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# In World First Transplant; A Man Received Genetically-Modified Pig Heart

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**Abstract:** ***Present paper aims to highlight great advancement in medical history where genetically altered heart from pig was transplanted to a man. For the first time in history, doctors successfully transplanted a genetically modified pig heart into a patient. With the patient doing well after three days, UMMC officials said that the genetically modified animal heart is functioning like a human heart without immediate rejection by the body. Pig hearts are used to study the anatomy of human hearts because they are very similar in structure, size and function to human hearts. These similarities, combined with the fact that they are much more readily available than human hearts, make them an ideal choice for research and study. There's a shortage of human organs for transplants and each day many patients die due to unavailability of organs on time.***

**Keywords:** Transplant, Heart, Xenotransplantation

On January 7, 2022, doctors in Maryland successfully transplanted a pig's heart into a human. "The breakthrough may lead one day to new supplies of animal organs for transplant into human patients.1

57-year-old David Bennett gave Mohiuddin's team a chance to jump straight to a human transplant. Bennett had been on cardiac support for almost two months and couldn't receive a mechanical heart pump because of an irregular heart beat. Neither could he receive a human transplant, because he had a history of not complying with doctors' treatment instructions. Given that he otherwise faced certain death, the researchers got permission from the FDA to give Bennett a pig heart.

The surgery went well and "the heart function looks great", Mohiuddin says. He and his team will monitor Bennett's immune responses and the performance of his heart. They will continue working towards controlled clinical trials, but Mohiuddin says they might apply to conduct more emergency procedures if the right patients come along.

The first person received a transplanted heart from a genetically modified pig in Baltimore, Maryland. It is assumed that with this advance will enable surgeons to give more people animal organs, but many ethical and technical hurdles remain.

"It's been a long road to get to this point, and it's very exciting we are at a point where a group was ready to try this, " says Megan Sykes, a surgeon and immunologist at Columbia University in New York City. "I think there's going to be a lot of interesting things to be learned. "

This incident opens a new door for further study and may bring revolutionary changes in medical treatment of patients which require organ transplantation. Many times the patient dies due to unavailability of organs from appropriate donors. This paper also aims to discuss about the similar cases and study which highlight how these studies can extend the life.

This procedure marks the first time that a pig organ has been transplanted into a human who has a chance to survive and recover. In 2021, surgeons at New York University Langone Health transplanted kidneys from the same line of genetically modified pigs into two legally dead people with no discernible brain function. The organs were not rejected, and functioned normally while the deceased recipients were sustained on ventilators.

Pig heart valves are routinely transplanted into humans, and some patients with diabetes have received pig pancreas cells. Pig skin has also been used as temporary grafts for burn patients. The combination of two new technologies — gene editing and cloning — has yielded genetically altered pig organs.

The researchers had applied to the US Food and Drug Administration (FDA) to do a clinical trial of the pig hearts in people, but were turned down. According to Muhammad Mohiuddin, the University of Maryland surgeon who leads the research team behind the transplant, the agency was concerned about ensuring that the pigs came from a medical-grade facility and wanted the researchers to transplant the hearts into ten baboons before moving on to people.

Aside from that, most research has so far taken place in non-human primates. But researchers hope that the 7 January 2022 operation will further kick-start clinical xenotransplantation and help to push it through myriad ethical and regulatory issues.2

Xenotransplantation has seen significant advances in recent years with the advent of CRISPR–Cas9 genome editing, which made it easier to create pig organs that are less likely to be attacked by human immune systems. The latest transplant, performed at the University of Maryland Medical Center (UMMC), used organs from pigs with ten genetic modifications.

Xenotransplantation is any procedure that involves the transplantation, implantation or infusion into a human recipient of either (a) live cells, tissues, or organs from a nonhuman animal source, or (b) human body fluids, cells, tissues or organs that have had ex vivo contact with live nonhuman animal cells, tissues or organs. The development of xenotransplantation is, in part, driven by the fact that the demand for human organs for clinical transplantation far exceeds the supply.

Currently ten patients die each day in the United States while on the waiting list to receive lifesaving vital organ transplants. Moreover, recent evidence has suggested that transplantation of cells and tissues may be therapeutic for certain diseases such as neurodegenerative disorders and diabetes, where, again human materials are not usually available.

Although the potential benefits are considerable, the use of xenotransplantation raises concerns regarding the potential infection of recipients with both recognized and unrecognized infectious agents and the possible subsequent transmission to their close contacts and into the general human population. Of public health concern is the potential for cross-species infection by retroviruses, which may be latent and lead to disease years after infection. Moreover, new infectious agents may not be readily identifiable with current techniques.3

Pigs are considered suitable heart donors because their hearts are roughly the same size and shape as human hearts. Pig hearts are used to study the anatomy of human hearts because they are very similar in structure, size and function to human hearts. These similarities, combined with the fact that they are much more readily available than human hearts, make them an ideal choice for research and study.

Like a human heart, a pig heart consists of four chambers: two atriums and two ventricles. Likewise, consistent with the structure of a human heart, it has four valves and an aorta. These similarities allow blood to flow through a pig's heart in the same way it flows through a human's heart. In fact, pig hearts are so similar to human hearts that tissue from pig hearts is used to make heart valve replacements for humans. Of course, the tissue is treated before surgery to decrease the likelihood of the recipient's immune system rejecting it.4

Transgenic technology has potentially solved many of the immunological difficulties of using pig organs to support life in the human recipient. Nevertheless, other problems still remain. Knowledge of cardiac anatomy of the pig (Sus scrofa) is limited despite the general acceptance in the literature that it is similar to that of man. A qualitative analysis of porcine and human cardiac anatomy was achieved by gross examination and dissection of hearts with macrophotography. The porcine organ had a classic 'Valentine heart' shape, reflecting its location within the thorax and to the orientation of the pig's body (unguligrade stance). The human heart, in contrast, was trapezoidal in silhouette, reflecting man's orthograde posture. The morphologically right atrium of the pig was characterised by the tubular shape of its appendage (a feature observed on the left in the human heart). The porcine superior and inferior caval veins opened into the atrium at right angles to one another, whereas in man the orifices were directly in line. A prominent left azygous vein (comparable to the much reduced left superior caval or oblique vein in man) entered on the left side of the pig heart and drained via the coronary sinus. The porcine left atrium received only 2 pulmonary veins, whereas 4 orifices were generally observed in man. The sweep between the inlet and outlet components of the porcine right ventricle was less marked than in man, and a prominent muscular moderator band was situated in a much higher position within the porcine right ventricle compared with that of man. The apical components of both porcine ventricles possessed very coarse trabeculations, much broader than those observed in the human ventricles. In general, aortic-mitral fibrous continuity was reduced in the outlet component of the porcine left ventricle, with approximately two-thirds of the aortic valve being supported by left ventricular musculature. Several potentially significant differences exist between porcine and human hearts. It is important that these differences are considered as the arguments continue concerning the use of transgenic pig hearts for xenotransplantation.5

Researchers in South Korea are expected to transplant pig corneas into humans within a year. A handful of groups across the US are also working toward pig organ clinical trials in the next few years, including a group at Massachusetts General Hospital in Boston that is starting a six-person clinical trial using "blankets" of pig skin to temporarily protect the skin of burn victims. At the University of Alabama at Birmingham's (UAB) medical school, researchers are planning to transplant pig kidneys into adults and hearts into struggling newborns.

For a pig kidney, heart or lung to keep a person alive, the human immune system has to be tricked into not recognising that it comes from a different species. That's where Crispr gene-editing technology comes in, enabling researchers to make targeted changes to a complete set of genes in many places simultaneously.

Transplant-ready pigs could do far more than just provide organs. Eventually, they could be used to produce the islet cells – clusters of hormone-producing pancreatic cells – needed by people with diabetes. Pig blood could be used to give transfusions to trauma patients and people with chronic diseases like sickle cell anemia, who often develop antibodies against human blood cells because they have had so many transfusions. Even dopamine-producing cells could be made by pigs, and transplanted into patients with Parkinson's disease.

Even if a pig organ can't last forever in a person, it should be able to buy someone time. At the moment, newborns can wait on the organ transplant list for more than three months for a new heart, often facing a mortality rate above 50%, says David Cleveland, a heart surgeon at UAB. Cleveland wants to use xenotransplantation to save babies born with congenital heart defects. "There's such a great need, " he says. Artificial hearts can keep adults alive while awaiting a transplant, but no such device exists for infants. There are clearly difficulties in using a pig heart permanently for a baby, but at least the pig heart could be used as a bridge.

Pig skin could also help burn patients, says Jeremy Goverman, the principal investigator of Massachusetts general's skin trial. Now, he often can't find swatches of human skin big enough to cover large wounds.6

There's a shortage of human organs for transplants—an average of 21 people die each day in the United States because they don't get transplants in time. Lungs or hearts can only stay functional on ice for a few hours, and so they often aren't used before they expire.

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