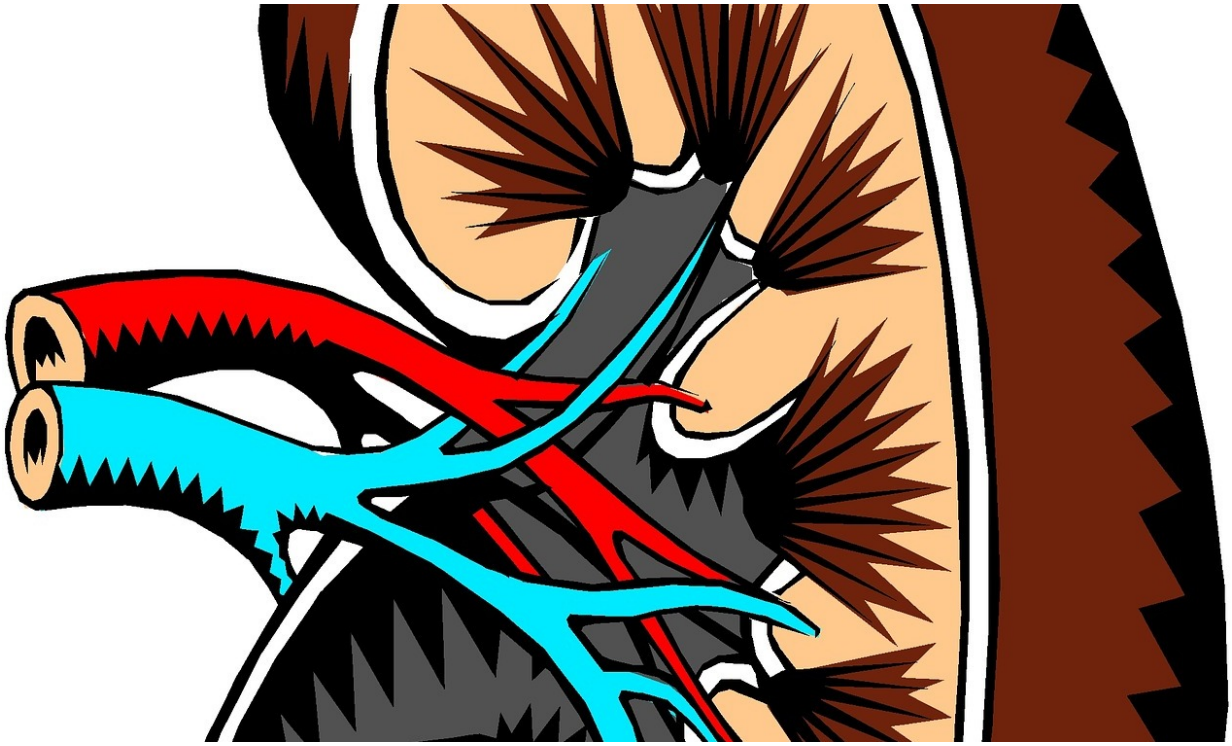
Drug therapy from lethal bacteria could reduce kidney transplant rejection

August 3 2017



Credit: CC0 Public Domain

An experimental treatment derived from a potentially deadly microorganism may provide lifesaving help for kidney transplant patients, according to an international study led by investigators at Cedars-Sinai.

The study, published in the *New England Journal of Medicine*, found that treating patients with the drug IdeS before transplantation significantly reduced, and in most cases eliminated, donor-specific antibodies that can cause rejection or failure of the new organ. These antibodies represent an often impenetrable immunologic barrier to transplantation.

IdeS is derived from an enzyme in the bacteria Streptococcus pyogenes, which causes disorders ranging from sore throats to life-threatening infections.

Stanley C. Jordan, MD, medical director of the Kidney Transplant Program at Cedars-Sinai, said the enzyme is the only one that can completely remove organ-rejecting antibodies and allow kidney transplantation to take place. He noted that, one hour after infusion of the enzyme, antibodies declined drastically.

"We found that IdeS could immediately cut patient antibodies in half, making them powerless to attack and injure a newly transplanted kidney," said Jordan, the study's lead author. "We can put a new kidney in a patient without it being rejected."

All people have human leukocyte antigens (HLA), proteins that are key to the immune system's defense against bacteria, viruses and other potentially harmful invaders. Patients develop antibodies to foreign HLA due to failed organ transplants, transfusions or pregnancy.

These antibodies persist over a patient's lifetime, causing their body to perceive a newly donated organ as a threat and so attack it. This response prevents patients from having a successful kidney transplant and they often remain on dialysis for years with diminished quality and length of life.

The study of IdeS involved two coordinated investigations, with a total

of 25 patients treated in the U.S. and Sweden. Twenty-four of the patients were transplanted successfully after receiving the investigational therapy.

The special enzyme is produced by Hansa Medical of Sweden.

"IdeS could change the way we treat antibody rejections overall," said Jordan, who also directs the Human Leukocyte Antigen and Transplant Immunology Laboratory at Cedars-Sinai. "We think this approach to preventing organ rejection has the potential to offer significant benefits to those in need of heart, lung, liver and bone marrow transplants."

Nearly 128,000 people in the U.S. are waiting for organ transplants, according to the Organ Procurement and Transplantation Network, with more than 105,000 needing new kidneys. Many of them wait years for an organ to become available, only to have their bodies' immune systems attack it.

"We need larger studies to confirm the promising results of this unique approach to removing patient antibodies that threaten newly transplanted organs," Jordan said. "And we want to investigate any long-term impact IdeS therapy may have on overall antibody production in patients."

More information: Stanley C. Jordan et al, IgG Endopeptidase in Highly Sensitized Patients Undergoing Transplantation, *New England Journal of Medicine* (2017). DOI: 10.1056/NEJMoa1612567

Provided by Cedars-Sinai Medical Center

lethal-bacteria-kidney.html