

# Opening the door to safer transplants

**Refined methods of typing and preserving organs can make transplants effective**

by Betty Corday

Most types of organ transplantation are generally considered to be experimental procedures. After a heady year of heart transplants in 1968, cardiac replacement has slowed notably. Liver transplants (SN: 2/21, p. 202) are still a last-ditch measure. But more than a decade's experience with kidney transplantation has transformed that operation from an experimental to a therapeutic procedure.

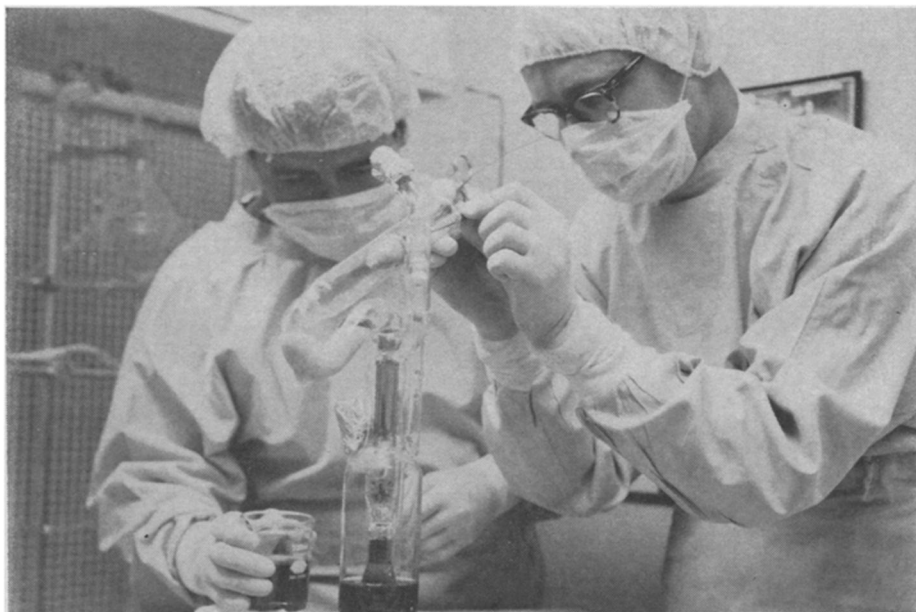
Widespread success with kidney transplantation, in fact, leads scientists to believe that other organ transplants will, in time, become effective, life-saving operations. But there are roadblocks.

The first is the still unsolved problem of immune rejection. The second is the scarcity of available donor organs—even kidneys—and the fact that organ-preservation and organ-banking techniques have yet to be devised.

In several ways the two go hand-in-hand. A transplanted organ is most likely to thrive in a recipient if it is genetically closely matched to the recipient's tissues. But because even preliminary typing takes a matter of hours, it is necessary to preserve the donor organ for some period before surgery. Presently, this is all but impossible with hearts, most successful with kidney transplants.

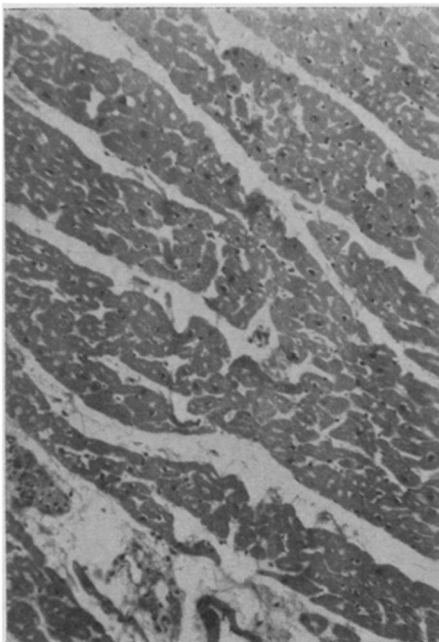
**The kidney transplanters** have not resolved all of their obstacles, but their continuing progress may point the way for other transplants.

For purposes of matching donor and recipient as closely as possible, two regional networks for kidney typing and sharing have been established within the last year. The Western network, covering Salt Lake City, Denver and the coast cities, has headquarters in



Photos: Biomedical Research Labs.

*Malinin (right): Modification in preservation systems will have to be devised.*



*Preserving the heart for 10 hours can damage the muscular fibers (right).*

Los Angeles, where Dr. Paul I. Terasaki of the University of California types tissue from patients who are transplant candidates in the various cities, and stores the information in a computer. When a donor kidney becomes available anywhere in the region, it is typed. The computer then selects the most closely matched patient. In the East, a similar network is headquartered at the Medical College of Virginia, headed by Dr. David Hume.

Current methods of kidney preservation can easily keep the donor organ functioning for 24 hours. However, Dr. Keith Reemtsma of the University of Utah says, "In reality, we can generally work much faster than that. Using com-

mercial and sometimes chartered airlines, we can get a kidney to a patient within about eight hours." The donor organ is flushed, cooled and put into a plastic bag for shipment.

"The running question," he observes, "is whether hypothermia—cooling—or continuous organ perfusion is the best method of preservation. Dr. Folkert Belzer of the University of California at San Francisco has shown very good results with a new perfusion technique." At present both preservation methods are effective only for short-term maintenance. Long-term banking remains far in the future.

Dr. Belzer perfuses donor kidneys with human plasma, treated to remove

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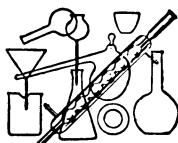
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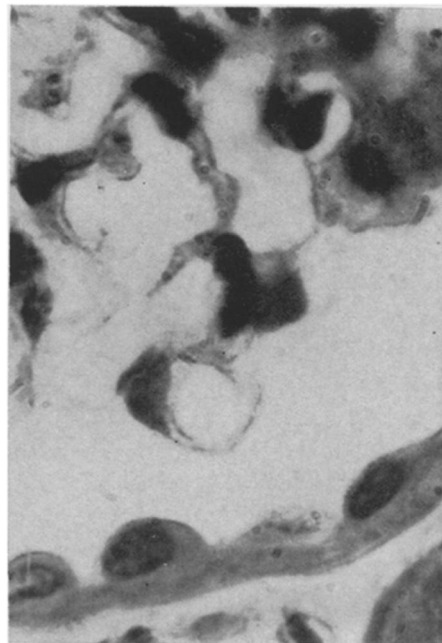
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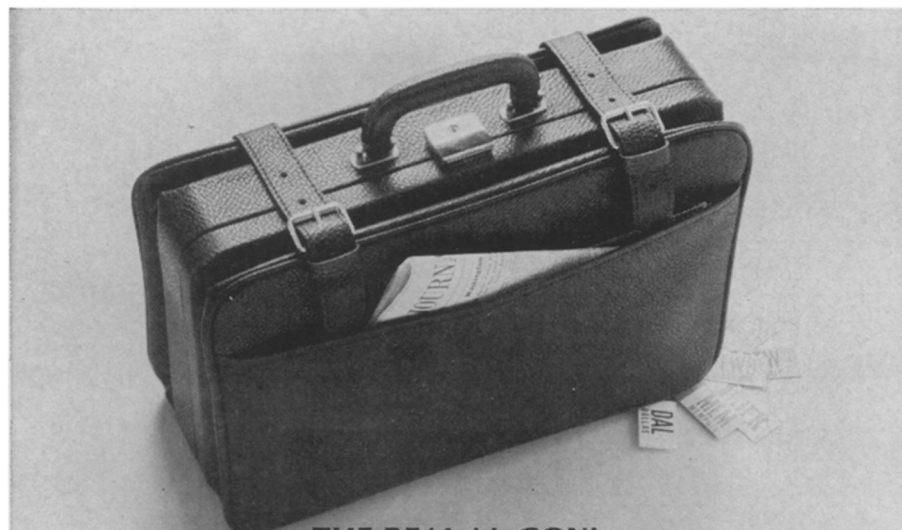
*Kidney storage damages blood vessels.*

lipoproteins that can lead to fat deposits, tissue swelling and the death of cells in donor organs. A pulsatile pump that mimics the action of the heart rhythmically pumps the plasma through the organ, causing little damage to its blood vessels. "Workers have used everything from whole blood to artificial fluids as perfusion media," Dr. Belzer says. "But we find that if we perfuse at low temperatures—50 degrees F.—the kidney does not need the red cells contained in whole blood to supply oxygen. There is enough oxygen physically dissolved in the plasma to meet its needs."

At present, the Belzer perfusion pump is compact enough to be carried around in the back of a truck. But it is not small enough for air transportation. "The technique," he says, "has been used successfully so far on kidneys for more than 60 patients. In one case, we kept a donor organ for 50 hours before implantation."

Another experimental approach to organ preservation is to treat the donor kidney with drugs such as chlorpromazine and magnesium sodium fluoride. These agents inhibit the level of metabolism within cells, thereby reducing the organ's need for oxygen. Prior to implantation, a drug antagonist will reverse the inhibiting effects of the initial drugs. In principle, this technique is analogous to cooling.

While progress in short-term preservation has facilitated tissue-typing prior to surgery, refinements in typing procedures themselves are also contributing to kidney transplantation success. Compatibility between donor and



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recipient, generally highest among relatives, is gauged according to similarities in two individuals' immune systems as measured in the H-LA, or histocompatibility locus antigen, system.

Two tests predominate (SN: 10/18, p. 358). In one, developed by Dr. Terasaki, leukocytes, or white blood cells, are reacted with antisera. In the other, designed by Drs. Bernard Amos of Duke University and Fritz Bach of the University of Wisconsin, leukocytes are reacted with antibodies from donor and recipient. Incompatible cells will be destroyed by the antisera or antibodies.

In newer tests intended to yield yet more specific information about compatibility, kidney cells themselves are reacted with antisera. "The idea," Dr. Belzer says, "is that the amount of kidney antigen on a leukocyte may be too small to be detected by current methods, whereas the antigens on the kidney cells themselves produce stronger, clearer reactions."

Once methods of preserving hearts and livers emerge, these typing tests can be performed to identify compatibility before transplantation. Some preliminary progress in heart preservation is reported by researchers at Baylor University in Houston. Dr. Edward B. Diethrich has succeeded in perfusing dogs' hearts for more than 24 hours and human hearts for more than nine hours without damaging the blood.

Dr. Theodore I. Malinin and his colleagues at the American Foundation of Biology in Bethesda, Md., report that temperature variations affect the time they have been able to maintain perfused monkey hearts. Low temperatures appear to be important. At 50 to 60 degrees F., monkey hearts functioned for as long as 10 days, at room temperature for only two days and at body temperature they survived no more than 24 hours. "Short-term preservation studies," Dr. Malinin explains, "are designed to assess and eliminate tissue damage that may result from perfusion and other treatment."

Unfortunately, long-term preservation will not necessarily be possible simply from refinements or extensions of techniques for short-term maintenance. And techniques for preserving one organ cannot be applied directly to others. Modifications in preservation systems will have to be devised specifically for hearts, kidneys, livers and other transplantable organs.

Says Dr. Kenneth Cell, director of the Navy Tissue Bank in Bethesda, "There are many parameters to control for each organ, including toxicity, temperature, oxygen intake and osmotic pressure; each organ will react differently." □

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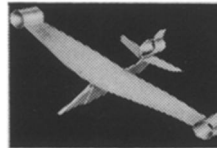
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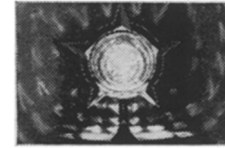
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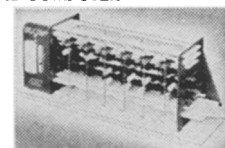
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