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IDWeek 2023: Investigating the Infectious Risk of Xenotransplantation

### Announcer:

You're listening to *Clinician's Roundtable* on ReachMD. On this episode, we'll hear from Dr. Jay Fishman about the current state of xenotransplantation where he'll discuss the infectious risks of transplantation and strategies for prevention. Dr. Fishman is the Director of Transplant Infectious Diseases and Compromised Host Program at Massachusetts General Hospital in Boston and a Professor of Medicine at Harvard Medical School. He'll be presenting on this topic at IDWeek 2023. Here's Dr. Fishman now.

### Dr. Fishman:

In the early era, when we first raised questions about the infectious risk of xenotransplantation, we identified a number of potential pathogens, including the porcine endogenous retrovirus, which my lab cloned and sequenced and put a damper on things for a while because of concerns about infectious risk.

The ability to knock out PERV genetically using CRISPR/Cas9 and other advances, such as the availability of antiretroviral medications, which could treat it if infection occurred, helped to reopen a field at a time when a number of companies were getting interested again in developing pigs as potential organ donors for humans. The background is very simple. We have a dramatic shortage of organs for people with end-stage organ failure, and pigs were of appropriate size, easier to breed, didn't carry some of the infectious risks associated with primates, and so had been a choice for a long period of time as a potential for human transplantation.

There were and are some immunologic barriers, which required research and some new innovation in immunosuppression that would allow these organs to be accepted by humans. And what has now happened with genetic manipulation is that some of the immunologic barriers, the metabolic barriers, particularly surrounding coagulation and some of the infectious disease barriers, have been overcome using genetic tools, which allows consideration of clinical trials.

With the improvement of immunosuppression and with the improvement of our knowledge in infectious disease, people were becoming poised to begin studies. And you may have seen what we call the decedent studies, the people who have volunteered their bodies after their death for use in studies where kidneys and hearts have been transplanted in by groups at NYU and the University of Alabama, to see if they would be acutely rejected or if any metabolic incompatibilities existed, and these organs survived quite well. In the midst of those kinds of studies was the first, and now the second, heart transplant at the University of Maryland where, surprisingly, the first recipient, who was quite deconditioned and quite ill going into transplant and had a series of complications as well, did quite well, lived for 61 days, and the second gentleman, apparently, is doing also quite well and is off various forms of support.

In some ways, what we're missing are clinical trials. We need to know more about each of the areas. We've learned a lot about the immunology of xenotransplantation, and as a result, we've established very good immunosuppressive regimens for eventual application in clinical xenotransplantation. I think the infectious disease risks are manageable, but we know that any immunosuppressed human is at risk for infection from the environment and from the hospital environment, and therefore, we're going to take an approach where we monitor those recipients for infectious disease.

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That was Dr. Jay Fishman discussing his 2023 IDWeek session on zee-no-transplantation. To access this and other episodes in our series, visit *Clinician's Roundtable* on ReachMD dot com, where you can Be Part of the Knowledge. Thanks for listening.