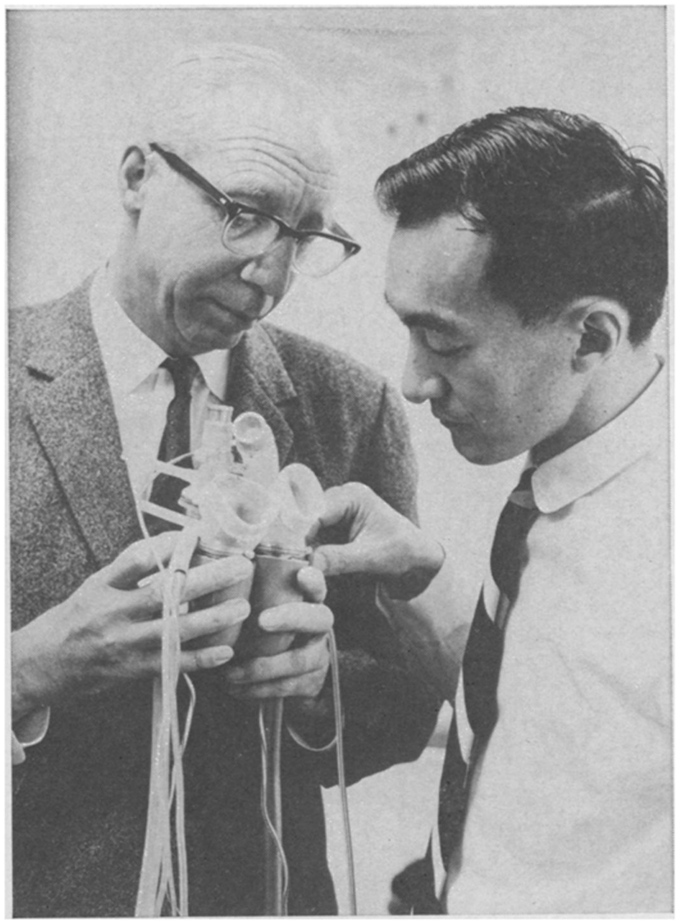
BIOMEDICAL ENGINEERING

A gathering of specialists



Photos: Univ. of Utah

Kolff and Kwan-Gett: An artificial heart with promise.

A unique symbiosis of engineering and medicine is tackling the problems of artificial organs

by Barbara J. Culliton

On April 10, Dr. Willem J. Kolff of the University of Utah will address a meeting of the American Society for Internal Artificial Organs in Washington, D.C. He intends to present to the group of researchers, many of whom have been frustrated for years by their inability to develop materials compatible with blood, evidence that there is finally light at the end of the tunnel.

Dr. Kolff, Dr. Donald J. Lyman, Dr. Horst Klinkmann and others from the team of biological and physical scientists and engineers who work together at Utah believe they have developed the materials that will make the advance of the development of artificial organs possible.

The progress, over the last three years, is at least in part the result of the fact that the team was designed across interdisciplinary lines, hand-picked by Dr. Kolff and by Dr. Keith Reemtsma, head of the department of surgery, who started the ball rolling.

In this article and another to appear next week, SCIENCE NEWS' editor in the biological sciences, Barbara J. Culliton, presents the results of their work and the organizational innovations that made it possible.

In the spring of 1967 Dr. Willem Johan Kolff, inventor of the artificial kidney, moved to Salt Lake City from Cleveland where he had worked for more than 20 years. Recruited by Dr. Keith Reemtsma, head of surgery, Dr. Kolff received a joint appointment to the departments of surgery and of engineering, and assumed direction of the division of artificial organs at the University of Utah. It was a new unit, tailor-made for him.

Dr. Reemtsma is a pioneer in the experimental use of organs transplanted from animal to man. He saw in Dr. Kolff a man who could capitalize on the university's strengths in medicine and engineering. "Dr. Kolff," he says, "is probably the best-known scientist in the field of applying engineering principles to medical questions; he has an uncommon ability to get people in various disciplines to work together on mutual problems."

Dr. Kolff set up headquarters in a single-story green building that looks like an army barracks, behind the modern university medical center, and proceeded to live up to expectations. In three years he has assembled a unique team of scientists, some drawn from within the university, some lured from without, whose pooled talents provide a singular ability to approach bioengineering challenges from all sides.

Drs. Kolff and Reemtsma gave them their mission: creation of a totally implantable artificial heart; development of heart assist devices for patients in cardiac failure; refinement of the artificial kidney.

Together they developed the plan of attack: Unite the surgeons and the chemists, the physicists and the cardiologists, the materials experts and the engineers.

Every morning at eight, Dr. Kolff gathers his staff for a strategy meeting to assess successes and failures and chart new solutions. Says Kent Beckman, the team's mechanical engineer, "The daily meeting gives each of us a chance to try out new ideas, seek advice, challenge each other."

According to bioengineers working on similar fronts at other institutions, the Salt Lake group is distinguished in three regards. The first is Dr. Kolff himself, who devotes much of his energy to catalyzing ideas among his staff and the rest to seeking funds to support their research. "I have a team of very bright, aggressive young scientists who must be allowed to follow their creative instincts," says the white-haired, Dutch-born scientist. "If I forced them all to face a single project in a limited way, ideas would evaporate. There would be no progress." So Dr. Kolff primes the intellectual pump and lets his collaborators run with their ideas.

The second quality that marks the Salt Lake bioengineers is an attitude or frame of mind that leads each member of the group to regard his colleagues as equals. There are neither chiefs nor Indians, and the medical men do not cater to the habit their profession has of looking down on any non-M.D.

The result is the answer to a felt need. Participants at a three-day meeting on bioengineering in Washington, D.C., in 1968 stressed again and again that the major handicap to a successful union between engineers and doctors is the fact that the two groups are either unwilling or unable to speak each other's language. "In Salt Lake," says a bioengineer from Case-Western Reserve in Cleveland, "they talk to each other."

The third feature that sets the team apart is its unique ability to translate its ideas into reality, without going off campus to solicit the aid of industry.

When Dr. Clifford Kwan-Gett, a surgeon and electrical engineer, wants to alter the design of his artificial heart, Tom Kesler, a master builder, fabricates a new one to specification. Within days it is ready for experimental trials in one of the division's several dozen sheep that live in a corral out back. Polymer chemists and materials specialists work together to conceive and execute designs of new membranes. Physicists and engineers team up to manufacture power supplies, all contributing to efficiency and flexibility. Dr. Kolff's catalysis seems to work. Progress has been rapid.

The ultimate goal of all research in artificial organs and devices is to create instruments that can be used efficiently and economically on a maximum number of patients. Presently the severest limiting factor in the development of artificial organs is the materials problem.

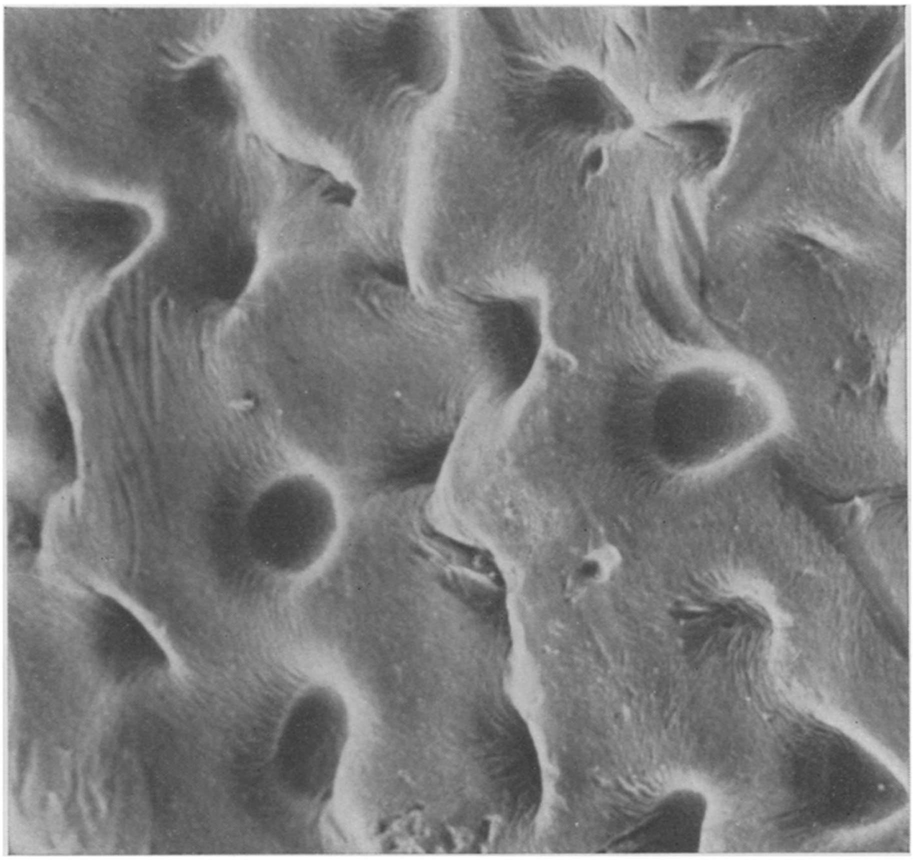
Blood has a natural and rapid tendency to clot whenever it comes in contact with a foreign surface, anything other than a blood vessel wall. The problem that has faced all researchers in the field has been one of designing a surface with which blood would react as it would with a blood vessel.

Silastic is used with varying degrees of success in most artificial devices now. In some cases it is coated with a layer of velour, a terry-cloth-like material that catches fibrin from the blood and eventually becomes covered with a layer of fibrin that separates the blood from the Silastic.

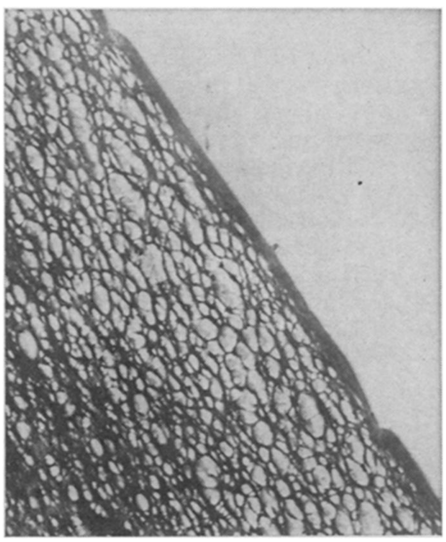
In other cases, the Silastic surface is disguised with a coat of heparin, an anticoagulant that can be chemically grafted to the inner wall.

Dr. Donald J. Lyman, a polymer chemist on Dr. Kolff's team, believes a protein coat, such as albumin, a natural blood component, may be the preferable way to create an interface between blood and material. But none of these is ideal.

"The real answer," Dr. Lyman be-

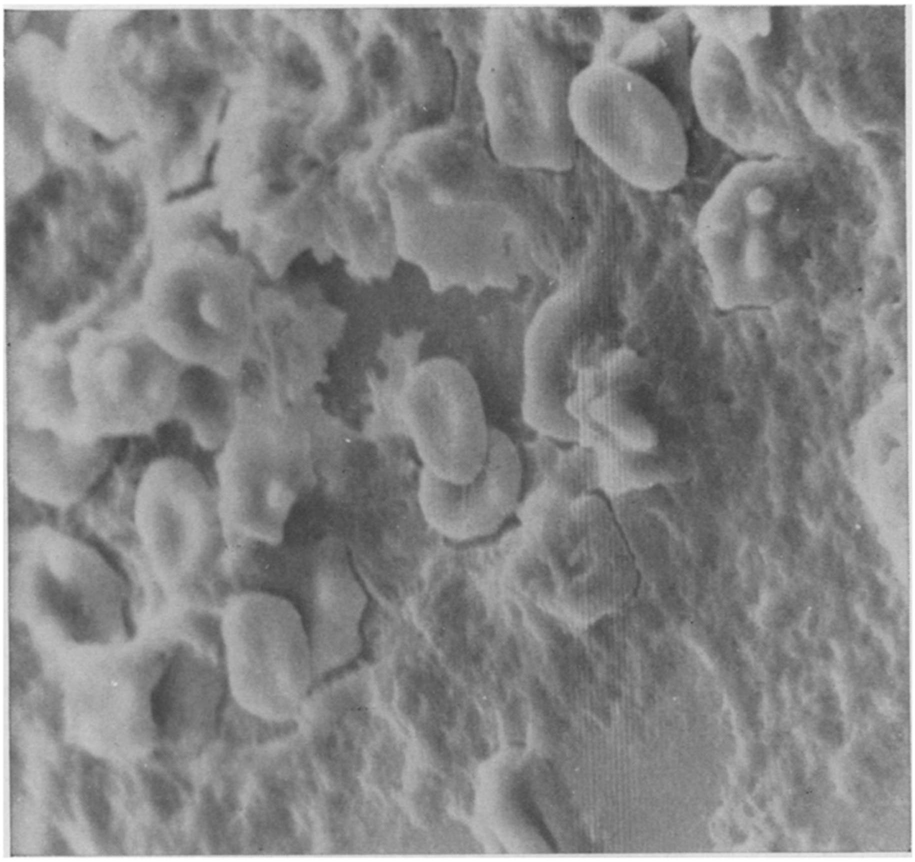


Pores in cellulose membrane pass toxic substances and retain blood cells.



Nephrophan: Larger pores, smoother.

Reemtsma: From cooperation, creation.



Clotted blood soon coats the surface, plugging up the filtering pores.

lieves, "is to design a material that itself is compatible with blood. If we can circumvent the need to coat an artificial vessel, we can stop worrying about what happens if the interior surface becomes scratched or worn."

Such material, a tailor-made polyurethane now in preliminary tests, may be at hand. If it proves to be the long-sought solution to the materials problem, as Dr. Lyman hopes, it will have applications for both artificial hearts and kidneys.

Dr. Kolff is optimistic, but maintains a certain perspective that favors conservatism. "If I speak as Willem Kolff the investigator," he says with delight, "I say it is no exaggeration that we have almost solved the materials problem. If I speak from my training as internist, I say 'Bah!' "

While work on artificial hearts and materials proceeds at a fairly rapid clip, total success is still years away. Perfection of the artificial kidney is closer at hand and Kolff's group is making clear headway.

"Supremacy in the heart field is up for grabs, but in the kidney arena, Dr. Kolff is definitely the man others are trying to beat," says a researcher from the East.

The first artificial kidney membrane was made of sausage casing by Kolff in occupied Holland during World War II. "On Sept. 11, 1945," he says, "we commenced dialysis on a woman who was the first to owe her life to the artificial kidney. It was then we proved it could work."

Since that time, he and others have modified and improved kidney dialyzers to the point that individuals using them can live without functioning kidneys upwards of seven years. But the technique is far from perfect.

First, it is expensive. The bill for a single patient undergoing dialysis in a hospital once or twice a week can go as high as $15,000 in the first year. In addition, there are not enough machines to go around. "Of the 40,000 persons in the United States alone who could be helped every year, we reach less than two percent," Dr. Kolff laments. A patient can be denied treatment because he is not between the ages of 15 and 45 years or because some committee fails to consider him a good citizen or an emotionally mature adult. Dr. Kolff finds this hard to take. "Have we come to the point at which we will let a man die because he is emotionally immature?" he asks.

A home dialysis training center at the university hospital is the beginning of a solution. There, under the direction of Dr. Horst Klinkmann, on leave from the University of Rostock, East Germany, patients and their families learn to use home dialysis units the size of a washing machine. The dialyzing solution is held in a tub made from the nose cones of old rockets and the kidney is powered by small machines developed at the Salt Lake center. "The idea," according to Roger Kirkham, chief administrator of the program, "is to reduce the cost of dialysis to $2,400 per year or less."

Cost, however, is not the only obstacle. In spite of the fact that patients can live for years on the machine that takes over the kidney's function of cleansing their blood, they become increasingly debilitated with time.

"After the first year or so," Dr. Klinkmann reports, "we begin to see signs of calcium disturbance and of neuropathy—reduced nerve conductivity—muscle wasting, loss of energy." Part of the trouble may lie in the cellulose membranes that filter waste materials from the blood. "We know we are removing really toxic substances," he explains, "but we may be leaving behind some molecules we should filter out, larger molecules such as creatine and uric acid which can build up to cause secondary complications."

Standard membranes of cellulose pose two problems. First, their pores are too small for the larger molecules to pass through. Second, within only a few hours they clog with blood.

Working with the East German Academy of Sciences, Dr. Klinkmann designed a new membrane called nephrophan. Larger pores permit passage of creatine and uric acid, and a smoother surface makes blood coating less of a problem. He thinks it is on the way into practice. Following clinical trials of nephrophan now going on at Salt Lake, "It may become widely used in the United States," he says.

Manipulating pore size is certainly a route to immediate improvement of kidney membranes but the Utah scientists are uncertain whether this will prove adequate as a final solution. Dr. Kolff would like to apply charcoal adsorption, used by other workers, as an adjunct to membrane dialysis. This is based on the theory that certain molecules that evade the membrane will be trapped on a charcoal column.

Dr. Lyman believes that the ideal membrane will be one designed to identify and selectively handle molecules on the basis of their chemical structure rather than physical size. "It amounts to creating a membrane of polymers that will function exactly like kidney tissue. We cannot do it yet, but it is not impossible."

(*Next: Toward the artificial heart.*)