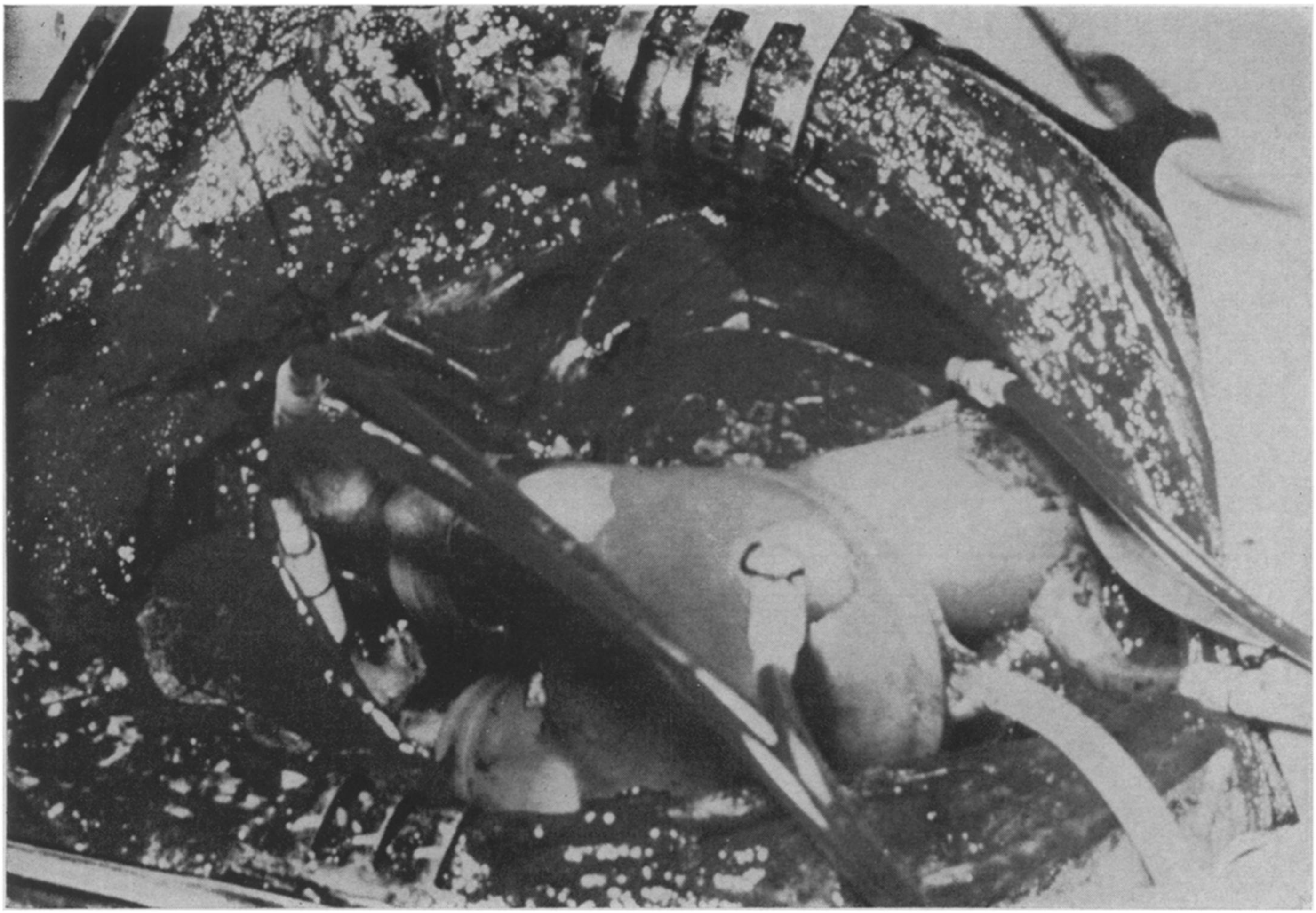


Photos: Univ. of Utah

BIOENGINEERING

Era of plastic hearts

Design advances and new sophistication in the creation of blood-compatible materials bring plastic hearts a step closer to reality

Dr. Kwan-Gett's latest diaphragm heart shows promise from trials in which it is totally implanted in the chest of a sheep.

by Barbara J. Culliton

A decade ago a totally implantable artificial heart fell more into the realm of fantasy than scientific possibility. In fact, many scientific societies and journals refused to accept papers describing research in that direction.

Since then the picture has changed dramatically. Scores of animal experiments at a number of institutions have proved the validity of the idea that an artificial heart is in the offing. Dr. Denton Cooley's pioneering and controversial implantation of a plastic heart into a dying man last spring (SN: 4/19/69, p. 375) suggested that the day of the artificial heart may not be far off.

There are problems, to be sure, and investigators predict that the first man-made hearts will have to be powered from outside the body rather than by fuel cells implanted within the chest. But the problems that remain are not insurmountable and the need for their resolution is critical.

Progress, according to Dr. Willem J. Kolff of the University of Utah in Salt Lake City, is steady and encouraging. Says Dr. Kolff, inventor of the artificial kidney and the first researcher to test a plastic heart in dogs in the United States, "Six hundred thousand individuals die per year in the United States from acute coronary heart attack alone. It behooves us not to be involved in either extreme enthusiasm or deep pessimism, but to continue to work quietly and urgently on the two possibilities with which these patients can be helped: heart transplantation and total replacement of the natural heart with an artificial pump."

In the United States and abroad, immunologists are working to unravel the complexities of the immune system that rejects transplanted organs; there is every reason to believe that when they do, men will live successfully with borrowed hearts, taken from human and perhaps animal donors. But even when that goal is reached, the demand for borrowed hearts is expected to outstrip the supply of live organs. Once perfected, plastic hearts could be made in unlimited quantity. Dr. Kolff, with his team of cardiologists, surgeons, engineers and chemists at Salt Lake, is among those investigators striving for their perfection.

From a clinical point of view, the challenge has several dimensions. The heart must be driven by a pump that can move adequate volumes of blood throughout the circulatory system—at least six or seven liters per minute—and match the natural beat of the human heart. The artificial organ must avoid causing physical damage to blood and be constructed of a material that is flexible, durable and compatible with blood. Dr. Kolff's group believes it is on the verge of achieving each of these goals.

There is still an additional consideration, however; one that precedes heart transplantation itself. If a patient comes into the hospital in heart failure, he is unable to withstand immediately the trauma of major surgery. The first step is to assist temporarily his failing heart. Because the left ventricle, which pumps oxygenated blood throughout the body, does most of the heart's heavy work, it is very often the chamber that fails first.

Dr. Hans Zwart, like Dr. Kolff a Dutch-born scientist, has developed a simple assist device that takes over the job of the left ventricle. After extensive testing on sheep—one pregnant ewe not only survived the procedure but subsequently gave birth to two healthy lambs—Dr. Zwart believes it is ready for human trials.

The surgeon thrusts a long, flexible cannula or tube through the axillary artery in the armpit, into the aorta and then into the left ventricle. Blood is sucked from the ventricle through a roller pump and fed back into the circulatory system through a cannula in the femoral artery in the groin. During this procedure, the left chamber deflates and rests while the right side of the heart continues to function as usual, supplying circulated blood to the lungs for oxygenation.

The Zwart method, which is being tested in animals at other institutions as well, has several attractive features. It precludes the need of opening a patient's chest for major surgery. The cannula itself is made of extremely thin glass reinforced polyurethane having an internal diameter almost as great as that of the artery itself, so that it can carry a sufficient load of blood. And to prevent blood from clotting when it comes in contact with the cannula surface, Dr. Zwart, working with Joseph Andrade, a bioengineer who recently joined the Salt Lake group, grafts a coat of heparin, an anticoagulant, to the interior surface. Traditionally, heparin is given directly to the patient; though it prevents clotting, continued doses can so disrupt the blood's clotting mechanisms that internal bleeding occurs.

"With luck," says Dr. Kolff, "Hans Zwart's assist device will give a man's heart time to rest and to recover and then that is that. But it cannot always recover. Then the artificial heart becomes important."

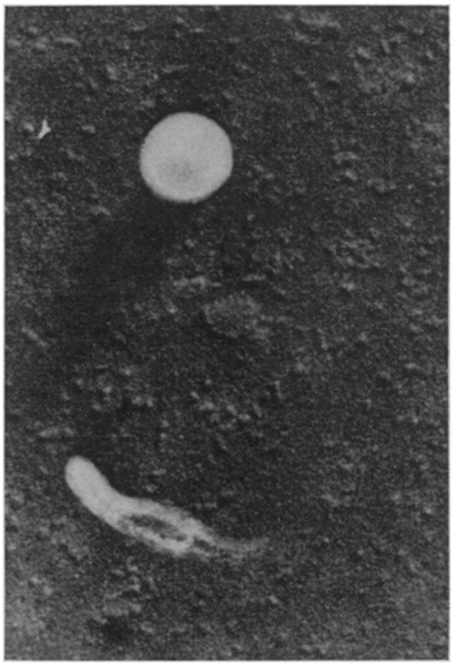
The most serious problem facing reseachers in this field is damage to the elements of the blood—red cells, platelets, proteins and white cells. On one hand there is damage from physical stress. With many existing heart designs, consisting of a flexible sac in a firm housing, the sac could expand too far, coming into physical contact with the outer wall, and break delicate blood cells. Salt Lake's Dr. Clifford Kwan-Gett has designed a diaphragm heart in which expansion and contraction are carefully controlled, and this source of blood damage is eliminated.

But even with this advance, blood clotting remains a major handicap. Blood has long been known to have a special aversion to any material other than the lining of a vessel wall, and the research objective in artificial organs has been to find a material that blood will tolerate. Dr. Donald Lyman, a polymer chemist who recently moved from the Stanford Research Institute to the University of Utah, believes that coating surfaces with protein, particularly albumin, a natural blood component, holds an immediate promise for success. Working with Andrade, one of the first investigators to apply techniques of chemical covalent bonding to the challenge of producing a non-thrombogenic surface, he bonds albumin to the interior wall of polyurethane tubing. "Our experiments show that the clotting incidence can be reduced essentially to zero and other workers are beginning to experiment with protein coating," Dr. Lyman reports.

But the ideal solution does not lie in coating existing materials. Coatings can be eroded or chipped away like the Teflon lining of a frying pan. The answer is to develop a material which in itself behaves like a protein coat or vessel lining.

A new material Dr. Lyman calls block copolyurethane may fill the bill. The synthetic plastic is constructed of high molecular weight polymers that are chemically bound together in repeating units like the cars of a railroad train.

Different polymers or chemical units have different known characteristics. Some have strong electrical charges; some weak. Some attract water molecules; some repel them. Some react with lipids; others do not. Dr. Lyman believes that by linking these polymer units together in carefully programmed sequence, it will be possible to design a plastic with almost any set of properties, according to need for hearts, vessels and kidneys.



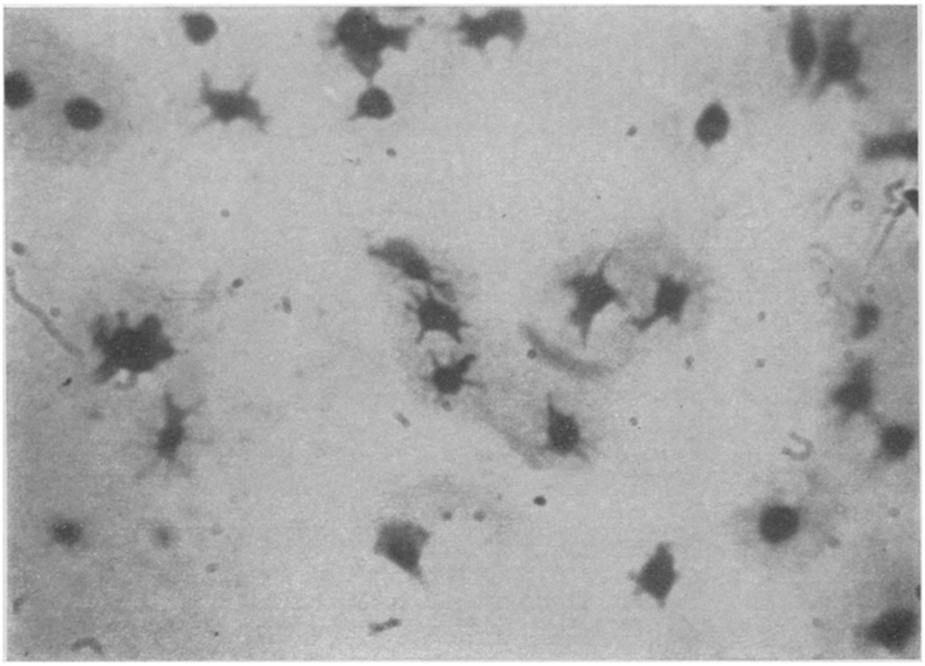
Blood proteins hold their shape.

So far, a single diaphragm heart has been constructed on one of these synthetic plastics which has the look and clarity of Saran wrap and is highly compatible with blood. That heart is about to be tested in a sheep.

In first approaching the problem of designing a material with a structure that would be compatible with blood, Dr. Lyman and his co-workers attempted to define, at the molecular level, what happens when blood comes into contact with a surface. Their insights have led not only to a new experimental material but have refined understanding of the clotting mechanism.

Classically, blood clotting has been described as a series of events initiated by a protein called factor XII. It was assumed that when factor XII comes into contact with a foreign surface, which happens, for example, when a vessel is injured, it becomes denatured; that is, the three-dimensional structure of the protein is disrupted and in its new and changed form it is able to trigger clotting.

To test this assumption, Dr. Lyman and his co-workers examined a series of blood proteins, including clotting factors, albumin and gamma globulin, brought in contact with a polished polymer surface. First, they measured the thickness of the layer of protein that adsorbed to the surface, finding it out of keeping with what they would expect to find if the molecules had been denatured or uncoiled. Then observations under the electron microscope



Platelets stick to foreign surfaces, entrapping red blood cells.

and by infrared spectroscopy confirmed their conclusion that the molecules were not denatured but held their normal configuration.

"We found no drastic physical or chemical changes in the blood protein," he says. "This finding, coupled with the observation that a clump of platelets appeared to accompany each site of clot formation, prompted us to investigate the role of platelets in the initiation of the clotting process."

Experiments revealed that when platelets adhere to foreign surfaces, their membranes disrupt, thereby initiating the formation of a clot. Indeed, comparative studies of platelet adsorption to various materials appear to corroborate the association. Exposed to Silastic, about four platelets adhere per unit area (20,000 square microns). Adherence to block copolyurethane is in the range of 0.2 or 0.3 platelets per unit area. With protein-coated material, the adherence is virtually zero, the Salt Lake researchers have found from repeated experiments with hearts and cannulas in adult sheep.

At this point, Dr. Kolff's team is waxing enthusiastic about its success, as it anticipates animal experiments of the heart of Dr. Kwan-Gett's design and Dr. Lyman's material. If sheep, used because of their large size and delicate vascular system (if their blood cells hold up, a man's will), can live on the artificial heart for long periods, the scientists' theories will be supported. "By a long time," says Dr. Kwan-Gett, "I mean weeks." In previous trials of artifical hearts, animals have survived up to 50 hours.

Lyman: Blood-compatible plastic.

Even if confirmation comes, trials in man are a few years away. Dr. Kolff's team itself will want extensive experience before considering experimenting on a patient. And, under a new policy established by the National Institutes of Health which funds much of the work, any experimental heart device must be reviewed by scientists at one of two test and evaluation facilities before going from animal to human trials. One of these new T & E facilities is at the Illinois Institute of Technology in Chicago. The other is in Salt Lake, where it will operate independently of Dr. Kolff's division of artificial organs. It will begin full-scale operations within the year. ☐