Doctor discusses pediatric heart pump trial

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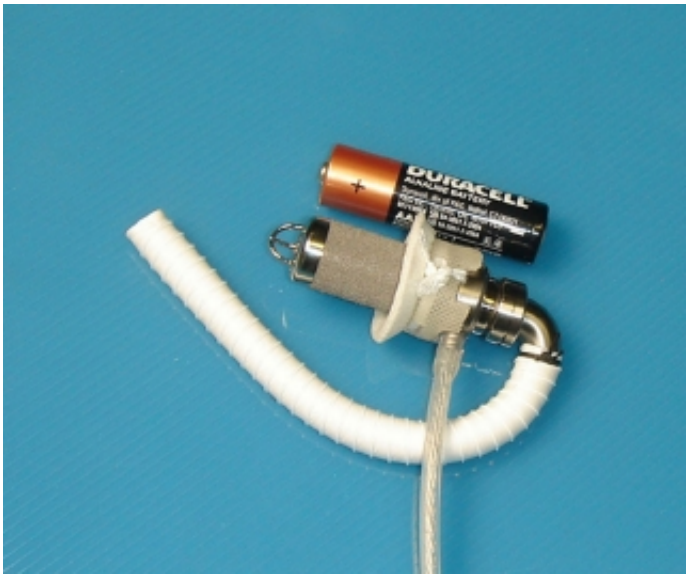

The Jarvik 2015 ventricular assist device is designed for young children with advanced heart failure who are awaiting a transplant. Stanford will be one of the sites testing the device. Credit: Jarvik Heart Inc.

During the wait for a heart transplant, patients with advanced heart failure can be supported with a ventricular assist device, an artificial pump that helps the heart move blood through the body. But the VAD now used for babies and small children—the Berlin Heart—has drawbacks. The pump carries a 30 percent risk of stroke and is unwieldy: The driver, which sits outside the body, is about the size of a shopping cart. For these reasons, children supported with the Berlin Heart must stay in the hospital until a donor heart becomes available. This can take months.

In recent years, researchers have developed a replacement for the Berlin Heart called the Jarvik 2015. The new device is a fully implantable pump that is roughly the length of a paper clip and as thick as an adult's index finger. After a series of successful animal studies, the Food and Drug Administration recently approved the first clinical trial of the device in humans. It's called the PumpKIN Trial after the NIH-sponsored Pumps for Kids, Infants and Neonates program that launched the research.

Christopher Almond, MD, an associate professor of pediatrics at the School of Medicine, is one of the trial's principal investigators. Erin Digitale recently asked him about the trial, which in May will begin enrolling children at Lucile Packard Children's Hospital Stanford and several other North American sites.

Q: How does a ventricular assist device support the patient's health?

Almond: Infants and small children with severe heart failure have an unacceptably high risk of death on the transplant waitlist. A VAD helps to keep the child stable and capable of safely waiting out the time until a donor organ is available. Also, it's really miserable having heart failure—patients tend to have trouble breathing; have severe fatigue that keeps them bedridden; and have nausea, vomiting and loss of appetite that lead to malnutrition. In addition to improving survival, a VAD alleviates many of these symptoms by ensuring enough blood can get to the body's organs when the heart is weak. The goals of VAD support are to allow you to breathe comfortably, engage in exercise and tolerate excellent nutrition so that you become a better candidate for heart transplant. Beyond that, we ideally would like kids to go home with their VAD rather than being stuck in an ICU for weeks or months.

Having a heart pump can also give transplant doctors more time to find a heart that is the best match for the patient. Both of these factors lead to better outcomes after heart transplant.

Q: The new pump is named for Robert Jarvik, MD, who has spent his career designing different ventricular assist devices, as well as the first total artificial heart. What were some of the biggest challenges he and his team faced in developing this tiny pump?

Almond: The main challenge of miniaturizing any pump technology is to design it in a way that does not crush fragile red blood cells as they pass through the device, which is spinning several thousand times per minute. An earlier version of the Jarvik 2015 pump tended to break red blood cells and had to be redesigned. Interestingly, a relatively minor design change caused a big reduction in the pump's red cell breakage.

A second challenge is that the flow rate through miniature pumps is much slower than for adult pumps, greatly increasing the chance that clots can form inside the pump. When clots form, they can break off and travel through the bloodstream to the brain, causing a stroke. For example, blood typically flows through an adult heart pump at 1.5 to 2 gallons per minute, making it less likely to slow down and clot. Blood flows through an infant pump at about one-eighth to one-quarter of a gallon per minute, making it more likely to clot. However, the Jarvik 2015 pump has a relatively low risk of clot formation.

Q: How will the trial work?

Almond: This multicenter, randomized clinical trial will enroll 88

patients at 22 pediatric heart transplant centers in North America. Stanford is providing leadership for the trial, which will enroll children with advanced heart failure who weigh between 18 and 44 pounds and need a heart transplant. They will be randomly assigned to receive a Berlin Heart or a Jarvik 2015, with half of the patients in each group. For the trial, all study participants will need to stay in the hospital so we can carefully evaluate the safety of the new pump. But if the pump proves to be safe enough, the longer-term goal is to discharge patients home with the device to wait for their heart transplant.

Q: How does Stanford's leadership role in this trial fit in with our larger history as a center of innovation in heart transplant?

Almond: Stanford has been a pioneer in developing cardiac transplantation and therapies for children with end-stage heart failure. In 1984, we performed one of the world's first heart transplants in a young child. We have been refining pediatric heart-transplant techniques ever since.

Stanford has also been a pioneer in the field of heart pumps. In 2004, Packard Children's was one of the very first U.S. hospitals to use the Berlin Heart. Until that time, the Berlin Heart had been used primarily in Europe. Under the direction of pediatrician David Rosenthal, Packard Children's petitioned the FDA to import the device from Germany for a 5-month-old boy, who was then the youngest child in the world to receive the pump. This little boy did well and got a heart transplant after 55 days. The novel use of the Berlin Heart in this child ended up on the front page of The New York Times and served to catalyze interest in the device across the United States. Stanford faculty provided important leadership for the multisite clinical trial of the Berlin Heart, which led to its FDA approval in 2011. Stanford physicians have been on the

forefront of the use of VADs in children with single-ventricle heart disease and in children with muscular dystrophy or other contraindications to heart transplant. Today, Stanford Children's Health has one of the busiest pediatric VAD programs in the country.

Provided by Stanford University Medical Center