THE ORGAN TRANSPLANT ODYSSEY

Although problems still plague the 30-year-old organ transplantation field, the outlook for organ recipients has never been better

By JOAN AREHART-TREICHEL

Like all of us, 54-year-old Willem Van Buuren of San Rafael, Calif., has some complaints. He tires easily and sleeps poorly and can't hold down a job because of these physical impairments. But as the world's second-longest lived heart transplant recipient, he has a lot to be grateful for, too.

He has a wife, three grown children and two grandchildren. He can walk, drive a car and travel. Occasionally he even finds himself a celebrity. When Barney Clark became the world's first artificial heart recipient last year, the press descended on Van Buuren to get his reaction to it. And some months ago he shared "more than a few glasses of wine" with the world's longest lived heart transplant patient, a Frenchman, and appeared with him on French television. But the best thing, Van Buuren says, is that the foreign heart he received in January 1970 has kept him alive all these years.

Many organ transplant recipients, of course, haven't been as lucky as Van Buuren. They have survived for far shorter time periods than 13 years — in some cases for only weeks or even days — because they experienced transplant surgery complications, because their immune systems rejected their new organs or because their new organs did not cure the diseases they were supposed to cure. But there is good news for those persons who are now getting a transplant: They will probably survive longer than those individuals who got a transplant a few years ago.

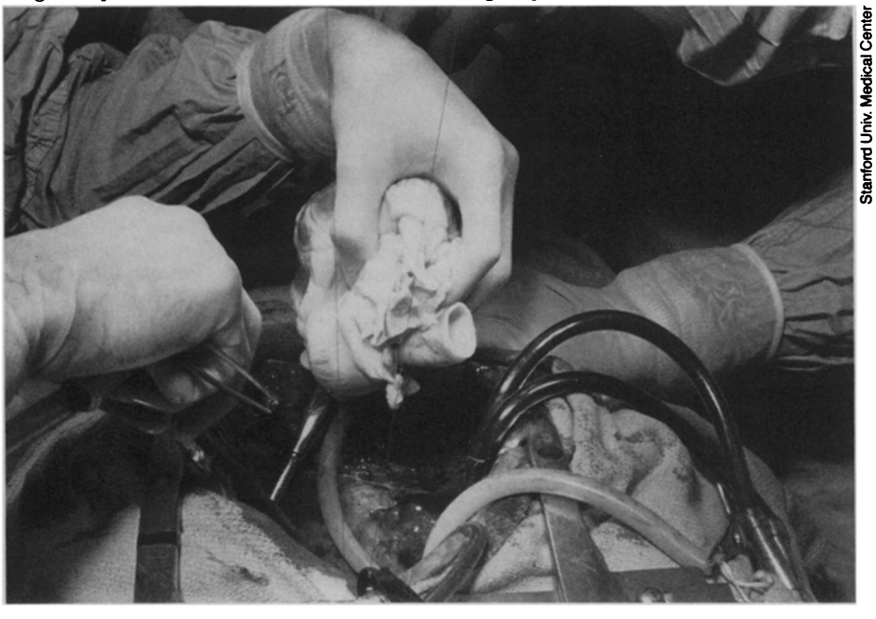
For instance, Paul I. Terasaki of the University of California at Los Angeles School of Medicine reported in the Aug. 26 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION that the one-year survival rate for patients getting kidneys from relatives is 97 percent today compared to 90 percent 10 years ago, and 90 percent for patients getting cadaver kidneys today compared to 73 percent 10 years ago. Similarly, Thomas Starzl, a liver transplant pioneer with the University of Pittsburgh, reported at a June National Institutes of Health (NIH) conference on liver transplantation that the one-year survival rate for patients getting liver transplants between 1980 and 1982 was 70 percent, compared to 33 percent for patients getting livers between 1963 and 1979. Survival for lung transplant recipients is also up, Norman Shumway and his transplant team at Stanford University Medical Center in Stanford, Calif., reported in the May 21 LANCET. Of the 39 lung transplants reported in the medical literature in the past, only two patients had ever survived beyond two months. By May of this year, seven of their patients had lived from two months up to two years.

One reason for this recent upsurge in organ transplant survival rates is improved surgical techniques. Since 1981, for example, Shumway and his team have used a combination heart-bilateral lung transplant technique instead of a single lung transplant method on terminally ill lung patients. The combination method provides blood vessel connections that are more likely to heal than does the single lung transplant method. Also, the former is more likely than the latter to prevent recurrent infection.

Along the same lines, Starzl reported at the NIH liver transplantation conference that a blood bypass technique developed in his lab is making liver transplantation a much less treacherous operation than it used to be. During transplantation, one of the large veins returning blood from the body to the heart has to be temporarily blocked, possibly endangering the patient's life. The new bypass technique compensates for the temporary blockage by routing blood from the obstructed vein externally to the upper half of the body.

A second ground for soaring transplant survival rates is scientists' recent chance discovery that if kidney transplant patients receive blood transfusions before transplantation, their immune systems are less likely to reject the foreign organs. How the transfusions blunt rejection "has not yet been resolved," says Henry Krakauer, chief of the transplantation biology branch at the National Institute of Allergy and Infectious Diseases in Bethesda, Md.

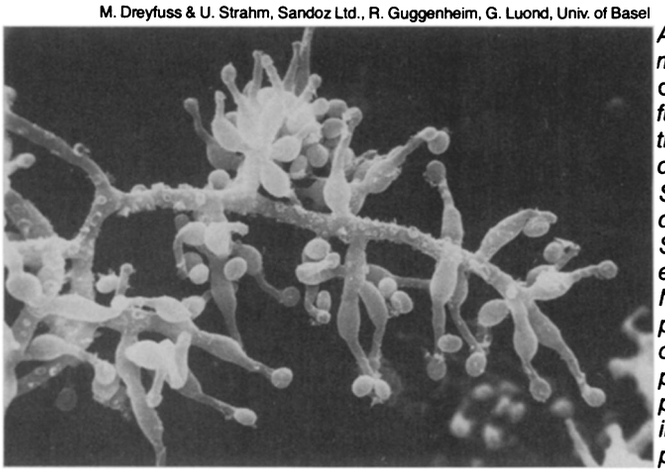
A third cause for rising transplantation survival rates is doctors learning that they can give patients lower doses of corticos-



Stanford Univ. Medical Center

A donor heart is inserted into a patient's chest during a transplant operation at Stanford University Medical Center.

M. Dreyfuss & U. Strahm, Sandoz Ltd., R. Guggenheim, G. Luond, Univ. of Basel



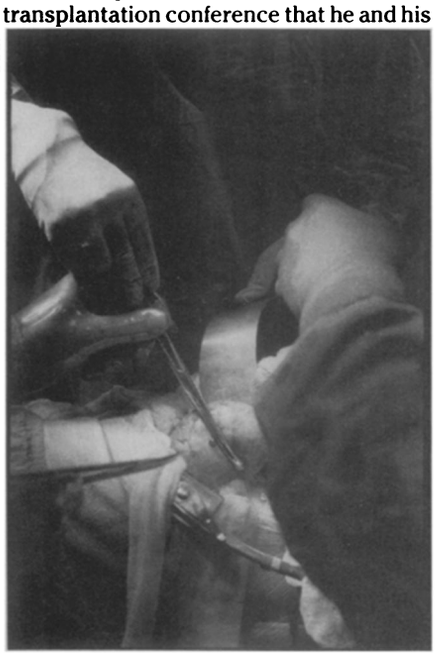
A scanning electron micrograph of Tolypocladium inflatum, *the fungus that makes the revolutionary drug cyclosporine. Scientists from Sandoz Ltd. in Basel, Switzerland, discovered the fungus in a Norwegian soil sample, then found that one of the fungus's products, cyclosporine, had unique immunosuppressive properties.*

teroids and other conventional immunosuppressive drugs than they used to and still prevent organ rejection. This way, Nicholas J. Feduska, a kidney transplant surgeon with the University of California at San Francisco, explains, one can still stop organ rejection but also reduce the risk of life-threatening infections that comes from excessive dampening of the immune system.

And yet a fourth explanation for spiraling transplantation survival rates is the recent introduction of a revolutionary new drug — cyclosporine — into the immunosuppression regimen. Shumway and his team reported at the first International Congress on Cyclosporine, held at the University of Texas Health Science Center at Houston in May, that the use of cyclosporine in heart transplant patients has reduced both postoperative infections and the incidence of organ rejection and is increasing patient survival. Eighty percent of their heart transplant patients who received cyclosporine are alive two years later whereas only 58 percent of those getting conventional immunosuppression are still living.

Starzl reported at the recent NIH liver transplantation conference that he and his colleagues have used cyclosporine on liver transplantation patients since 1980, and that 18-month survival figures indicate that it is superior to conventional immunosuppressive drugs. The 18-month survival rate with cyclosporine is 65 percent, compared to only 28 percent with conventional immunosuppression.

UCSF



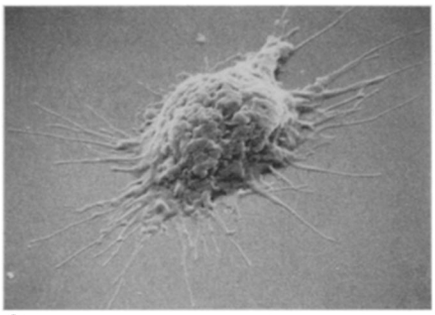
A patient gets a kidney at the University of California, San Francisco, the world's largest kidney transplant service.

The reason why cyclosporine is superior to conventional immunosuppressants in preventing organ rejection and reducing postoperative infections isn't totally clear. However, it is probably due to cyclosporine's unique ability to keep the immune system from rejecting a foreign organ while still allowing it to fight infectious organisms and cancer. In other words, cyclosporine probably dampens only certain fighters in the body's immune system, not all of them, as do conventional immunosuppressants. For instance, there is some evidence that cyclosporine represses killer T cells, which seem to be the major culprits in acute rejection episodes, but that it does not interfere with natural killer cells, which are thought to be major immune defenders against infectious organisms and cancer.

Regardless of its mode of action, though, cyclosporine is not the final answer to the transplant rejection-infection problem, says Bruce A. Reitz, a heart and heart-lung transplant surgeon at the Johns Hopkins Medical Institutions in Baltimore. David E. R. Sutherland, a pancreas transplant surgeon with the University of Minnesota School of Medicine in Minneapolis, agrees. The reason: It still impairs to some degree the immune system's ability to fight infectious organisms and cancer. Nonetheless, potentially even more selective immunosuppressant methods than cyclosporine are in the hopper and promise even greater longevity to persons getting transplants in the next decade or so.

For example, as Charles B. Carpenter of Harvard Medical School reported at a National Kidney Foundation science writers seminar earlier this year, scientists are now attempting to make monoclonal antibodies (mass-produced, highly specific antibodies) that react against killer T cells, yet not against other kinds of T cells that help make up the immune system. Such antibodies could conceivably then be injected into an organ transplant recipient in hopes that they would zap the killer T cells and prevent organ rejection, yet not impair the rest of the immune system and its ability to fight infections.

Yet another approach reported at a July organ transplantation symposium in Bar Harbor, Maine, might prove to be the elixir of the organ rejection-infection dilemma because it would eliminate immunosuppression altogether. And if it pans out, it would undoubtedly extend the life span of persons receiving organ transplants. Willys Silvers of the University of Pennsylvania School of Medicine in Philadelphia and colleagues have found, in rodents, that if a donor organ or donor organ material is stripped of immune cells called macrophages before transplantation, the organ or organ material will be accepted by a recipient who is immunologically incompatible with the organ or material. The stripping is done with high-pressure oxygen or monoclonal antibodies specific for the macrophages.



The Upjohn Co.

Stripping donor organs of macrophages (above) may prevent organ rejection.

So far Silvers and his team have achieved this success only with the thyroid gland, the parathyroid gland and the islet of Langerhans (tissue in the pancreas which secretes insulin). "It will be much harder to get large organs almost free of macrophages," he admits. "But if this is accomplished, transplants may be accepted with impunity." □