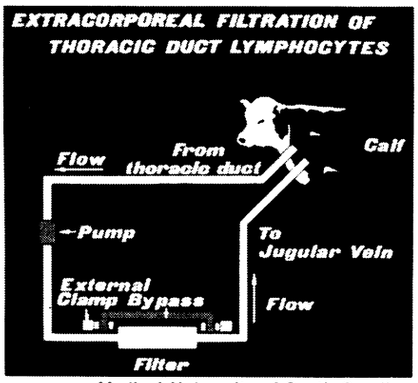
A possible answer to transplant rejections

Lymphocytes are a type of white blood cell that circulates throughout the lymph and blood systems of the body. They are probably the chief body defense against infection and foreign substances. So the challenge of suppressing the immune reaction by which the body rejects organ transplants is to eliminate only those lymphocytes that fight antigens from foreign tissue. If all the lymphocytes are rendered ineffective, a person's resistance to infection is drastically reduced.

It is obvious, especially from the numerous heart transplantation deaths over the past several years, that selective immunosuppression is yet to be achieved. Many transplant recipients die not because their bodies reject the foreign organ tissue but from infection that occurs because immunosuppressive drugs depress all their immune responses. Now a group of researchers at the Medical University of South Carolina—surgeon Charles T. Fitts, immunologist Robert J. Sharbaugh, microbiologist Charles D. Graber, bioengineer Thomas S. Hargest and medical student James A. Majeski—are carefully retesting and refining a new technique that they believe may answer the need for selective immunosuppression for organ transplants.

Fitts presented their preliminary findings at a meeting of the Society of University Surgeons in San Francisco in February. Their presentation drew encouragement from some of the scientists present, such as the well-known immunologist Robert Good of the University of Minnesota. Last week Sharbaugh reported his team's most recent results at the annual meeting of the American Society for Microbiology in Philadelphia. During the early phase of the investigative studies, they learned that lymph dialysis, the filtering of lymph through a semi-permeable membrane, resulted in severe depletion of lymphocytes. They theorized that lymphatic drainage might be a way of removing lymphocytes. They tested the idea by draining lymph from cows.



Medical University of South Carolina
The closed-circuit filter system.

"But even with mechanical assistance, this wasn't easy," Sharbaugh explains. Lymph was shunted from the thoracic duct of a cow continuously day and night so that lymphocytes could be collected by centrifugation and the remaining lymph fluid, containing protein and electrolytes, could be returned to the cow's circulation. What is more, the lymph was exposed to air and possible contamination during processing, thus rendering the cow susceptible to infection. So about two years ago the group devised a closed-circuit filtration system whereby lymph could be removed without exposing it to contamination.

But even under these conditions, removal of all lymphocytes still lowered the animal's general resistance to infection. Obviously an organ transplant patient, under similar conditions, would have his general immune protection placed in jeopardy. Encouraged by some experimental work in Europe, the Charleston group initiated efforts to filter out only those lymphocytes that react against a specific antigen from, say, a donor organ.

It is known that only a few of the lymphocytes of the body react against any one antigen. Glass beads were coated with a particular antigen and placed into the filtration system. As the lymph cells sensitized to the particular antigen passed through the filter, they would attach themselves to the antigen-coated beads. Sharbaugh and his colleagues were delighted when the idea worked.

Since then, they have been carrying out double blind studies to confirm that the technique is indeed successful. Cows are sensitized against both tuberculosis and the fungus disease histoplasmosis. TB antigen is then put on the filter. The lymphocytes that fight TB apparently attach themselves to the antigen traps, thus causing the cow to lose its immunity to TB antigen, but not its immune response to histoplasmin antigen. This evidence comes from tuberculin and histoplasmin skin tests. Reversing the situation, histoplasmin antigen is placed on the filter, and sensitized lymphocytes attach themselves to the antigen on the filter. This time the cow remains immune against TB antigen, but has lost its immunity against histoplasmosis.

All this is mounting evidence, Sharbaugh and his colleagues believe, that selective immunosuppression is indeed being accomplished by passing lymph through a closed-circuit system where decoy antigen particles, placed on a filter, trap specific lymphocytes. They have strong hopes that antigen from a donor organ might be used in the same manner to trap lymphocytes from an organ transplant patient who would otherwise reject the transplanted organ.


Medical University of South Carolina
Sharbaugh checks a lymph filter.

But, Sharbaugh cautions, "Clinical application is some way down the road."

Meanwhile further studies are under way to confirm that the technique selectively immunosuppresses at the cellular and subcellular levels. Lymph cells divide and multiply more than usual in the presence of a target antigen. So Sharbaugh is measuring cell division of lympocytes passing through an antigen filter. Those lymph cells that are supposed to be trapped by their target antigen should be dividing more. ❑

AMA asks moratorium on embryo implants

In Britain Robert G. Edwards and Patrick C. Steptoe of Cambridge University have been able for some time to fertilize human eggs outside the mothers' bodies and grow the resulting embryos to the blastocyst stage—the period where an embryo would normally become attached to the uterine wall of the mother.

Apparently the only thing keeping them from going ahead and reimplanting one of these eggs in the mother—creating in effect a semi-test-tube baby—is ethical considerations. In an editorial in the May 1 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, the AMA proposes that Edwards and Steptoe not make such an attempt until the ethical questions surrounding it are weighed, and the technique has been successfully carried out in animals. The AMA editorial expresses particular concern over risks of serious abnormalities or sacrifice of the child being grown.

Why the AMA has singled out a moratorium on a semi-test-tube baby is not clear, since other "genetic engineering" feats that raise comparable ethical questions are already available to society—artificial insemination of women with sperm from a sperm bank and prenatal diagnosis of birth defects with an option for abortion (SN: 10/30/71, pp. 294, 298). ❑