Transplanting pig hearts into sick babies may be a promising temporary treatment option

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Xenotransplantation—transplanting organs from animals into humans—is one step closer to becoming a possibility for infants awaiting human heart transplantation, according to research presented by

University of Alabama at Birmingham researchers at the annual Society of Thoracic Surgeons meeting today.

"Our study showed a high probability that a genetically engineered pig heart could be implanted in an infant to keep the baby alive until a human heart becomes available, without concern for early rejection," said David C. Cleveland, M.D., associate professor in the Division of Cardiothoracic Surgery. "The ability to use pig hearts would provide an inexhaustible source for organ transplantation."

Cleveland and colleagues from UAB analyzed how an infant's blood serum would react to a "triple-knockout" pig—a pig that has been genetically modified to delete all three major antigens that are known to react with natural human anti-pig antibodies. This immune monitoring was conducted in 70 infants less than 1 year of age using a blood test known as flow cytometry.

The 70 infants were separated into two groups. Group one consisted of 50 infants who had never been exposed to any surgical procedure or blood transfusion, and group two consisted of 20 patients who had undergone previous heart surgery, blood transfusion or exposure to biologic tissue patches (pig or cow).

The level of reactivity of human antibodies to pig cells is important because, if the level is high, it suggests that early rejection would occur following a heart transplant. In this respect, the researchers found that no infants in the first group had any immunoglobulin M (IgM) antibodies directed to TKO pig red blood cells, while only one infant showed a "very weak" immunoglobulin G (IgG) reaction. IgM is usually the first antibody to react against pig tissue. IgG is the most abundant antibody in the human body. In group two, one of the 20 patients had an IgM reaction to TKO pig blood cells, and two had an IgG reaction; but in all cases the reactions were very weak.

"The reactivity of the infant's serum to TKO pig red blood cells was almost zero, indicating no antibody binding and therefore no killing of the pig cells," Cleveland said.

Scarcity of organs in the U.S.

Encouraged by the UAB findings and the tremendous progress that has been made in the field of xenotransplantation research during the past 20 years, Cleveland says he is confident there is potential for a genetically engineered pig heart to support the life of an infant for weeks or months until a human donor heart becomes available.

"This would be especially important because very few human organs become available for transplantation into infants—particularly those with complex congenital heart disease," he said. "Furthermore, using mechanical assist devices in infants is suboptimal."

According to the United Network of Organ Sharing, more than 114,000 people are on the waitlist for organs in the United States, and nearly 3,200 of them are waiting for new hearts. Of those 3,200, approximately 50 are infants. The relative sizes of both the patient's body and the donor organ are considered when matching donors to recipients, which is why small children most often receive donations from other infants or young children. Information from the U.S. Department of Health and Human Services shows that, in 2016, 135 pediatric organ donors were babies younger than 12 months. In addition, each year the number of people added to the waitlist continues to be much larger than the number of donors who become available, worsening the organ shortage in the United States.

"The need is so great in infants," Cleveland said. "As we've increased our ability to keep really critically ill babies alive, we've increased the number of babies with significant heart failure. There's no good option

treatment for these children."

Why pigs?

Material from domestic pigs—heart valves—has been used routinely and safely for medical purposes for a long time. Cleveland says pigs can be bred and raised in large numbers, and genetic engineering of their hearts is relatively easy.

Provided the pigs are treated humanely, use of pig parts may present less of an ethical dilemma than using organs from other animals.

"The present evidence is that the public would accept a pig heart transplant if it were life-saving," Cleveland said.

Although much more work is needed before xenotransplantation trials in humans can begin, this research has moved an important area of study significantly forward. Cleveland says the next phase is the transplantation of TKO pig hearts into non-human primates to demonstrate long-term survival.

Provided by University of Alabama at Birmingham