chat with you and thanks for taking the time. And heads up, so their book The Insider's Guide to Living Kidney Donation: Everything You Need to Know if You Give or Get the Greatest Gift will be released sometime spring this year, 2021. So put that on your preorder list and check it out. It's fantastic. |
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| Erin Allmann Updyke |  | Ugh, that's awesome. |
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| Erin Welsh |  | Hi, I'm Erin Welsh. |
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| Erin Allmann Updyke |  | And I'm Erin Allmann Updyke. |
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| Erin Welsh |  | And this is This Podcast Will Kill You. |
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| Erin Allmann Updyke |  | And today, if you haven't figured it out yet, we're talking about organ transplantation. |
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| Erin Welsh |  | Like of all different kinds! |
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| Erin Allmann Updyke |  | It's gonna be- |
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| Erin Welsh |  | So big. |
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| Erin Allmann Updyke |  | It's very large and it's a hard one in some ways to fit into our normal format. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | So heads up, this episode is gonna be a little more different than traditional. |
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| Erin Welsh |  | (laughs) I think it'll be good though, I think it'll be... I'm very excited to learn all about the mechanics and immunology of organ transplantation. |
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| Erin Allmann Updyke |  | Me too. Great, I'm glad you said immunology cause we're not gonna talk about mechanics. |
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| Erin Welsh |  | I mean, you know, vein to vein, artery to artery. |
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| Erin Allmann Updyke |  | Yeah, that's not, I don't know anything about that, so. (laughs) Spoilers. |
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| Erin Welsh |  | (laughs) Well, before we begin, I guess we have some business to take care of. |
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| Erin Allmann Updyke |  | We always do. Let me check, it's quarantini time! |
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| Erin Welsh |  | Quarantini time. What are we drinking this week? |
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| Erin Allmann Updyke |  | Nothing other than 'On Ice'. |
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| Erin Welsh |  | On Ice. And as you can guess, On Ice is a drink served on ice. |
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| Erin Allmann Updyke |  | On Ice. |
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| Erin Welsh |  | It is made of whisky and pomegranate juice and lime juice and some bitters and a little splash of club soda. And guess what? It is served on ice. |
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| Erin Allmann Updyke |  | On Ice. (laughs) |
|  |  |  |
| Erin Welsh |  | And we will post the full recipe for the quarantini as well as the nonalcoholic placeborita on our website thispodcastwillkillyou.com as well as all of our social media channels, so be sure to follow us there. |
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| Erin Allmann Updyke |  | Absolutely. Any other business to attend to? |
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| Erin Welsh |  | There's the usual things. We have transcripts now. |
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| Erin Allmann Updyke |  | Yay! |
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| Erin Welsh |  | And we are getting so many of the back ones, we're getting so many of the current ones, so if you want to check out any of these transcripts, go to our website and click on the TRANSCRIPTS tab and you will see what is there. |
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| Erin Allmann Updyke |  | Also on our website you'll find a link to our bookshop.org affiliate account as well as our Goodreads list and merch. |
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| Erin Welsh |  | Merch! I was like, what else do we have there? (laughs) |
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| Erin Allmann Updyke |  | I forgot, yeah I forgot there for a second. But we have incredible merch. |
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| Erin Welsh |  | We really do. Okay, well. I'm kind of like ready to get down to business. |
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| Erin Allmann Updyke |  | Me too, me too. It's a big one so let's take a quick break and then dive in. |
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| Erin Welsh |  | Sounds great. |
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| TPWKY |  | (transition theme) |
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| Erin Allmann Updyke |  | So like I said, this is a different sort of episode. So the biology section is gonna be a little bit different in that we are going to focus on very broad strokes themes that are involved in all organ transplantation. |
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| Erin Welsh |  | I'm excited. |
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| Erin Allmann Updyke |  | Me too. So in dealing with organ transplants, whether we're talking about solid organs like lungs, livers, and kidneys and hearts, like the organ part that you probably think of, as well as tissue transplants like heart valves and skin and bone. There are kind of a few big categories of issues that might arise or things that might become complications. So of course there are medical complications especially because in the case of organ transplantation, a person who's undergoing organ transplantation is probably pretty sick, right? And so there are likely other medical complications aside from just the organ that needs replacing. And there also could be complications with the donor depending on whether it's a living donor or a deceased donor and what medical conditions they may have had or what the cause of death may have been. So that's like a whole category is medical complications. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | We're not gonna talk about those. They exist, that's all we need to know for the purposes of today. Additionally, because we're talking about literally moving organs or tissues from one person to another, for the vast majority of organ and tissue transplants there are major surgical complications to contend with. And the degree of surgical complication is gonna vary very widely, like bone marrow, relatively small, versus entire face transplant or entire hand transplant. |
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| Erin Welsh |  | Oh my gosh. |
|  |  |  |
| Erin Allmann Updyke |  | Right. And there's everything in between from skin grafts to livers to partial livers to single kidneys, etc. so there's a huge potential for surgical complication. Again, I don't know anything about that, so we're not gonna talk about like how you hook up one artery to another. However there is at least one category that I do feel that I can talk about and it happens to be by and large one of the biggest hurdles and what I suspect, based on, I don't know much about the history, but I suspect most of the history of organ transplantation, the biggest issues were in fact this hurdle. |
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| Erin Welsh |  | Exactly. |
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| Erin Allmann Updyke |  | Yeah. And that is neither medical nor surgical but immunologic. |
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| Erin Welsh |  | Mm-hmm. |
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| Erin Allmann Updyke |  | All right. So that's what we're gonna focus on. We're talk through these immunologic complications both in the short term and the long term, how we can actually recognize them, prevent them from happening now, and then how we can also manage in the long term. |
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| Erin Welsh |  | Sounds great. |
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| Erin Allmann Updyke |  | All right. So first we'll touch on the big immune system components that we have to take into consideration in order to find a matching donor, like what does it mean to be a matching donor? |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | And then we'll briefly go through what happens if things don't go exactly according to plan or aren't perfectly matched and different kinds or rejection that can happen. So the first big hurdle and the easiest one to cross in fact is blood type. Boom. |
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| Erin Welsh |  | Mm-hmm. Standard. |
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| Erin Allmann Updyke |  | So blood type as in A, B, AB, or O. So a donor in general has to have a matching blood type in order for an organ not to be rejected. The question is what are these blood types exactly and why is it so important that they match? So I can't believe we've never, have we ever talked about blood types? |
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| Erin Welsh |  | We briefly touched on it in the hepatitis C episode and then but really what we did, we spent most of the time being like, 'We should do an episode on blood and blood types.' And then... |
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| Erin Allmann Updyke |  | Typical! Well, here we go. Promise finally realized. |
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| Erin Welsh |  | (laughs) |
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| Erin Allmann Updyke |  | So basically, A and B represent antigens which are glycoproteins, little proteins that are found on the surface of our red blood cells. However, these antigens are also on the surface of a huge variety of our cells including the lining of our blood vessels. So we think of them as you blood type, like your red blood cells, but these proteins are found on the surface of a whole bunch of cells. If you have type A blood, that means that your cells have that A antigen on their surface, and what naturally happens in everyone who is type A is shortly after birth, you start to produce antibodies against the B antigen. If you have type B blood, it's the opposite. You have the B antigen and you make natural antibodies against the A antigen. |
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| Erin Welsh |  | How does your body know what the B antigen looks like if you have type A blood? |
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| Erin Allmann Updyke |  | It's a good question. So our bodies are constantly making antibodies against all kinds of different things and whether or not they kind of keep them in our memory and continue making antibodies against them just depends on whether we recognize them as actually foreign. Why it is that we all make antibodies against the one protein that we don't have, I don't really know. It's a good question. |
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| Erin Welsh |  | And so I'm AB, does that mean I don't make antibodies against...? |
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| Erin Allmann Updyke |  | Exactly! |
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| Erin Welsh |  | Cool, okay. |
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| Erin Allmann Updyke |  | So you as a type AB are a universal acceptor for blood and things like that cause you don't make any antibodies. I on the other hand am type O, which means I make antibodies against A and B. So your blood would kill me, Erin. |
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| Erin Welsh |  | (laughs) |
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| Erin Allmann Updyke |  | But you could take my blood any day. |
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| Erin Welsh |  | Wow! I don't like the metaphors that are being implied by this. (laughs) |
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| Erin Allmann Updyke |  | (laughs) That is really funny, actually. Okay listen. In the case of organs, if you have a mismatch of blood type ABO, when you try to put in that new organ that's of a different blood type, those preformed antibodies that you already have will immediately recognize this new organ as non-self and will attack it, resulting in what we know as hyperacute rejection. So that means it's not just in the short term but it's within less than 24 hours, an organ will fail. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | And a lot of times... I mean essentially this should never happen in modern times but if it ever did, a lot of times it's so instant that like if you try to say, hook up a kidney as you're waiting where it should pink up, it will then de-pinkify, essentially. |
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| Erin Welsh |  | Oh interesting. Okay, yeah. |
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| Erin Allmann Updyke |  | So Rh, which is the positive and negative in your blood type, is Rhesus factor. And people either have it and then they're Rh positive or they don't have it and then they're Rh negative. There's two reasons that it doesn't not matter as much for organ transplantation, whether you're positive or negative. And one is that while A and B antigens are expressed on a wide variety of tissues, the Rh factor is only on red blood cells. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | And so when you're doing an organ transplant, you flush that organ to get rid of all of the blood so you're not giving that person any red blood cells directly. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | And the other reason is that because unlike A and B, we don't automatically make antigens against Rh, if you're Rh negative, unless you've been previously exposed to it. |
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| Erin Welsh |  | Okay, so that's the whole like where you hear about it during pregnancy and second pregnancies and so on. |
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| Erin Allmann Updyke |  | Right, that's why it's important in pregnancy. Yeah. Exactly. |
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| Erin Welsh |  | Interesting. |
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| Erin Allmann Updyke |  | Okay. So that's A, B, and O and that's a really easy one to deal with because there's only three blood types, right, four. There's A, B, AB, and O. If you get those right, you're good. The next one is more complicated. The next big immunologic hurdle are the HLA proteins or human leukocyte antigen proteins. So to understand these, and I'm gonna be 100% honest, researching this episode was the first time I actually understood what HLA was. |
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| Erin Welsh |  | I am so excited to hear you explain them because I kept coming across this kind of thing in my readings and I was just like, I can't, I don't know what the relevance is... Okay. |
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| Erin Allmann Updyke |  | Let me break it down so simply for you. |
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| Erin Welsh |  | (laughs) Great. |
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| Erin Allmann Updyke |  | I'm really thrilled to do this. So to understand what HLA proteins are, we have to think back for a second to our vaccines episode. In that first part of our vaccines episode, we went through the immune system play, right. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | And we talked a lot about how the immune system responds to things like pathogens or any other non-self what we call 'antigens' which is just non-self material. In act one of our play, our white blood cells like macrophages are the first ones to recognize this non-self, whether that's pathogens or whatever bits and bobs of little pieces of protein and stuff that they find. Those white blood cells then engulf this material, they go, 'Hmm, this isn't me, I don't recognize this' and then they present it on their surface to T cells who are there waiting, like a flag, right? |
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| Erin Welsh |  | Mm-hmm. |
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| Erin Allmann Updyke |  | So it turns out that the proteins that are on the surface of our white blood cells that actually do this process, that actually present those antigens to the T cells, those are HLA proteins. So you can think of HLA proteins as like the flagpoles that our cells use to present different flags, different little peptides or antigens or whatever, to our immune system to start the process of our immune system mounting a response. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | Cool? |
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| Erin Welsh |  | Very cool. Why are there different like- |
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| Erin Allmann Updyke |  | Lemme, we'll keep going. (laughs) |
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| Erin Welsh |  | (laughs) |
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| Erin Allmann Updyke |  | I know what question you're gonna ask, let me preempt you and continue going. So as it turns out, the immune system is a little more complicated than our immune system play was. |
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| Erin Welsh |  | Ah, what? |
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| Erin Allmann Updyke |  | I know, who knew? (laughs) There are two different classes, so two different entire classes of HLA proteins. HLA class I is found on a huge range of our cells, like almost every cell, and it presents all kinds of intracellular material. So like if a virus infects, let's say, your epithelial cells in your nose, then those epithelial cells will present on HLA class I. They'll be like, 'Hey, I found this piece of a virus! Can you come check this out?' Okay? |
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| Erin Welsh |  | Mm-hmm, mm-hmm. |
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| Erin Allmann Updyke |  | So that's HLA class I. HLA class II are the ones that we kind of talked about already and that we talked about more in our vaccines episode. Those are found on the surface of white blood cells that engulf foreign material and then present it to the T cells. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | Okay. This is very complicated. Within those two classes of HLA proteins, there are six different subgroups. So there's A, B, and C for class I and then there's, I think it's like DR, DQ, and DS. I might've gotten that wrong and somebody's gonna yell at me for it. And then within those six subgroups there are tons of additional variations, like person to person differences, I think we found a couple thousand different individual variations. |
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| Erin Welsh |  | Mm-hmm. |
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| Erin Allmann Updyke |  | And so unlike the ABO system where you have four things to contend with, now we have six different subgroups and lots more individual variation within that that we have to contend with. Yes, Erin? I can tell by your intake of breath that you have a question. (laughs) |
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| Erin Welsh |  | (laughs) And so how do we recognize other like non-self HLA? And what happens? |
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| Erin Allmann Updyke |  | Great question, Erin. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | So what you're kind of getting at gets into the timecourse of these types of rejection that we see. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | Because what you're kind of asking is... So in the case of an ABO incompatibility, we already have antibodies against that foreign blood type. In the case of HLA, you may or may not already have anti-HLA antibodies. So when we are looking, and this is totally jumping ahead from my notes, but that's fine. When we look at trying to match someone for organ transplantation, we have to look not only at their HLA profile and the donor's HLA profile but you also have to look at do the recipient or the donor have any anti-HLA antibodies against any of those other classes? You may or may not. So if you've ever had a blood transfusion, if you've ever had any other tissue transplantation, then you'd be at much higher risk of having those. If you haven't then there's a good chance that you might not have any HLA antibodies. |
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| Erin Welsh |  | Okay. Gotcha. |
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| Erin Allmann Updyke |  | Preformed. That doesn't mean that you couldn't then form them, but we'll talk about how we deal with that in a second. |
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| Erin Welsh |  | Okay. Gotcha. |
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| Erin Allmann Updyke |  | Great question. So because these HLA proteins are proteins that are found on cell surfaces that are directly involved in invoking immune responses, there are two different ways that a recipient's body can react to a mismatch in donor HLA. They can do so either directly by recognizing that foreign HLA on, for example, a donor white blood cell, just like they would respond to their own white blood cell except they say, 'Hey, that whole HLA protein? I don't like that.' And then respond to that whole protein. Or alternatively some of those proteins on the surface of the donor cells might get broken at some point and then the recipient's antigen-presenting cells or white blood cells would pick up little bits of donor HLA that they find and then present those, very much in the same way that they would present any other pathogen or whatever to T cells. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | So that indirect response is thought to be something that's more important later, like later in the course of a graft rejection for example, whereas that direct response is thought to be more important earlier after transplantation. |
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| Erin Welsh |  | Okay. Mm-hmm. |
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| Erin Allmann Updyke |  | Oh my gosh that was a lot of acronyms and immunology. |
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| Erin Welsh |  | (laughs) |
|  |  |  |
| Erin Allmann Updyke |  | But essentially from there, once a recipient's immune system recognizes that foreign HLA, they do exactly what their immune system is supposed to do, they respond in any number of different ways either by making a bunch of antibodies against it or activating natural killer cells or cytotoxic T cells, whatever. They just mount an immune response to try and kill anything with that HLA protein, which means the brand new organ that you just transplanted. |
|  |  |  |
| Erin Welsh |  | So you can match blood types, how close can you get to matching HLA? Can you? |
|  |  |  |
| Erin Allmann Updyke |  | You can match subgroups definitely, like the six different subgroups you can match. Certainly siblings are the easiest to match, you have a 25% chance of having a perfectly matched sibling just based on genetics. But those individual little polymorphisms I think would be a lot harder to match. How much those matter in the grand scheme of antibodies, I don't actually know. |
|  |  |  |
| Erin Welsh |  | Okay. |
|  |  |  |
| Erin Allmann Updyke |  | But for those six groups. And it also varies organ to organ exactly how close the match has to be to ensure good graft survival. |
|  |  |  |
| Erin Welsh |  | Ooh that is very interesting. |
|  |  |  |
| Erin Allmann Updyke |  | Yes, please don't ask me anymore details than that. (laughs) |
|  |  |  |
| Erin Welsh |  | Ugh, you're killing me. |
|  |  |  |
| Erin Allmann Updyke |  | I know, I'm sorry. But if you also think about it... So HLA class I, that's the one that's found on the majority of cells so that's for most transplants going to be the most important. HLA class II is found on white blood cells, so if you're transplanting something with white blood cells involved then that one's going to be more important. |
|  |  |  |
| Erin Welsh |  | Okay. |
|  |  |  |
| Erin Allmann Updyke |  | Etc etc. There are also non-HLA proteins called minor histocompatibility proteins which also vary but they aren't major players in solid organ transplantation, that's why they're minor histocompatibility. |
|  |  |  |
| Erin Welsh |  | Gotcha. |
|  |  |  |
| Erin Allmann Updyke |  | All right. So that's the basic underlying immunology. But now the question is what happens if there is a mismatch. Like what does transplant rejection actually look like? |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | I'm not gonna go into a ton of detail because the truth is the exact symptoms that you see vary a lot based on organ and exactly what symptoms you're gonna have will depend on what type of transplantation you're talking about. But there are a few large scale ways that we classify it, either by timecourse or by immune response. So by timecourse you have hyperacute rejection, which we kind of already talked about and that's if you have preformed antibodies that immediately within 24 hours go ahead and attack that new organ. You can also have acute rejection anywhere from 6-90 days, there is a little window period those first few days where if things go really wrong it's like a whole different classification, accelerated rejection. But acute rejection is sort of in those first couple of months and that can actually be either antibody or cell-mediated, so it could be mostly an antibody response or it can be a cell-mediated response, either way. |
|  |  |  |
|  |  | And then you have chronic rejection. And so this is what can happen if someone has a transplant, seems fine for several months, but then later, could be months later, could be years later, that graft starts to get rejected. And this again can also be either cell or antibody-mediated. And to some degree there's going to be chronic damage in essentially every graft eventually, and exactly when that happens depends in part on how well those organs are matched, so how well each HLA and everything matches and also on how good of immune suppression you get and kind of everything overall. Does that make sense? |
|  |  |  |
| Erin Welsh |  | Yeah, it's a tricky line to walk. |
|  |  |  |
| Erin Allmann Updyke |  | Right, yeah. So every recipient and donor has to be checked for their blood type as well as their HLA profile as well, like we said, if they have any preformed anti-HLA antibodies in their blood. And then like I said too, how strict you have to be depends in part on the organ that you're transplanting. But no matter what organ and no matter how well you are matched, basically everyone who undergoes an organ transplant of any kind is going to be on at least some immunosuppressive drugs. I'm not gonna get into all the different types of immunosuppressive drugs because that is - hoo - that's a whole thing. There's a lot of different ones and we've come very far in the amount of immunosuppression that we can do, however all of our immunosuppressants are still very general, they're not specific. So in general the goal is to just reduce overall white blood cell activation, growth, or downstream effects which means that because these are acting on our entire immune response, they make people more susceptible to infectious disease as well as cancers, since our immune system normally helps fight off infection and take care of any mutated cells that could turn into cancer in our own body. |
|  |  |  |
| Erin Welsh |  | Right. |
|  |  |  |
| Erin Allmann Updyke |  | So usually immunosuppression is very high, right, after the transplant or even sometimes starting before the transplant and then can be tapered down but is usually for the entire life of the graft, which is the new organ. So yeah. That's the biology of organ transplantation. |
|  |  |  |
| Erin Welsh |  | Oh wow, okay. |
|  |  |  |
| Erin Allmann Updyke |  | Oh! I did wanna give a quick shoutout to graft versus host disease. |
|  |  |  |
| Erin Welsh |  | Yes. |
|  |  |  |
| Erin Allmann Updyke |  | So graft versus host disease is what it sounds like. The graft is the new donor tissue vs host, which is the recipient, and so that is when the donor tissue is an immunologically active tissue that then recognizes and attacks recipient cells. So this is a problem most commonly in bone marrow transplantation where you're literally giving someone stem cells that become white blood cells whose job it is to find and eliminate non-self and they are now surrounded by non-self. |
|  |  |  |
| Erin Welsh |  | Oh boy. It's like the Trojan Horse of... |
|  |  |  |
| Erin Allmann Updyke |  | Right, yeah. But it's also a problem in the case of intestinal transplantation as well, which is not surprising considering how immunologically active intestines are. |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | So HLA and especially HLA class II, which is the white blood cell HLA- |
|  |  |  |
| Erin Welsh |  | Uh huh. |
|  |  |  |
| Erin Allmann Updyke |  | Matching and pretreatment with immunosuppression in the recipient is really important in these cases. |
|  |  |  |
| Erin Welsh |  | Okay. |
|  |  |  |
| Erin Allmann Updyke |  | Because graft versus host, it's pretty easy to prevent but it's very difficult to treat once it's established. And it's atrocious, it's a horrible disease. |
|  |  |  |
| Erin Welsh |  | Yeah. Yeah. Obviously we've come a long way since early transplants. How often does that happen now? |
|  |  |  |
| Erin Allmann Updyke |  | That's a good question, I don't actually know the statistics on it. |
|  |  |  |
| Erin Welsh |  | Okay. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah, I think it's pretty rare because I don't think we'd be able to continue doing transplants if this was something that was super common. There may be some degree of it a little bit, and I actually remember learning that in a very small amount in a disease for example like leukemia, if you have those donor cells actually helping to eliminate the last bits of any cancer that might still be there, a little bit of graft versus host might not be a terrible thing. |
|  |  |  |
| Erin Welsh |  | Okay. |
|  |  |  |
| Erin Allmann Updyke |  | But in general, graft versus host is not good. (laughs) |
|  |  |  |
| Erin Welsh |  | Yeah, yeah. Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. And so immunosuppression is really important to prevent that. They also, I will say the other thing that they do to prevent it is if you transplant just stem cells and not any already activated T cells, so you make sure that when you transplant you flush out any active T cells, that also greatly reduces the risk of graft versus host. |
|  |  |  |
| Erin Welsh |  | That makes sense. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. So that now is truly the biology of organ transplantation. Erin. |
|  |  |  |
| Erin Welsh |  | (laughs) |
|  |  |  |
| Erin Allmann Updyke |  | I don't know anything about this history and I can't wait to learn it. |
|  |  |  |
| Erin Welsh |  | Oof, let's take a quick break first. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| TPWKY |  | (transition theme) |
|  |  |  |
| Erin Welsh |  | Okay, Erin. Let's talk organ transplantation. |
|  |  |  |
| Erin Allmann Updyke |  | Yes! |
|  |  |  |
| Erin Welsh |  | I actually have a little note in here that I wrote 'put on your grafting boots, Erin' but I think that's just cause we've been watching too much Love Island. |
|  |  |  |
| Erin Allmann Updyke |  | (laughs) Oh my god that's the best use of that phrase! I love it! My grafting boots are on. |
|  |  |  |
| Erin Welsh |  | (laughs) Okay. Here we go. So as you can imagine, there are many early myths and traditional tales that tell stories of body parts being replaced, of limbs regrown or reattached. There are tales of a magic glue from tortoises that is strong enough to reattach human body parts. |
|  |  |  |
| Erin Allmann Updyke |  | What? |
|  |  |  |
| Erin Welsh |  | Noses and ears being removed and then replaced by wax, a heart replacement from the underworld- |
|  |  |  |
| Erin Allmann Updyke |  | Ooh. |
|  |  |  |
| Erin Welsh |  | Grafting a premature baby onto a god's thigh until it grows large and strong enough to be born. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | Yeah. (laughs) At the core of some of these stories was a philosophical question: can a heart or a head or hand replacement make the recipient take on the feelings or thoughts or personality of the donor? |
|  |  |  |
| Erin Allmann Updyke |  | Ooh. |
|  |  |  |
| Erin Welsh |  | In other words, what make you you? It was a question of identity. While other stories use the instance of organ or limb replacement as simply like a plot point or to demonstrate the power of a god or goddess or saint. But whatever the reason, there's one thing that unites these early stories and myths and that is that in them body part replacement was pretty much just symbolic, it was not seen as a medical operation or like something that could actually happen. |
|  |  |  |
| Erin Allmann Updyke |  | Right, it wasn't real, it was mythology. |
|  |  |  |
| Erin Welsh |  | Right. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | And what I wanna do in this section is to trace the history of organ transplantation from the first people who looked at these myths or thought of limb replacement and thought, 'I wonder if we could actually do this, like really.' |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | And then I'll start there and then I wanna take us all the way through the first big burst of successful transplantation in the mid 20th century. Like I wanna talk about the immunological and surgical developments that led to that period being the period of organ transplantation. Why then? |
|  |  |  |
| Erin Allmann Updyke |  | Why now? Yeah. |
|  |  |  |
| Erin Welsh |  | Yeah. This is a massive history, as I've said, and not just because of the incredible growth or technologies that allows for transplantation to become this almost everyday reality, but also because of the ethical conversations that were happening alongside and were often outpaced by these developments. So just a warning, this won't be an entirely comprehensive history, just an overview but don't worry, I will recommend lots of further reading. The story of organ transplantation starts earlier than you might expect and it doesn't start with a reattached hand or a transplanted kidney. It starts with skin grafts. |
|  |  |  |
| Erin Allmann Updyke |  | Mm-hmm. |
|  |  |  |
| Erin Welsh |  | Skin grafts and their widespread use in ancient and then renaissance times led to building a lot of the knowledge base on how our bodies heal themselves and how our immune systems often reject tissue that is not ours. The ancient Hindu Sanskrit text Sushruta Samhita from around the 6th century BCE, that's like a long time ago, lays out in impressive detail how to perform tissue replacements using skin flaps from the person who was injured. And this type of plastic surgery was practiced with regularity for hundreds of years in India before the knowledge spread more widely to East Asian cultures, Arab surgeons, and then to Europe by the Renaissance. |
|  |  |  |
| Erin Allmann Updyke |  | Did you say in the 6th century BCE? |
|  |  |  |
| Erin Welsh |  | 6th century. |
|  |  |  |
| Erin Allmann Updyke |  | What!? |
|  |  |  |
| Erin Welsh |  | Yeah and so I wanna clarify here I mean autografts, so like from the person's thigh. |
|  |  |  |
| Erin Allmann Updyke |  | Right, from the self. Yeah. |
|  |  |  |
| Erin Welsh |  | Yeah. There's like schematics and like 'here's how you fix a nose'. It's pretty amazing. |
|  |  |  |
| Erin Allmann Updyke |  | That's amazing. |
|  |  |  |
| Erin Welsh |  | Yeah. And it pretty much went unnoticed until the Renaissance in other places. And then there, in the Renaissance, especially in Europe it was taken up by a lot of different surgeons and expanded upon because of the increased demand caused in part by syphilis and the spread of syphilis. Cause tertiary syphilis can cause your nose to fall apart. |
|  |  |  |
| Erin Allmann Updyke |  | Fall off. Mm-hmm. |
|  |  |  |
| Erin Welsh |  | But using skin flaps from someone to surgically prepare facial disfigurements on that same person is, you know, that's not whole organ transplantation. |
|  |  |  |
| Erin Allmann Updyke |  | Right. |
|  |  |  |
| Erin Welsh |  | Like we would consider that plastic surgery. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | So from the 1700s to the 1800s, there was a shift in scientific research trends from observation, which had been made possible through advancement in technology like microscopes and like stethoscopes and other tools. |
|  |  |  |
| Erin Allmann Updyke |  | Right. |
|  |  |  |
| Erin Welsh |  | And so it went from observation to experimentation, where researches could test hypotheses to learn the things that might not be as easily observed. And among this new era of experimentation was of course transplantation. Skin grafts became increasingly popular, and not just autografts, so like from one person to that same person, and not just on humans. Researchers began playing around with allografts, so skin from another individual of the same species, on humans and animals. So like from one dog to another. |
|  |  |  |
| Erin Allmann Updyke |  | Right. |
|  |  |  |
| Erin Welsh |  | And then also some xenografts, so like skin from another species entirely or organs from another species entirely. |
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| Erin Allmann Updyke |  | Like put a pig organ into a dog or etc. |
|  |  |  |
| Erin Welsh |  | Exactly. Happened a lot. Pig's or goat's kidney into a dog. Whatever. Anyway, there were lots of kind of out there experimentations and some of them, most of them, all of them were unsuccessful but there were several key things learned during this time like up to the 1900s that I'll kind of just go over. Number one was that blood flow could become reestablished with autografts. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | Number two, diseases could be transplanted along with the tissue. |
|  |  |  |
| Erin Allmann Updyke |  | Ooh, that's an important one. |
|  |  |  |
| Erin Welsh |  | Hugely important. So like doctors were finding syphilis, for example, pop up in the recipient's tooth transplants. |
|  |  |  |
| Erin Allmann Updyke |  | Oh. Tooth transplants?! |
|  |  |  |
| Erin Welsh |  | Yeah, they were really popular in the 1700-1800s. |
|  |  |  |
| Erin Allmann Updyke |  | What? |
|  |  |  |
| Erin Welsh |  | I don't think they actually worked, but... |
|  |  |  |
| Erin Allmann Updyke |  | I don't think... |
|  |  |  |
| Erin Welsh |  | No. But you can still give someone syphilis that way, so. (laughs) Even if the transplant itself didn't work. |
|  |  |  |
| Erin Allmann Updyke |  | (laughs) Wow, okay. |
|  |  |  |
| Erin Welsh |  | Number three. Xenografts, so like from one species to another, just they don't work. The heart of a pigeon can't really replace the heart of a rabbit and this kind of reinforced the idea that there were significant biological differences between species, which even though it sounds sort of self-evident to us now, like that was still kind of up for debate. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah, yeah. |
|  |  |  |
| Erin Welsh |  | And number four, very thin skin grafts worked better than whole chunks of skin. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. Yeah. Just those first few layers. |
|  |  |  |
| Erin Welsh |  | Yeah, exactly. The growth in experimental transplants during this time meant that transplantation also was no longer just a fascination for the medical community. The vast possibilities that transplantation seemed to present bled into the public arena where some of these possibilities were laid out in fiction books such as Frankenstein by Mary Shelley, or The Island of Doctor Moreau by H. G. Wells. |
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| Erin Allmann Updyke |  | Oh! I haven't read that one. |
|  |  |  |
| Erin Welsh |  | It has a bunch of like composite animals, monstrous animals. |
|  |  |  |
| Erin Allmann Updyke |  | Ooh. |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | How fun. |
|  |  |  |
| Erin Welsh |  | And ethical questions were raised as to donor willingness, for example, so like prisoners and other disenfranchised individuals were often quote unquote like 'volunteered' as donors and philosophical questions were asked about transferrable personality characteristics or the unnatural extension of life. Some snake oil salesmen took advantage of the public's fascination with transplantation, as per usual. |
|  |  |  |
| Erin Allmann Updyke |  | As per usual. |
|  |  |  |
| Erin Welsh |  | And they promised renewed virility or manliness by transplanting, get this, small slices- |
|  |  |  |
| Erin Allmann Updyke |  | Don't say weiners. |
|  |  |  |
| Erin Welsh |  | Well, close. (laughs) Quite close. Small slices of goat testes into human testes. |
|  |  |  |
| Erin Allmann Updyke |  | (laughs) What? Why goat? |
|  |  |  |
| Erin Welsh |  | I don't know why goat. |
|  |  |  |
| Erin Allmann Updyke |  | Just easily accessible? |
|  |  |  |
| Erin Welsh |  | Yeah, maybe there's like a size thing to them too? I don't know. |
|  |  |  |
| Erin Allmann Updyke |  | Goat testicles. |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | Just bits of 'em. |
|  |  |  |
| Erin Welsh |  | Yeah, just slices. |
|  |  |  |
| Erin Allmann Updyke |  | Just little bits. |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | Into your testicles. |
|  |  |  |
| Erin Welsh |  | Mm-hmm. This didn't work, obviously. |
|  |  |  |
| Erin Allmann Updyke |  | Didn't work. (laughs) |
|  |  |  |
| Erin Welsh |  | And this misguided procedure, misguided is an understatement... But it wasn't the only bit of misinformation that remained from this period. With the biggest one being that most people seemed to believe, like researchers seemed to believe that allografts between humans worked. And there was no issue. |
|  |  |  |
| Erin Allmann Updyke |  | No issue. |
|  |  |  |
| Erin Welsh |  | Which is very interesting that that was like the prevailing thought. Maybe it's because expectations weren't very high to begin with or the definition of a successful transplant was not how you or I would define it or people would define it nowadays. |
|  |  |  |
| Erin Allmann Updyke |  | Right, yeah. |
|  |  |  |
| Erin Welsh |  | But yeah, doctors and surgeons from this time seemed to think that skin grafts with donated tissue were largely successful. |
|  |  |  |
| Erin Allmann Updyke |  | Oh, well skin grafts... Yeah, yeah, yeah. |
|  |  |  |
| Erin Welsh |  | But they didn't work. |
|  |  |  |
| Erin Allmann Updyke |  | (laughs) |
|  |  |  |
| Erin Welsh |  | They just didn't work. What would often happen is that it may have appeared to work in that the donor skin would wither away and become shrunken and then eventually fall off, in the meanwhile if the wound was not severe enough, the person's own skin would recover. |
|  |  |  |
| Erin Allmann Updyke |  | I see. |
|  |  |  |
| Erin Welsh |  | But besides that, people were barely blood typing at this time. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | I thought they might've just got lucky where- |
|  |  |  |
| Erin Welsh |  | It's possible. |
|  |  |  |
| Erin Allmann Updyke |  | You know there are some populations where there's a lot of one blood type, so maybe they just... |
|  |  |  |
| Erin Welsh |  | Sure, I mean it's possible, you know, even a broken clock is right twice a day but... |
|  |  |  |
| Erin Allmann Updyke |  | (laughs) |
|  |  |  |
| Erin Welsh |  | I don't know about how that applies to allografts, skin grafts. (laughs) Anyway. This wide belief in the fact that allografts were easy peasy, a-ok for skin, that caused a bit of a hurdle later on in immunological advancements. And that being said, there were some types of transplantations or grafts that were successful including bone grafts, which because basically the bone just provided like a surface where the host cells could grow, and corneal grafts. And those were successful often because rejection is uncommon, host cells can't reach corneas because there are no blood vessels that nourish the cornea, etc. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | And these promising advancements overall encouraged surgeons to expand their horizons a bit in terms of transplantation. Surgeons attempted whole gland transplantation, which was met with mixed results. I say mixed because often spontaneous improvement in gland function was incorrectly attributed to the transplanted glands, which were... Yeah. |
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| Erin Allmann Updyke |  | Wait, what glands? |
|  |  |  |
| Erin Welsh |  | Like thyroid. |
|  |  |  |
| Erin Allmann Updyke |  | Oh. |
|  |  |  |
| Erin Welsh |  | Right. Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | Weird. |
|  |  |  |
| Erin Welsh |  | But these transplanted glands were almost without a doubt rejected. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | Yeah. And then other whole organ transplantation began to take place with allografts of human to human kidney but also xenografts of all kinds, so like goat to human. None of these transplants was ultimately successful and the recipient often died within a few days of the surgery. |
|  |  |  |
| Erin Allmann Updyke |  | And these are often recipients, are these in this case, who actually need a new organ to survive? Or are these medical tortures that are being... |
|  |  |  |
| Erin Welsh |  | From what I could read, it was people who this was the last resort type of surgery. Now the donor on the other hand, there wasn't necessarily consent and this was like pre legal discussion of what consent would mean from someone who is deceased. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | But yeah, from what I can tell, at least I did not come across any medicalized torture. I'm sure that they happened but I don't think that they contributed to the body of knowledge and so they maybe just didn't make it into the history. If that makes sense. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah, yeah, yeah. Definitely. |
|  |  |  |
| Erin Welsh |  | So the question at this point is what would it take for successful transplantation to occur? So in the history, we're around the early 20th century right now and we're still five decades away from the first successful whole organ transplant. And there are some major hurdles to overcome before we get there. These next decades are largely spent asking and answering what I like to think of as the how and the why of organ transplantation. So the how meaning basically the technical or mechanical aspects of the procedure, how to best suture the vessels, where organs should be placed in the body, how to prolong organ life outside of the body. And the why is what i take to basically mean the immunology. Why does rejection happen? Because if we can understand that, we can maybe prevent it from occurring. |
|  |  |  |
| Erin Allmann Updyke |  | Ooh, fun. |
|  |  |  |
| Erin Welsh |  | Yeah. So I talk a lot on this podcast about the huge impact that germ theory had on sanitation infrastructure, microbiology techniques, vaccine development, and overall public health. I bet you didn't think I was gonna mention germ theory in this, did you? |
|  |  |  |
| Erin Allmann Updyke |  | I didn't expect it, honestly. |
|  |  |  |
| Erin Welsh |  | (laughs) Well I didn't either, but as I was reading it occurred to me that one thing that I don't really mention either ever or at least as often as I should is the huge implications that germ theory had for the field of immunology. |
|  |  |  |
| Erin Allmann Updyke |  | Oh, yeah. |
|  |  |  |
| Erin Welsh |  | Essentially like creating it. |
|  |  |  |
| Erin Allmann Updyke |  | Created it, yeah. |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | Cause if these are things that can be passed from human to human, our body is taking them in and doing something with them. What is our body doing? That's immunology. |
|  |  |  |
| Erin Welsh |  | Exactly, exactly. |
|  |  |  |
| Erin Allmann Updyke |  | Ooh! |
|  |  |  |
| Erin Welsh |  | Disease is not just an imbalance in the body's humors but if we use the battle lingo that a lot of people often use in describing infectious disease, it's due to tiny invaders attacking the body's organs. So it stands to reason or it stood to reason that if there were tiny invaders, there must also be like tiny defenders. |
|  |  |  |
| Erin Allmann Updyke |  | Right. |
|  |  |  |
| Erin Welsh |  | So this recognition that there was a biological basis for non-self material and then a subsequent attack mounted against it would prove to be a huge step forward in transplant science. |
|  |  |  |
| Erin Allmann Updyke |  | Wow! |
|  |  |  |
| Erin Welsh |  | And this also, I find this really interesting, this wasn't a one-way transfer of knowledge, it wasn't just form immunologists telling transplant surgeons 'this is what works, this is what doesn't work, this is how whatever'. These experimental transplants gave immunologists the opportunity to study the body's immune response. |
|  |  |  |
| Erin Allmann Updyke |  | Oh yeah. |
|  |  |  |
| Erin Welsh |  | Leading to the observation that rejection was not just this passive response with the donor tissue or organ dying, but a very active immune reaction. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | It's cool. (laughs) |
|  |  |  |
| Erin Allmann Updyke |  | I'm getting chills a little bit. |
|  |  |  |
| Erin Welsh |  | Ooh! Yay! And in some ways, these observations led to a changing paradigm of immunity where it wasn't all dictated just by antibodies, this humoral immune response. And also a more complete understanding of, especially in the case of transplant science, what the lymphocyte actually does. Which was previously just thought to be a stationary thing that didn't do anything. |
|  |  |  |
| Erin Allmann Updyke |  | Really? |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | They're like, 'Oh here's this cell, it just hangs here?' |
|  |  |  |
| Erin Welsh |  | It just hangs here and waits. It was like a more passive thing. |
|  |  |  |
| Erin Allmann Updyke |  | They're everywhere! |
|  |  |  |
|  |  | Yeah, yeah. So in the early 20th century, the first couple of decades did see a lot of progress particularly in this realm, in experimental transplantation and in observations on the immune response to a transplanted skin or transplanted organ. But the overall rate of progress in transplant science slowed to a near crawl during and after WWI. Really the only field of transplant science that didn't experience a decline due to the war was, as you might guess, skin allografts in humans because of lots of disfigurements from bombs and battle wounds. |
|  |  |  |
|  |  | So the 1930s then began this slow climb back towards methodical research and transplant science and experimental transplants of whole organs began in earnest. It was more like, 'Let's measure this.' Not just like, 'Hey, you know what? Let's spin the...' What do you call those things at a casino? |
|  |  |  |
| Erin Allmann Updyke |  | Roulette? |
|  |  |  |
| Erin Welsh |  | No, not roulette. 'Let's do the slot machine of a dog kidney and a monkey heart into a pig,' or something like that. |
|  |  |  |
| Erin Allmann Updyke |  | (laughs) Got it. I see. I see what you're saying, the slot machine. |
|  |  |  |
| Erin Welsh |  | (laughs) So it was more like, 'Okay, let's take careful notes at the very least'. And part of this was helped along because technical advancements in surgical procedures had been developed in the previous decade, so suturing and vascular surgery techniques developed by French surgeon Alexis Carrel, which eventually earned him the Nobel Prize in 1912, these techniques allowed for the mechanics of transplant surgery to become a reality during this time. |
|  |  |  |
| Erin Allmann Updyke |  | Right. That makes sense. |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | It makes sense to that that stayed as being important during the war because that would be very necessary. |
|  |  |  |
| Erin Welsh |  | Mm-hmm. Right. And another key mechanics development that I'll mention is the profusion pump developed in the 1930s also by Alexis Carrel, who had teamed up with Charles Lindbergh of all people. Also in doing the research I learned that they were both eugenicists and Nazi sympathizers. |
|  |  |  |
| Erin Allmann Updyke |  | Typical. |
|  |  |  |
| Erin Welsh |  | Yeah. So anyway... |
|  |  |  |
| Erin Allmann Updyke |  | I'm not even surprised anymore, Erin. |
|  |  |  |
| Erin Welsh |  | I know. |
|  |  |  |
| Erin Allmann Updyke |  | And this person was a Nazi and this person. |
|  |  |  |
| Erin Welsh |  | I mean, yeah. That's the history of scientific research in the 1930s and 40s for the most part. |
|  |  |  |
| Erin Allmann Updyke |  | You know, everyone's a eugenicist. Mm-hmm. Especially medical research. |
|  |  |  |
| Erin Welsh |  | Yes, yeah, a lot, a lot. But anyway. The profusion pump allowed organs to survive outside the body during surgery which was a crucial development for transplants as well as for open heart surgery. And other technical advancements during this time such as how cold the organ should be kept and how long it could be considered viable. All of these contributed to surgeons having the tools and technical knowledge that would allow them to perform whole organ transplants by the 1930s and 1940s. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | So like, the technical stuff is down. |
|  |  |  |
| Erin Allmann Updyke |  | Right. They've got the surgery complications done. That's why I didn't talk about them, I knew they were easy. (laughs) |
|  |  |  |
| Erin Welsh |  | Exactly. (laughs) Oh yeah, super duper easy. In 1933, Ukrainian Yurii Voronoy performed the first human allograft kidney transplantation from a cadaver donor, so six hours after death. |
|  |  |  |
| Erin Allmann Updyke |  | What? What? 1933? |
|  |  |  |
| Erin Welsh |  | Well, okay. I didn't say successful. |
|  |  |  |
| Erin Allmann Updyke |  | Oh got it, got it. You're right, you're right. (laughs) |
|  |  |  |
| Erin Welsh |  | (laughs) So pump the brakes. |
|  |  |  |
| Erin Allmann Updyke |  | This is the first human cadaveric transplant where we know how to do this surgically, is it going to work otherwise? Like we know that the surgery wasn't the issue here, so if it didn't work, it wasn't because of that. Whereas any previous ones would've just been like a crapshoot. |
|  |  |  |
| Erin Welsh |  | I think it might've been that. In the literature this seems to be what people often point towards as being the first one. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | Yeah. And then there were a bunch of additional transplants performed throughout this time in the 30s and 40s. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | Not like tons but, you know. A good number, yeah. And of course, just like Voronoy's transplant, they all failed. The surgeons and the transplanted organs were all losing this fight against the immune system and it was starting to look like a lost cause. Until WWII. So unlike WWI, the need for applied surgical and medical research was very clear in the midst of the second world war, and the high rate of burns really highlighted the importance and potential of skin grafts in treating those burns. During WWII, a young zoology graduate student at Oxford named Peter Medawar saw firsthand the horrible pain and excruciating experience that a burn victim could go through when a British pilot's plane crashed into his neighbor's garden. The pilot survived the crash but 60% of his body was covered in burns. |
|  |  |  |
| Erin Allmann Updyke |  | Oh no. |
|  |  |  |
| Erin Welsh |  | And Medawar knew about skin grafts and how allografts were used as short term treatments for burns in the hopes that the body could start the healing process before the graft was rejected. And Medawar attempted to heal the fallen pilot with tissue culture slurries or tiny slices of skin, basically like painted on the raw areas, but nothing worked and the pilot eventually died of infection. |
|  |  |  |
| Erin Allmann Updyke |  | Ugh. |
|  |  |  |
| Erin Welsh |  | But this experience would then launch Medawar onto a research path that laid the groundwork essentially for the future of successful transplantation. |
|  |  |  |
| Erin Allmann Updyke |  | Wow. |
|  |  |  |
| Erin Welsh |  | Yeah. Cause at the time he was a zoology student, he wasn't sure what exactly he wanted to do, and then he had this experience and was like, 'The pilot could have survived if those skin grafts weren't rejected. So how can I prevent rejection?' So pretty cool. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | Answering those questions would require like a lot of untangling of these immune system mysteries that had long been untouched in a way. And now that he had landed on a career path, Medawar sought opportunities to explore these questions using both clinical and laboratory experiments, which made him kind of unusual in that respect. He teamed up with a Scottish plastic surgeon named Tom Gibson and that's where he got the opportunity to observe firsthand the use of allografts to treat burns as a graduate student. And together they made the observation that a second graft from the same donor was rejected more quickly than the first. Very interesting. |
|  |  |  |
| Erin Allmann Updyke |  | Very. |
|  |  |  |
| Erin Welsh |  | This finding, and it was also I have to say more of a rediscovery since it had been observed before but then I was lost to the lost era of organ transplantation. This finding was published in a 1943 paper and it would end up being hugely instrumental in the field of transplant science since it firmly established rejection as an immune response. Medawar continued his research by looking at skin grafts between rabbits, like the timing of rejection, pigment spread, and the immunological basis or rejection. Then came a very fortunate meeting that would end up paving the way for successful transplantation. |
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|  |  | At an international conference in Stockholm in 1949, a Scottish veterinarian asked Medawar if he knew how to distinguish between fraternal and identical cattle twins. And Medawar was like, 'Yeah of course, you just need to like exchange skin grafts between the twins and see how long they last. If they last forever, you've got identical twins. If they slough off, fraternal.' The vet called him up later and was like, 'Hey, can you demonstrate this in person?' And so Medawar drove up and performed a bunch of grafts and none of them rejected, which was absolutely not what they were expecting. Like even all of the fraternal twin grafts took, suggesting that the twins shared some sort of blood flow in utero where they like got used to one another. This eventually led him to realize that tolerance could be acquired, that the immunological barrier could be broken, and that the co-mingling of fluids between two unborn organisms in utero would allow them or could allow them later as adults to accept each other's foreign tissues and have their body fail to recognize it as non-self. |
|  |  |  |
| Erin Allmann Updyke |  | I'm speechless. |
|  |  |  |
| Erin Welsh |  | (laughs) I mean, yeah. There's more about these cows in particular and why they were important but like, I tried to do as succinct as possible. And then this, suddenly here was a way, at least a suggestion that you could manipulate immunity and that you could bypass this enormous hurdle that had so far prevented organ transplantation from being an actual, viable option. |
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| Erin Allmann Updyke |  | And just as a refresher on the time that we are here, do we know yet about blood types? Do we know anything about what it is that's causing the incompatibility? |
|  |  |  |
| Erin Welsh |  | We know about blood types. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
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| Erin Welsh |  | And so there was at least that. So the Voronoy, the first kidney transplant, that was also mismatched blood type, which could have contributed of course to the failure. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | But that was about it. Like there was some inkling of these other major histocompatibility complex type things but I don't really know exactly how much we knew about that as it related to things other than infectious disease. |
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| Erin Allmann Updyke |  | Okay, got it. |
|  |  |  |
| Erin Welsh |  | Because I think that was the larger context that we understood the immune system at that time, for the most part. |
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| Erin Allmann Updyke |  | Of course. Yeah, yeah. |
|  |  |  |
| Erin Welsh |  | Right. So yeah. |
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| Erin Allmann Updyke |  | Okay, thanks. |
|  |  |  |
| Erin Welsh |  | No prob. And so after finding this out, after this cattle experiment, Medawar along with colleague Rupert Billingham and graduate student Leslie Brent began experimenting with different methods of immunosuppression on mice using spleen cells to induce chimerism in order to prevent rejection. And they met with some success, some limited success. And eventually Medawar was awarded a Nobel Prize in 1960 for all of his efforts. |
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| Erin Allmann Updyke |  | Wow. |
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| Erin Welsh |  | And the key take-home from all of this research that he did was that rejection was not inevitable. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | You could overcome it. So while Medawar was hard at work at untangling the mysteries or the human immune system, many surgeries were still tinkering away at transplantation and they seemed to focus in particular on kidneys. Why the kidneys, you might ask? Well, for one, most people have two of them so replacing- |
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| Erin Allmann Updyke |  | That was my guess. I was like, we have two, so that's an easy one. (laughs) |
|  |  |  |
| Erin Welsh |  | (laughs) Yeah, we have two. So yeah, so replacing one didn't seem like as much of a death sentence as something like trying to replace a liver or heart, almost ensuring death at that point. |
|  |  |  |
| Erin Allmann Updyke |  | Right. |
|  |  |  |
| Erin Welsh |  | The other thing is that kidney disease was really common in the first half of the 20th century with conditions like crush syndrome, thanks to all of the bombings and people trapped under the rubble in WWII, like bringing that to light, Bright's disease, acute renal failure, chronic nephritis, all of these things occurred quite frequently. And the other thing is that in these pre-antibiotic times, infections were often likely to cause lasting kidney damage. |
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| Erin Allmann Updyke |  | Mm-hmm. I never thought about that. |
|  |  |  |
| Erin Welsh |  | Yeah. And so there was a substantial amount of focus on the kidneys and on kidney disease. And in terms of transplants, kidneys happen to be more available because a common treatment for hydrocephalus was to remove one kidney so that cerebrospinal fluid could be drained to the bladder like through the vessel- |
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| Erin Allmann Updyke |  | Through the ureter? |
|  |  |  |
| Erin Welsh |  | Yeah, exactly, through the ureter. So there'd be like spare kidneys. |
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| Erin Allmann Updyke |  | (laughs) That's really interesting. I never knew that. |
|  |  |  |
| Erin Welsh |  | (laughs) So also the importance of kidney disease during this time is also kind of illustrated by the fact that artificial kidney machines were developed during WWII. |
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| Erin Allmann Updyke |  | Wow! |
|  |  |  |
| Erin Welsh |  | And those represented this enormous step forward for treatment of kidney disease. |
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| Erin Allmann Updyke |  | That long ago, wow. |
|  |  |  |
| Erin Welsh |  | That long ago, yeah. But a lot of people at the time when these machines were first developed saw them as prolonging misery and not increasing the quality of life at all. And so throughout the late 1940s and into the early 1950s, several experimental kidney transplantations were attempted, and none were ultimately successful. These transplants did do a couple of things, though. They demonstrated that a kidney could be transplanted into another person and regain functionality as evidenced by urine production. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | And they illustrated that as always the immune system stood in the way of a successful transplant. Enter surgeon Joe Murray. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | Before training as a plastic surgeon, Murray had worked as an army doctor in Valley Forge Hospital where he treated wartime burn victims and developed firsthand experience in the potential power of skin allografts. He happened to treat someone whose skin, whose allografts took really well, like kind of stayed on there a lot longer, so I wonder if it was just a fortuitous match in some way. But that kind of like really lit the fire under him and after his time in the army was up, he decided to become a surgical resident with a focus on transplants of all kinds. In addition to studying transplant surgical techniques and tracking the timeline for rejection, he also studied Peter Medawar's research. And Murray, who was then a surgeon at Brigham Hospital, came to the conclusion that while there were several barriers that needed to be addressed in order for there to be long term transplant success, there was at least one solution for all of them that he could think of: identical twins. |
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| Erin Allmann Updyke |  | Ooh! Good one. |
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| Erin Welsh |  | Yup. On October 15th, 1954, the Brigham transplant team received a phone call about a 22 year old patient, Richard Herrick, who was close to death with Bright's disease and was seeking dialysis. And they called Brigham because Brigham had an artificial kidney machine. |
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| Erin Allmann Updyke |  | Okay. |
|  |  |  |
| Erin Welsh |  | Initially there was some hesitation from Brigham with the doctor in charge of the artificial kidney feeling that this would just be a way to prolong a long and painful death. But just as the phone call was about to end, the doctor who had called added, 'By the way, this patient has an identical twin.' And for Joe Murray, this was the opportunity that he had been waiting for. He had been training for this for over ten years. And for Ronald Herrick, Richard's twin brother, the decision to donate was absolutely a no-brainer. It was unbearable to watch his brother and best friend slowly die and he said he would do anything to help him, even giving him his own kidney. Joe Murray, the surgeon, wasn't entirely without reservations. Like what if the twins weren't actually identical and the kidney was rejected? |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | What if Richard's condition left him too sick to survive surgery? There were many, many what ifs to consider but the one that overruled them all was: what if this works? The questions about the twins identical status were laid to rest with ample genetic screening and a test skin graft and the kidney transplant was scheduled for December 23, 1954. For hours the transplant team worked, removing a kidney from Ronald to replace his twin's diseased ones, suturing artery to artery, vein to vein. And once every stitch was finished came the moment of truth. For an hour and 22 minutes, the transplanted kidney had been entirely without blood flow. The clamps on the arteries were then released, allowing blood to flow into the new kidney which promptly turned pink and began producing urine. So much urine that the surgeons were laughing about it cause it had to be mopped up from the surgery floor. |
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| Erin Allmann Updyke |  | Oh goodness, they forgot to put a catheter in him. (laughs) |
|  |  |  |
| Erin Welsh |  | (laughs) Maybe it overflowed, who knows. |
|  |  |  |
| Erin Allmann Updyke |  | Maybe. |
|  |  |  |
| Erin Welsh |  | At least at the outset the transplant seemed entirely successful. And it was. For eight years, Richard lived with his brother's donated kidney until that kidney too developed Bright's disease and he passed away. |
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| Erin Allmann Updyke |  | Ugh. |
|  |  |  |
| Erin Welsh |  | Very sad, but this was huge. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | Like monumental. |
|  |  |  |
| Erin Allmann Updyke |  | Oh my goodness. |
|  |  |  |
| Erin Welsh |  | Yeah. |
|  |  |  |
| Erin Allmann Updyke |  | 1954 |
|  |  |  |
| Erin Welsh |  | 1954, December 23. And for his work on the surgery, Joe Murray was awarded a Nobel Prize in 1990. |
|  |  |  |
| Erin Allmann Updyke |  | Wow. |
|  |  |  |
| Erin Welsh |  | Yeah. And it's interesting because in retrospect, this first successful organ transplantation was hugely important not because it necessarily opened the doors to more transplants, because in many ways this transplant was seen as kind of a one off, like so many things had to align in order for it to happen. Identical twins, young, one very healthy, one sick. But what it did was it breathed life into the field of organ transplantation and injected a much needed dose of optimism after what seemed like years and years of near wins but overall losses. |
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| Erin Allmann Updyke |  | Losses, yeah. Absolutely. Just that sense of hope, like it's been done once. |
|  |  |  |
| Erin Welsh |  | Yep. And popular support as well for organ transplantation which had definitely waned. |
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| Erin Allmann Updyke |  | Yeah, yeah, yeah. Especially with like 22 year old that you saved doing it? That would be... |
|  |  |  |
| Erin Welsh |  | Oh my god, there are some very cute pictures of them like in the hospital and afterwards. Yeah, it's very sweet. After the success of 1954, there was a bit of a lag in terms of transplants. There were more twin transplants that were performed but there wasn't this huge upswing in transplants overall, mostly because the issues with rejection still remained, right. But progress in that realm was also being made. Bone marrow donation seemed in some cases to help prevent rejection before and organ was transplanted and experiments involving total body irradiation prior to transplantation also showed limited success. So for instance, one recipient of a kidney from his fraternal twin lived for 20 years after receiving some limited irradiation. And this surgery was in a way an even more successful accomplishment than the first kidney transplant. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | But as you may remember from our radiation episode, radiation is not harmless. |
|  |  |  |
| Erin Allmann Updyke |  | No. |
|  |  |  |
| Erin Welsh |  | And people began to look for other ways to minimize the immune system reaction following transplantation. So next came chemical immunosuppression. The ability for certain chemicals to suppress the immune system was not a new discovery or a new concept. At the very least, during WWI researchers had observed mustard gas was able to reduce the immune system and some drugs used in cancer therapy like 6-MP were found to reduce immune responses. Tissue typing and the importance of blood type were also key in developing a protocol for preventing rejection but for much of the 1950s and into the 1960s, success following a transplant was absolutely not guaranteed or like even likely. |
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| Erin Allmann Updyke |  | So by the 60s they also knew, okay, it's not just blood type,we also have these tissue antigens we have to deal with. |
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| Erin Welsh |  | Right. Tissue antigens. But it was still like even with that knowledge, it doesn't, yeah. |
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| Erin Allmann Updyke |  | It's not enough. |
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| Erin Welsh |  | It's a small- |
|  |  |  |
| Erin Allmann Updyke |  | (whispers) Because there are thousands. |
|  |  |  |
| Erin Welsh |  | Yeah. (laughs) It's a small step. And so yeah, the glow of the 1954 and then the limited success of the later 1950s transplants started to kind of fade away a bit. |
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| Erin Allmann Updyke |  | Okay, okay. |
|  |  |  |
| Erin Welsh |  | But then in 1963, there was a conference organized by the National Research Council to review the status of human kidney transplantation. Many of the surgeons at the meeting were reporting low success rate, low success rate, everyone's dying, people were like, 'Should we even be doing this anymore?' The mood was just incredibly grim. |
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| Erin Allmann Updyke |  | Very grim. |
|  |  |  |
| Erin Welsh |  | And then a young surgeon named Thomas Starzl spoke up. And he was like, 'Hi, actually, I have survival rates in patients that are actually kind of decent.' And they were so high in fact that the rest of the surgeons were like, 'We don't believe you. How are you doing this?' So then he was like, 'Okay, well what I'm doing is I give azathioprine and prednisone, the steroid.' |
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| Erin Allmann Updyke |  | Ooh, I was waiting for you to say prednisone. (laughs) |
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| Erin Welsh |  | (laughs) And steroids had been tried on their own before but they didn't really seem to work and so it was this combination that had led Starzl to stumble upon this greater than 70% survival rate like one year following the surgery for kidney transplantation. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | Whereas like everyone else was like, 'Yeah I've had one in ten patients live for a month.' Or something. Like just really remarkable. |
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| Erin Allmann Updyke |  | Oh my god. Wow. |
|  |  |  |
| Erin Welsh |  | And so this protocol absolutely revolutionized the field of kidney transplantation. Transplant units were started in hospitals around the world, like it was huge. And this also opened the door for other whole organ transplants. Surgeons started to consider other organs to transplant like liver, lung, intestines, pancreas, and of course the heart. The first heart transplant was performed in early December 1967 in Cape Town, South Africa by Christian Barnard. This first attempt had limited success. The patient died after 18 days due to the immunosuppression regimen, but the second attempt the recipient lived for two years. Which is pretty amazing. |
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| Erin Allmann Updyke |  | Wow! Yeah. |
|  |  |  |
| Erin Welsh |  | Yeah. And then not many people had success after him, like I don't know what he did that was so magical but yeah. |
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| Erin Allmann Updyke |  | So good. |
|  |  |  |
| Erin Welsh |  | And so with these developments, especially once Starzl's immunosuppressive cocktail was out and about, that sort of really opened the door for everything, that really broke the dam for transplants. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah! |
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| Erin Welsh |  | And so the transplant science at this point wasn't quite off and running but it was steadily walking, like incrementally growing in knowledge, refining surgical and immunosuppressive technique, and that actually did leap a bit forward with the development of cyclosporine in 1976. But the next few decades are just sort of like a list of firsts, right. So we see the first pancreas, the first liver, the first intestine, the first lung, and other organs successfully transplanted. |
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| Erin Allmann Updyke |  | Mm-hmm. |
|  |  |  |
| Erin Welsh |  | And before I hand it over to you to talk about where we are today, I wanna talk about how alongside the steady growth of transplant science, there's one thing that lagged far behind or at least a little behind and that was the ethics of transplantation. And this is where science had definitely outpaced the law. And I touched on this a little bit earlier but questions like who was in charge of the body after death? Was it the next of kin? Were the deceased person's wishes during life legally binding? And then later when artificial ventilation had been developed, there was this new ethical dilemma or how to define life and death. For legal purposes, not to mention the philosophical implications, was someone on a ventilator but without brain activity considered alive? |
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|  |  | And this was a crucial question for successful transplantation of organs other than kidneys, like the heart or the liver or the lungs. Organs that became rapidly damaged after death. When transplantation first became a reality, many of these questions didn't yet have legal answers and it would take some time, not only for the legality to be sorted out but also the public perception. But eventually rulings came out that did address some of these things. So it was ruled that permission could be given from the donor's relatives after death and that if someone wanted to donate tissue after death they could put that in writing. And also brain death was defined medically and legally in 1968 by a Harvard committee. |
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|  |  | And then advancements in organ storage and long-distance transport also gave rise to the formation of a transplant waiting list. And naturally criteria had to be developed about who gets on the list and their place on the list. So when I looked it up I found the different criteria were medical urgency, blood and tissue type, and size match with the donor, time on the waiting list, and then the proximity between the donor and the recipient were just some of the criteria. And some of these ethical debates around organ transplantation have definitely continued through today just as the technology for transplantation has developed enormously. And I think in reading this I realized I had kind of taken organ transplantation for granted in some ways. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Like obviously I knew that it was this huge, incredible surgical feat but I don't think it was until this episode that I realized just how much baseline knowledge needed to be built, how many surgeons and scientists were involved in these developments, I only mentioned like a handful of them, and how brave some people were to say, 'Yeah, I volunteer to give my kidney.' Or 'I volunteer to have my heart replaced.' |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | There are some things I feel like in medical science that seem inevitable, some discoveries, some developments, but organ transplantation really doesn't seem that way to me. Seems like pushing forward in an incredible way. Like this is not very long ago at all. |
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| Erin Allmann Updyke |  | Right! Right. |
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| Erin Welsh |  | It's incredible. At the same time it feels so recent and also surprising to me that like 1954 was the first successful... Like that's incredible. |
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| Erin Allmann Updyke |  | That's...yeah. |
|  |  |  |
| Erin Welsh |  | Yeah. We've come a long way since that first kidney transplant and, Erin, I'm excited for your to tell me now where we stand. |
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| Erin Allmann Updyke |  | Oh, I'll try my best. |
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| Erin Welsh |  | (laughs) |
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| Erin Allmann Updyke |  | We'll take a quick break. |
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| TPWKY |  | (transition theme) |
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| Erin Allmann Updyke |  | So why don't we start with kind of the best news? |
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| Erin Welsh |  | Oh. |
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| Erin Allmann Updyke |  | I think overall the best news. |
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| Erin Welsh |  | Excellent. |
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| Erin Allmann Updyke |  | And that is how much better we do with overall survival than many of the scenarios that you said. Overall, and I'll again just kind of keep this broad, for all transplant types of entire organs and partial organs, there is an initial pretty rapid decrease in survival and that is because of the things that we talked about in the biology section, that kind of acute onset of graft failure. But overall, about 70% of grafts will be functioning at ten years when you look at the overall transplant numbers. |
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| Erin Welsh |  | That's amazing. |
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| Erin Allmann Updyke |  | Yeah. Isn't it? |
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| Erin Welsh |  | That is amazing. |
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| Erin Allmann Updyke |  | Yeah, it's really, really incredible. And for some particular organs, you know, it can be a little bit better and a little bit worse. For example, lungs tend to be overall the worst. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | With maybe a five year survival of only 50-60% at most institutions. But for example in infants who need a heart transplant, they can have a 90% ten year survival. |
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| Erin Welsh |  | Holy cow! |
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| Erin Allmann Updyke |  | Right, yeah. So it really varies still but we've definitely come an incredibly long way in terms of overall survival. If we look at the global numbers, which I think is really interesting to do, there is a global database, it's literally called the Global Database on Donation and Transplantation. (laughs) |
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| Erin Welsh |  | Uh huh. (laughs) |
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| Erin Allmann Updyke |  | And according to that database, at least from 2007, they do have some more updated data but this was synthesized nicely. So in 2007 there were around 100,000 solid organ transplants worldwide. I think the number from 2018 was a little higher, around 140,000, so not a huge increase but an increase. Of those in 2007, 68,000 were kidney transplantations. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | So kidney by far is the largest. And the numbers for kidney transplantations, I actually do have the more recent numbers for that. So in 2019 there were 98,000 kidney transplants worldwide. 98,000 kidney transplants! And that's out of 150,000 total organ transplants. |
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| Erin Welsh |  | Wow! |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | So what do you think happened inbetween 2007 and 2019 to lead to so many more... Is it just infrastructure? Is it need? Is it... |
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| Erin Allmann Updyke |  | I would guess that it's infrastructure because there are certain countries that disproportionately do a lot of the transplants and so I wonder is it a wider geographic range of where transplants are being done and that is what is causing those numbers to go up. |
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| Erin Welsh |  | Gotcha. |
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| Erin Allmann Updyke |  | Whereas it was unavailable in some parts of the world and now it is becoming available. I don't know for sure if that's the case but my guess would be that would be at least part of it. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | Yeah, lemme throw some other numbers out at ya. For liver transplants, total worldwide: 34,000 in 2019. Heart transplants: 8500 in 2019. So by far kidney is the biggest but there's pancreas, there's hearts, there's lungs, you can do partial livers, you can do entire livers, and then there's also differences in how many of those come from living donors vs deceased donors. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | So yeah. We do a lot of transplants overall. Although I have to say it was also a smaller number than what I expected. |
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| Erin Welsh |  | Really? Okay. |
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| Erin Allmann Updyke |  | Yeah, yeah. It was like, 150,000, that's a lot. But there's a lot of people. So another thing we could take about is how many people need organs. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | And there is a huge discrepancy in the number of people who need organs who are on waiting lists who don't ever actually get an organ. In the U.S., according to U.S. organ donation statistics, there are 100,000 people that are on the transplant waiting list as of September 2020 for only less than 40,000 transplants generally performed in a year. And so in the U.S. at least, 17 people die everyday waiting for an organ transplant. |
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| Erin Welsh |  | Oh my gosh. |
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| Erin Allmann Updyke |  | To look at some other countries, I have statistics on the U.K. as well. So in the U.K. for example in 2010, it's a little older statistic, but there were 8000 people on the waiting list for an organ transplant in general. And if you look at heart transplants, which are one of the less commonly performed transplants, while 62% of people who need a heart would get a transplant within a year, 12% will die on the waiting list and another 7% will be removed from the waiting list for some other medical reason. Like they're no longer a candidate. And that's for hearts. For lungs it's even worse. 27% of people will either die or be removed from the waiting list and only 31% will be transplanted. So we definitely have a big mismatch in terms of need even in the countries that do a ton of transplants. That's not even mentioning places where this just isn't even a possibility, where kidney failure is either dialysis if that's available or a death sentence. |
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| Erin Welsh |  | I have a question about the makeup of the list in terms of like does it follow proportionately the transplants that are actually performed? Like do you see most of the list being made up of people who are on the list for a kidney? |
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| Erin Allmann Updyke |  | Oh, good question. That's a really good question. I actually don't know, they don't have those particular statistics off the bat on... Let's see, here we go. Okay. They actually have a graph here and no. |
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| Erin Welsh |  | Interesting. |
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| Erin Allmann Updyke |  | I mean, well, yes and no. So kidneys are by far the biggest need however even though it's the most commonly performed, there's the biggest gap by far between needed and received for kidneys. |
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| Erin Welsh |  | Oh, okay. Okay. |
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| Erin Allmann Updyke |  | So a lot more people need kidneys than get them especially. And then it goes down proportionally from there, liver, heart, lung, and then other is all infrequent enough that it's just combined on this graph so I can't tell you more data. But if you wanna know more you could go to organdonor.gov and they have a lot more statistics there. |
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| Erin Welsh |  | Gotcha. |
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| Erin Allmann Updyke |  | But yeah, so I guess the biggest question is kind of where do we go from here? We've come a very long way, like you kind of walked up through, Erin, it's still far from perfect. But in general there's kind of two big gaps, at least that I see. One is long-term tolerance of grafts and the other is organ availability, right? |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | There, like we already said, are thousands of people who die every year on waiting lists and on top of that, no organ from another person can function precisely as well as the original. So there's a lot of room for improvement in both of those regards. And it's kind of a question of where do we go from here? Like what direction do we take? I will say there are people doing work on all fronts. There was a paper from 1998 that was published in Nature that was like, 'New directions for organ transplantation! We figured it out! Here's how you're gonna use animal tissues! Xenografts are the way of the future!' (laughs) |
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| Erin Welsh |  | Uh huh. (laughs) |
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| Erin Allmann Updyke |  | We still don't really do xenografts with the exception of tissues, not full organs, and so the research on using animal organs is still well within animal model stages, we have a very long way to go before we're using pig hearts in a human. But there is another kind of technology that has the potential to ensure not only organ availability, to overcome that hurdle which we know is huge, but to also overcome essentially all immunologic barriers. |
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| Erin Welsh |  | Ooh! |
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| Erin Allmann Updyke |  | And that would be - it is Twilight Zone. |
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| Erin Welsh |  | (hums Twilight Zone theme) |
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| Erin Allmann Updyke |  | It's using your own stem cells to 3D print a new organ. |
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| Erin Welsh |  | It is the coolest thing, one of the coolest things ever. |
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| Erin Allmann Updyke |  | It is. Still every time I think about it I get re-blown away all over again. |
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| Erin Welsh |  | Mm-hmm, mm-hmm. |
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| Erin Allmann Updyke |  | We're not there (laughs) is the long and short of it. But there is proof of concept in at least some of this. Like we can induce cells to become pluripotent stem cells, which is what you would in theory need. And then we can induce those to differentiate into specific cell types. And at least in mouse models, that's been shown to potentially help a mouse live longer even with a disease. |
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| Erin Welsh |  | That's amazing. |
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| Erin Allmann Updyke |  | And there are a lot of different companies across the globe that are working on 3D printing with bioengineered tissue things like ears, because it turns out ears are kind of a good starting point. But even as far as those go, we still do have a really long way to go before we're 3D printing new hearts or kidneys for people. But I do think it's kind of the way of the future and the future is now. |
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| Erin Welsh |  | It absolutely is. |
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| Erin Allmann Updyke |  | It really is. |
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| Erin Welsh |  | And it all seems very promising and just a matter of time kind of a thing. |
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| Erin Allmann Updyke |  | It does, it does. There's a couple of great articles out there that we'll link to that have a lot more detail on kind of where we are at in this process, so if you'd like to read more. Speaking of which, should we talk about our sources? |
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| Erin Welsh |  | Sources, let's do it. I wanna shout out a couple of books. On is by David Hamilton and it is called 'History of Organ Transplantation'. |
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| Erin Allmann Updyke |  | Well, appropriate. |
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| Erin Welsh |  | Yes, it is thorough, it is great. Another one is called 'Borrowing Life' by Shelley Fraser Mickle and that is more specifically about the first kidney transplantation and a very interesting read. And I have a few papers and I will post those to the website. |
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| Erin Allmann Updyke |  | Excellent. A couple of resources that I wanna especially shoutout, one is 'The Immunology of Organ Transplantation' article in Surgery, 2017 by Phillips and Callaghan. And another is 'Transplantation Immunology: Solid Organ and Bone Marrow' in the Journal of Allergy and Clinical Immunology, 2010 by Chinen and Buckley. There's a bunch of other resources including more detail on the Global Database on Donation and Transplantation. You can find the list of all of our sources for this episode and every single one of our episodes on our website thispodcastwillkillyou.com under the EPISODES tab. |
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| Erin Welsh |  | Absolutely. Thank you again so much Carol and Betsy, it was so much fun. And again, keep an eye out for their upcoming book. |
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| Erin Allmann Updyke |  | I can't wait to read it, I wish I got to talk to them too. |
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| Erin Welsh |  | Oh my gosh, they were great. And we will also link to Carol's website where you can find more information about the book as well as some great resources that she links to for especially like living donors for kidneys and so on. |
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| Erin Allmann Updyke |  | Excellent, awesome. |
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| Erin Welsh |  | Thank you to Bloodmobile for providing the music for this episode and all of our episodes. |
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| Erin Allmann Updyke |  | Thank you to Exactly Right network of whom we are very proud to be a part. |
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| Erin Welsh |  | And thank you to you, listeners, for sitting through this very long episode on organ transplantation. |
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| Erin Allmann Updyke |  | I hope that you guys had fun because I did. |
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| Erin Welsh |  | I did too. Okay, well. Until next time, wash your hands. |
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| Erin Allmann Updyke |  | You filthy animals! |