The artificial organs program at The Cleveland Clinic Foundation: past, present, and future[1]

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The artificial organs program at the Cleveland Clinic was reorganized in 1967. Active circulatory support programs, metabolic and immunoassist programs, and biomaterials and biocompatibility programs have been established during the past 16 years. A skeletomuscular assist program is in the process of being integrated into the artificial organs program. The main emphasis in the circulatory assist program is on the development of a permanent totally implantable artificial heart. In addition, a clinical temporary ventricular assist device, a permanent implantable ventricular assist system (electrical and thermal), and a nonpulsatile circulatory support system are included in the circulatory assist program. The metabolic and immunoassist program is directed toward the development of a system to modulate the human immune system in an effort to treat and prevent metabolic and immunological diseases. The biomaterials and compatibility program is devoted to the study of the interaction between "human spare parts" and/or artificial organs and human tissues and organs. Various types of innovative systems to replace or augment human organs are included in the scope of the artificial organs program, including the artificial heart, circulatory assist devices, artificial kidney, hepatic assist, pancreatic assist, immunoassist, oxygenator, and biomaterials.

Index term: Artificial organs

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Artificial organs research was started at The Cleveland Clinic Foundation when Willem J. Kolff, M.D., joined the staff in 1950. During his 17-year tenure, the artificial kidney became the most effective and widely used artificial organ. More than 60,000 patients in the United States and approximately 200,000 worldwide are maintained by the artificial kidney.

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Total artificial heart research was initiated in 1957 along with the introduction of various types of assisted circulation, including intra-aortic balloon pumping. As early as 1956 a membrane oxygenator was developed and is in the mainstream of cardiopulmonary bypass techniques today. Aided by blood oxygenation techniques, the Cleveland Clinic is one of the leading medical institutions in open-heart surgery.

The Cleveland Clinic was the first institution in the world to establish a "Department of Artificial Organs," specializing in research, development, and clinical application of artificial organ technology for the advancement of therapeutic medicine. The Department of Artificial Organs, initially a part of the Research Division, later became a part of the Division of Surgery. It was composed of three groups: basic research, hemodialysis, and cardiac perfusion. An active kidney transplantation program including organ preservation technologies, using both living and cadaver donors, was initiated by the Department of Artificial Organs.

When Dr. Kolff moved to the University of Utah in 1967, the Department of Artificial Organs was abolished and an Artificial Organs Research Laboratory was established. Now, 16 years later, it is worthwhile to recapitulate the activities of its programs and its future goals. The Artificial Organs Research Laboratory, after demonstrating successful program developments, was redesignated the Department of Artificial Organs in 1971. In 1973 the Department's facilities were expanded. It presently has 45 full-time investigators, clinicians, and support personnel. Some of the Department's current work is described in other papers in this issue: Kambic et al, Yozu et al, Smith et al, and Malchesky et al. Kambic et al outline the progress made in the cardiovascular program. The original paper by Yozu et al presents the preclinical evaluation of a biolized temporary ventricular assist device. Smith et al outline the metabolic assist program, and Malchesky et al highlight a specific aspect of it.

The artificial organs program is one of five research programs at the Cleveland Clinic. The Chairman of the Department of Artificial Organs is also the Scientific Director of the artificial organs program.

Philosophy of the artificial organs program

From its beginnings, the primary goal of the Department has been to meet the needs of clinicians by providing improved artificial organ technologies, new methods of therapy, and new tools for the investigation of the disease process. It is hoped that by supplying various types of "human spare parts" and artificial organs for end-stage organ failure, the health and quality of life of patients can be improved. Our second major goal is the establishment of basic scientific programs that will lead to better understanding of human physiology when natural organs and tissues are replaced with man-made devices. The interactions of biological tissues and organs with man-made tissues and organs are continually investigated. For example, the use of artificial kidneys in the treatment of chronic renal failure provided expanded knowledge of the essential renal functions and the pathophysiology of end-stage renal failure. The availability of cardiac prostheses of known hemodynamic performance and control characteristics further increases the knowledge in circulatory physiology and pathophysiology. The understanding of the biocompatibility of man-made tissues and organs provides new insights in the understanding of the calcification (or atherosclerosis) processes, excessive tissue buildup (or carcinogenic) process, and other immunological processes occurring in the cardiovascular system with artificial or diseased natural surfaces. Artificial organs are unique tools for studying physiology and pathophysiology.

The third goal is the development of innovative concepts and approaches for the replacement or support of human organ systems, e.g., a pulseless circulatory system, selective macromolecule removal systems, and biolization (a process to make synthetics more biologically acceptable) of artificial surfaces.

Recently, the direction of artificial organs has changed. In the past, emphasis had been on treatment of end-stage disease. Emphasis is now on the development of technology for therapeutic treatment and prevention of disease and its progression. The most notable concept is that of immunomodulation, which affords treatment and prevention of various autoimmune diseases. The treatment of cancer and atherosclerosis may be possible through this process.

Organization of the artificial organs program

In fulfilling these goals it is essential that basic and clinical research programs be carried out by a multidisciplinary team. *Table 1* lists the various types of engineers, scientists, and medical doctors and their wide variety of specialties and subspecialties. The Department of Artificial Organs has

Table 1. Department of Artificial Organs, full-time personnel (August 1983)

Scientists/engineers		Medical		Support	
Biochemist	1	Cardiologist	1	Nurse	1
Biologist	1	Cardiovascular surgeon	7	Technician	11
Biomedical engineer	3	Endocrinologist	1	Secretary	3
Chemist	1	General surgeon	2		15
Chemical engineer	3	Nephrologist	1		
Electrical engineer	1	Immunologist	1		
Mechanical engineer	3	Immunopathologist	1		
	13	Internist	1		
		Physiologist	1		
		Veterinarian	1		
			17		
Total 45					

For individuals holding two or more specialty degrees, only the major and/or highest degree is tabulated.

established a comprehensive research capability including in-house prototype hardware production, various types of in vitro component and system performance test apparatus, and acute and chronic in vivo test facilities, including small and large animal housing. The experimental team can easily become a clinical team when developments reach the clinical stage. From the initiation of a concept through the fabrication of prototypes, evaluation of performance and reliability, testing of efficacy and safety, to the final clinical application, all stages can be performed in the Department's facilities. This capability assures the successful development and evaluation of various types of artificial organs.

The Cleveland Clinic has traditionally given high priority to training postgraduate fellows. Eighteen research fellows from different parts of the world, including Asia, Europe, and South America, are studying in the areas of circulatory assist, hepatic assist, pancreatic assist, pulmonary assist, immunological assist, and biomaterials. The preferred term of training in the Department of Artificial Organs is at least two years. Many of the Department's alumni play leading roles internationally in implementation and development of artificial organs.

The Department's research activities have been divided into four areas: circulatory support, metabolic and immunological assist, biomaterials, and compatibility. A skeletomuscular assist program is in the planning stages in conjunction with the Department of Orthopaedic Surgery. A successful program can be assured only if there is close, integrated collaboration with clinical departments. It is also important that each program combines the medical/biological and engineering specialties of its team members. *Figure 1* shows the Department's table of organization. Each scientific program has dual leadership even though one program manager is specified. When the program is in the design, fabrication, or in vitro characterization stage, the engineering or scientific director is in charge, with the medical or biomedical director playing a secondary role; however, when the project progresses to in vivo or clinical studies, the medical/biological director takes charge and the engineering/scientific director plays the secondary role. This dual leadership provides a balance between the scientific and medical disciplines.

Circulatory support program

Table 2 lists the six active programs in this area. The initial emphasis on the total artificial heart with pneumatic actuation was reviewed critically in 1976. Until 1976, the feasibility of a total artificial heart was not demonstrated; however, in that year the Department of Artificial Organs was able to keep a calf alive on a total artificial heart for five months.[1] Termination of the experiment was due to the growth of the experimental animal; the implanted cardiac prosthesis was too small to accommodate the circulatory needs of a 200-kg recipient. No major physiological or hematological abnormalities were observed during the period of total artificial heart implantation. At that time it was decided that the continuation of long-term survival olympics would not contribute any additional information. The pneumatic actuation system requires an extracorporeal drive system with percutaneous actuation tubes. A patient with this type of total artificial heart would be tethered for life to the machine with the threat of infection through the percutaneous tubes. Therefore, although it was shown that a pneumatically actuated, biolized total artificial heart could be used clinically with-

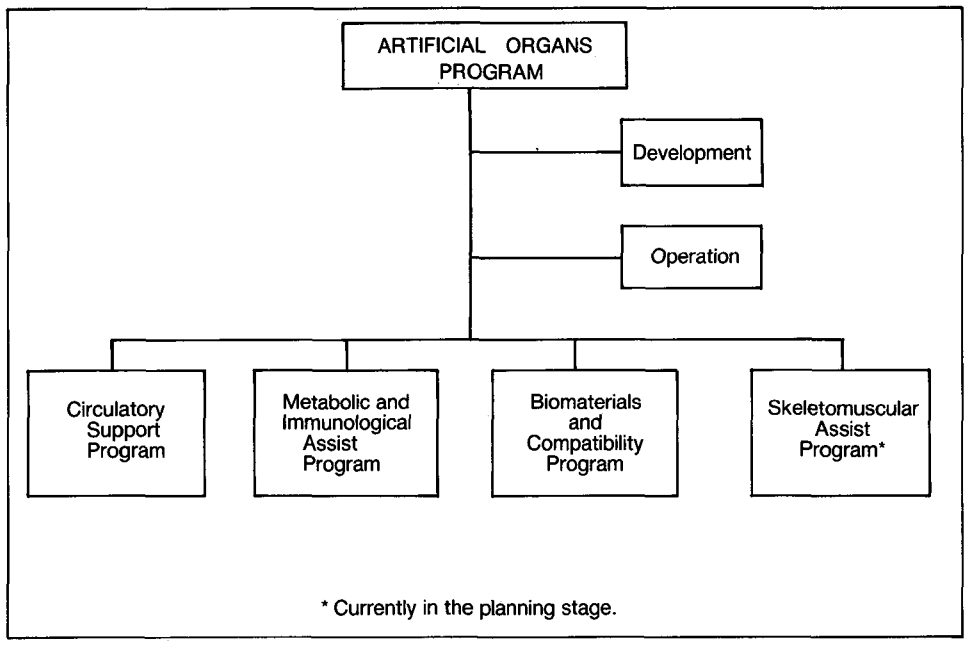

Fig. 1. Artificial Organs: table of organization.

out any further development or modification, it was concluded that this system would have only limited clinical applications and could not provide full rehabilitation of the patient. The total heart objective was then shifted to the development of a completely implantable total heart system (*Figure 2*) that could promise a near-normal life-style for a patient.

In clinical practice there are many occasions requiring circulatory support systems (*Table 3*). To meet the variety of clinical needs, different systems are required. The extent to which temporary assist devices can reverse myocardial dysfunction has not been clearly defined. Other areas of uncertainty remain: to what degree can a permanent left ventricular assist device support circulation, and who, among the total patient population really require ventricular replacement? A strategy was established that called for the use of a minimal cardiac prosthesis. Progression should be from minor and short-term application to major and long-term application.

A universal multipurpose cardiac prosthesis that would be applicable for temporary, perma-

Table 2. Circulatory support program

Temporary ventricular assist program
Permanent ventricular assist program
Permanent implantable electrohydraulic LVAS
Permanent implantable thermal-pneumatic LVAS
Permanent implantable thermal-hydraulic LVAS
Permanent implantable total artificial heart program
Nonpulsatile circulatory support program

LVAS = left ventricular assist system.

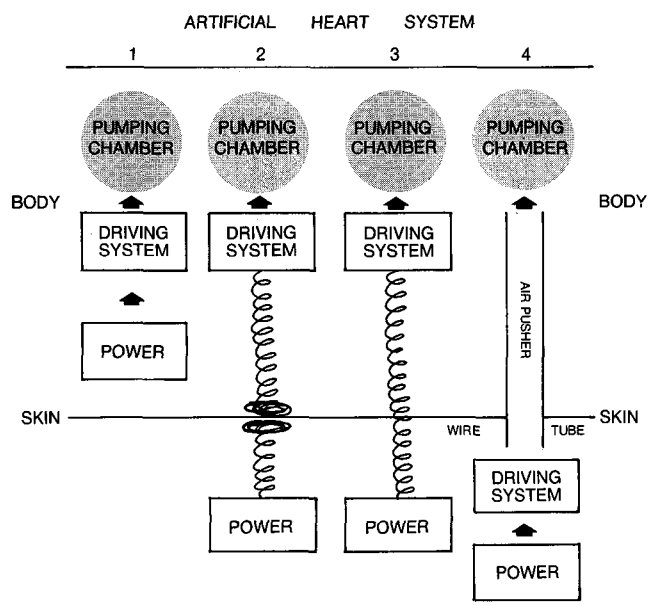

Fig. 2. Cardiac prosthesis with pneumatic actuation (System 4) requires external drive system and power supply. The totally implantable cardiac prostheses currently being developed at the Cleveland Clinic are a combination of systems 1 and 2. Power can be transmitted through intact skin to the implanted driving system. Without the outside power supply, the cardiac prosthesis will operate with the implanted auxiliary power supply for 0.5–2 hours with the electrical system and 8–10 hours with the thermal system.

Table 3. Types of mechanical circulatory support devices

A.	Circulatory assist devices
1.	Temporary assist (2 weeks)
a)	left ventricular assist (TLVAD)
b)	right ventricular assist (TRVAD)
c)	biventricular assist (TBVAD)*
2.	Permanent assist (2 years)
a)	left ventricular assist (PLVAD)
b)	right ventricular assist (PRVAD)
c)	biventricular assist (PBVAD)*
B.	Heart replacement (total artificial heart)
1.	Temporary replacement (TTAH)* with heart transplantation (1 month)
2.	Permanent replacement (PTAH)* (2 years)

* Two-pump system.
Temporary assist: parts of all of the system can be outside the body; permanent prosthesis: preferably the entire system, including actuation, is implanted inside the body.

nent, biventricular, and total assist was deemed necessary. The development of such a universal cardiac prosthesis was begun in 1977. Also, a temporary clinical ventricular assist program was initiated during 1977 utilizing a commercially available external centrifugal pump.[2] So far, 12 patients have received this type of temporary circulatory assistance (*Figure 3*). Developments in the Cleveland Clinic's universal cardiac prosthesis have been continuing since 1977[3] (*Figure 4*). The basic design is a long-term implant inside the chest cavity. It is also designed to be coupled with various types of implantable energy and actuation systems under development in the United States through the National Institutes of Health. Adaptation of the CCF universal biolized pump is shown in *Table 4*. This prosthesis has been applied clinically as a temporary extracorporeal ventricular assist device in 3 patients. Permanent assist devices are now in the system development and evaluation stage. Goals for completion of preclinical studies are 1987 for the electrically-powered system,[4] and 1989 for the thermal energy-powered system.[5] Preclinical system evaluation of the totally implantable artificial heart[6] is expected to be completed by 1991 (*Fig. 5*). The Cleveland Clinic circulatory assist program's clinical time line is shown in *Figure 6*. In addition, projects on the development of biomaterials, heart valves,[7] and small vascular prostheses are underway.

One innovation in the Department of Artificial Organs has demonstrated that totally pulseless circulation is possible.[8] Animals with two nonpulsatile blood pumps can be maintained with near

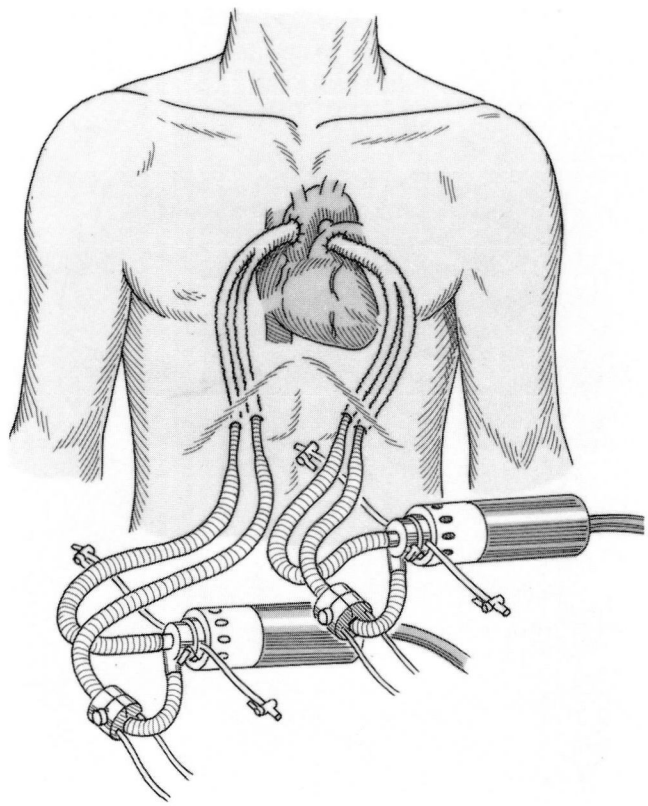

Fig. 3. Simple application of a temporary biventricular assist device utilizing commercially available centrifugal pumps. Seven left ventricular assists (three long-term survivors), two right ventricular assists, and three biventricular assists have been performed to date.

normal physiology for more than three months.[9] If this type of circulatory support is feasible, cardiac prostheses can be made much smaller, more efficient, and more durable without heart valves or a volume-shifting compliance system.[10]

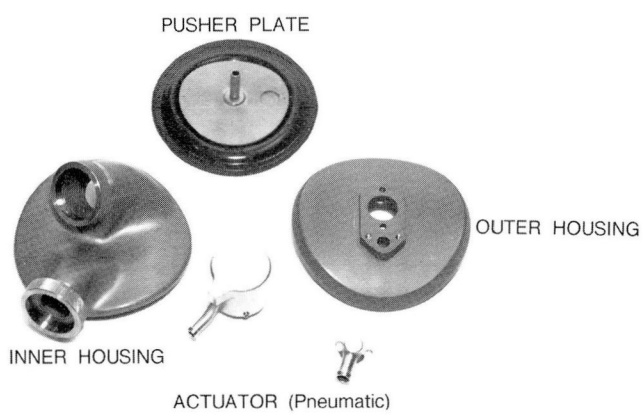

Fig. 4. Components of the multipurpose universal cardiac prosthesis. The same components are used in all the pumps, regardless of the intended clinical application. Various types of activators can be accommodated.

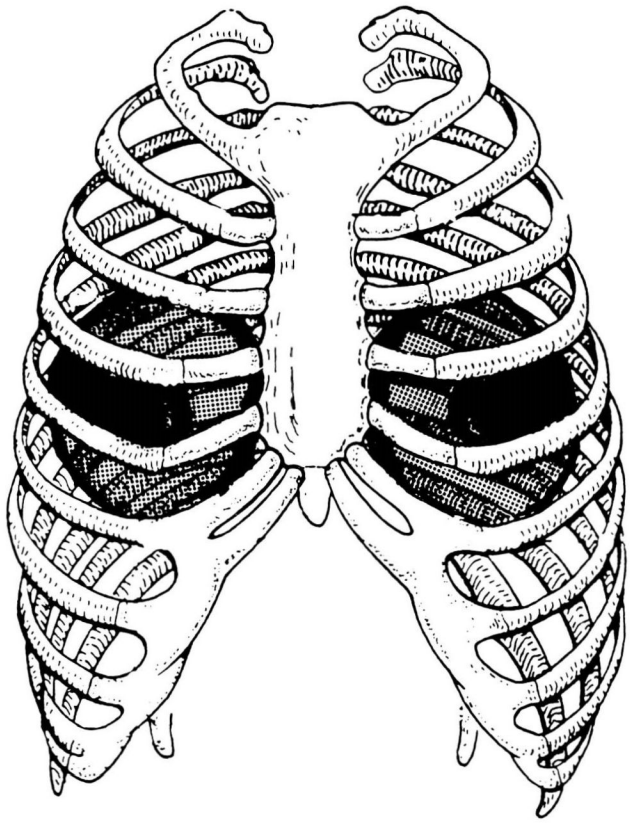

Fig. 5. The future totally implantable total artificial heart. Two of the left ventricular assist systems currently under development will be used for this application. The systems are implanted in the chest cavity, not in the pericardial cavity. This allows for its application not only in total replacement, but also in biventricular assist.

Metabolic and immunological assist program

The metabolic assist program was established in 1968 and was later expanded in 1978 to include immunological assist. Achievements are summarized in *Table 5*. Included in this program are developments in the artificial kidney, oxygenator, artificial pancreas, hepatic assist, artificial blood and plasma treatment systems for macromolecule removal (immunoassist). The initial emphasis on the artificial kidney was redirected to the on-line plasma treatment systems for metabolic and immunological assist during 1974.[11] At that time dialysis research had been oriented toward basic clinical studies, and interest arose in extending the extracorporeal treatment technologies developed for management of renal failure to other disorders. In 1972, microporous hollow fibers and sheet membranes became available,[11] which led to other innovations. The development of an effective hepatic assist remains a difficult problem, since treatment of blood for metabolic disorders is much more complex and difficult than is treatment of plasma. The availability of on-line plasma separation from whole blood provided incentives for further developments. Attempts to create an artificial liver were started more than 20 years ago,[12] utilizing freeze dried liver tissue preparation; however, the nonavailability of proper microporous filter membranes halted this research for ten years. Metabolic assist devices using plasma filters and multiple sorbents were initiated in 1974,[13] and in 1977, the Departments of General Surgery and Gastroenterology cooperated in a clinical hepatic assist program.[14] The initial emphasis was on the treatment of acute hepatic insufficiency, and later efforts were directed toward chronic liver support.[15] One patient suffering from sclerosing cholangitis has been participating in the chronic liver support program for the last two years, and has received over 100 treatments.

Table 4. Adaptation of CCF universal biolized pump

1. Temporary LVAD (CCF pneumatic)
2. Permanent LVAD
Electromechanical LVAD (TECO System)
Electrohydraulic LVAD (Nimbus System)
Thermopneumatic LVAD (Nimbus System)
Thermohydraulic LVAD (University of Washington System)
3. Total artificial heart

Adaptable to most of developing circulatory support systems of the National Institutes of Health.

Selective removal of macromolecules with cascade double filtration was initiated in 1975. Realizing the limitations of this technology, in 1979, on-line treatment of plasma for removal of macromolecules in the treatment of autoimmune diseases was developed by Malchesky et al and Nosé et al.[11,16] In one technique, cryofiltration, the plasma is separated from whole blood with a membrane plasma separator and then passed through a cooling unit. Cryogel that forms during the cooling process is removed by a second filter, the cryofilter (*Figure 7 and 8*). Cryogel differs from the classically measured cryoprotein; it is composed of various types of macromolecules including immunoglobulins, immune complexes, complement and activated complements, antibodies and other substances together with fibrinogen and albumin[17,18] (*Table 6*).

Patients suffering from autoimmune diseases

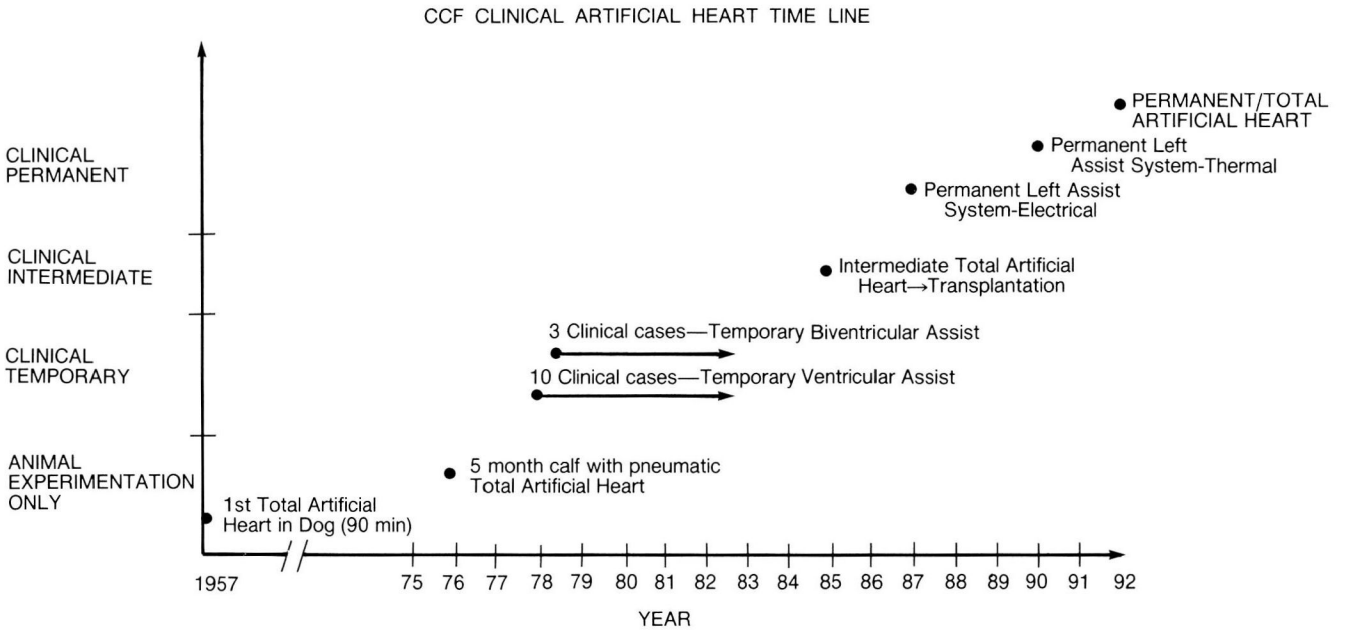

Fig. 6. The Cleveland Clinic Foundation, clinical artificial heart time line.

generate higher levels of cryogel in comparison to those generated from normal plasma. This cryogel is highly concentrated in macromolecules associated with the disease state.[19] Appreciable reductions in pathologically related macromolecules can be achieved in individual treatments, at present, being used in the management of rheumatoid arthritis; one patient has been treated for more than three years. Three treatments per week were necessary initially; however, only one treatment every two months appears to control her clinical symptoms. In 15 patients undergoing this technique, a 92% improvement has been shown. Similar results are being reported by other institutions using this technique. These results are much more promising than plasma exchange (58%) or leukocytapheresis (85%). Overall improvement of 90% with cryofiltration treatment is achieved when all published results up to April 1983 are reviewed.[20] This method of treatment is also applicable to other autoimmune diseases and metabolic diseases such as acute liver failure with multiorgan failure. It may be possible to arrest or reverse other diseases such as renal failure, cardiomyopathy, and atherosclerosis.[21] If this is possible, the number of candidates for hemodialysis or cardiac prostheses may be reduced. With the high costs of hemodialysis maintenance (currently 2 billion dollars a year and increasing)[22] and the expected high cost of maintaining patients with cardiac prostheses (5,000 to 50,000 projected recipients per year),[23] the reduction of potential candidates for this maintenance is imperative.

Results of studies at our institution and elsewhere have shown that alteration of humoral factors by cryofiltration subsequently alters cel-

Table 5. Metabolic assist program

	Accomplishments
1968–1974	Development through clinical testing of two artificial kidneys
1968–present	Development of analytical models for optimization of dialysis therapy
1974–1977	Design of membrane oxygenator for cardiovascular surgery
1973–1976	Research on biological agents for detoxification in chronic renal failure
1968–1970	Pioneering research on artificial blood and liquid-liquid type blood oxygenator
1974–1978	Research on biocompatible sorbent technology for blood detoxification
1972–1976	Early development of membrane plasma separation technology
1978–1982	Development of drug infusion systems, clinical applications in insulin infusion
1976–present	Development and clinical application of membrane plasma separation with on-line sorptive detoxification using multiple sorbents for acute and chronic liver support
1979–1980	Development of on-line plasma treatment systems for autoimmune diseases
1980–present	Clinical applications of cryofiltration, plasma exchange and on-line plasma treatment systems

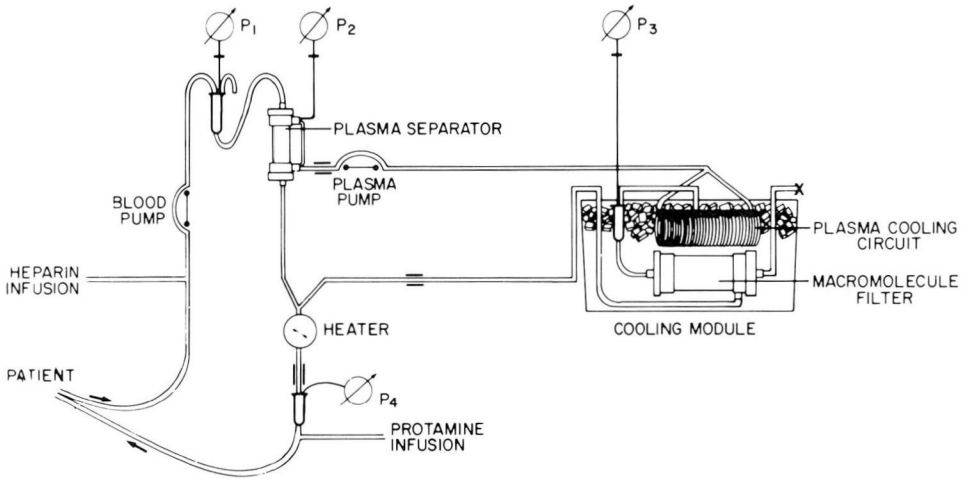

Fig. 7. Plasma separation and filtration circuit for clinical on-line removal of cryoproteins.

lular immunology, normalizing its function. There are some indications that the removal of macromolecules such as immunosuppressive acidic proteins and immune complexes might produce favorable results for the treatment of certain types of cancer.

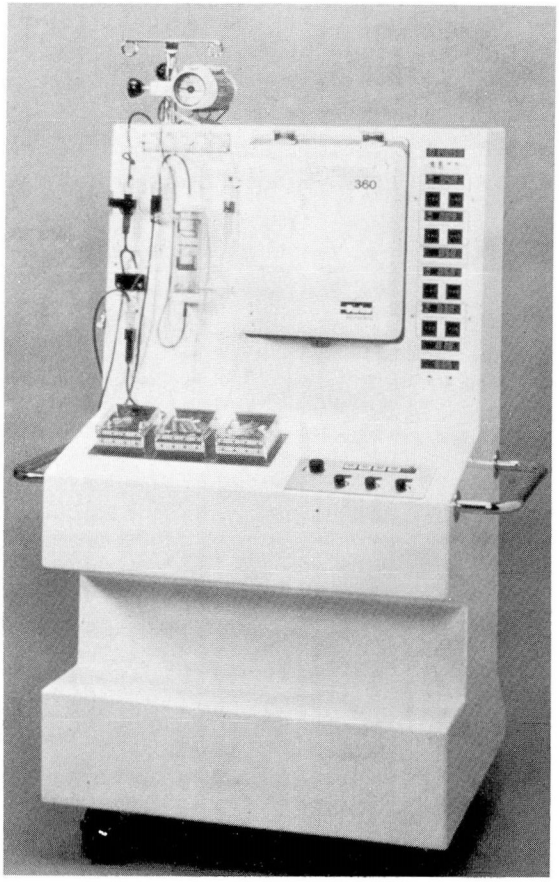

Fig. 8. Continuous cryofiltration system for treatment of immunological diseases. The primary filter can be seen on the left. The macromolecular filter and cooling unit are contained inside the large square lid on the right.

Other projects of the metabolic and immunological assist program include the development of an open-loop miniaturized insulin delivery pump[24] (*Figure 9*), and membrane oxygenators[25,26] (*Figure 10*). Both of these types of devices have a large clinical demand. A miniaturized drug delivery pump can be used for insulin delivery to the diabetic patient, and also for various types of continuous drug delivery including anticoagulation, cancer chemotherapy, pain control, and nutritional management. The membrane oxygenator is useful for open-heart surgery as well as for extracorporeal respiratory support. In the past, studies were carried out to support renal function with wearable systems. Isolated intestinal loops were created in dogs and filled with dialysate and sorbents.[27] To develop a biological replacement for the natural kidneys, soil bacteria were investigated[28] for the ability to degrade urinary waste products. Combinations of bacteria were isolated. The possibility exists that with certain types of bacterial combinations or enzyme systems and with water absorbents, an implantable renal replacement is feasible.

Table 6. Composition of cryogel

Cryoprotein	Complement
Immune complexes	Activated complement
Immunoglobulin	Endotoxin
Fibronectin	Antibody
Fibrinogen	Albumin

Composition of cryogel varies as a function of the disease state; it is affected by temperature, pH, electrolytes, and the addition of macromolecules such as heparin.

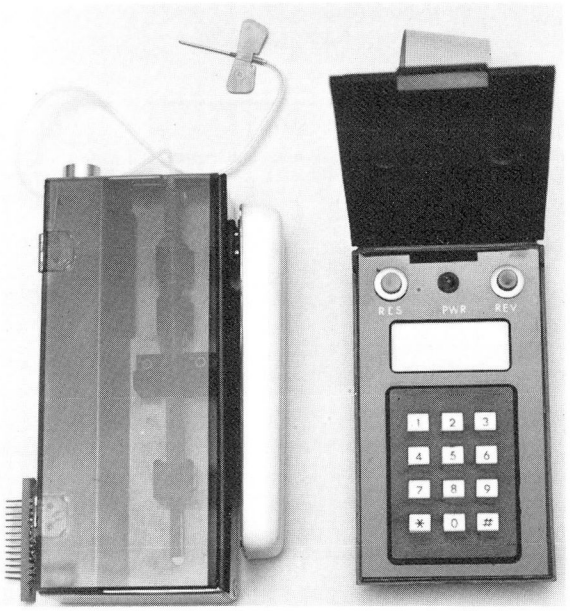

Fig. 9. Small, open-loop insulin delivery pump that can be worn by the patient. The batteries and syringes enable delivery of approximately one week's supply of insulin.

Biomaterials and compatibility program

Initially, the biomaterials program focused on blood compatibility because one of the major problems with the cardiac prosthesis had been thromboembolic phenomena. The introduction of smooth surface polyurethane and pseudoneointima-forming surfaces made possible the use of clinically acceptable pump systems. However, complete elimination of thromboembolism from smooth surfaces and limitation of pseudoneointima growth on fabric or flocked surfaces were difficult to achieve. The introduction of the "biolization hypothesis"[29] and the biolized cardiac prosthesis[3] significantly reduced thromboembolic occurrences even with implantations of the pumps for up to seven months.

Typically, the biolized surface is created by coating the inside surface of the pump with purified gelatin and crosslinking it with aldehyde.[30] This hydrophylic smooth surface does not attract platelets or fibrin. Transient deposition of white cells is seen two weeks after implantation; however, these white cells do not remain on the biolized surface but generally detach within a few days. This attachment and detachment process continues throughtout the period of implantation. So far there has been no evidence of even partial monolayer cellular coverage in up to seven months of implantation. This biolized surface seems to be resistant to calcium deposit and infection. All the cardiac prostheses produced since 1977 in our Department have this type of surface treatment. Because it does not promote cellular deposition, it may be ideally suited to small vascular prostheses. This is currently being studied, as well as blood compatibility related to hemodialyzers, plasma filters, and oxygenators.

During the last four decades, cellulose membranes have been used for hemodialyzers. Since they are effective for removal of uremic toxins, and since other types of membranes were not available, in-depth blood compatibility studies of hemodialyzers were not carried out until recently. The transient reduction of leukocytes at the onset of a dialysis procedure was noticed as early as 1960,[31] but its importance was not recognized for some time. Later it was considered to be related to complement activation[32] and could be alleviated if more blood-compatible polymeric membranes such as polymethylmethacrylate (PMMA) were used.[33] Multiple use of dialyzers produces less leukocyte reduction and complement activation .[33] Formaldehyde solution is used for sterilization in multiple use of dialyzers. The surface of the dialyzer is covered by the patient's protein after its first use; these surface proteins are subsequently crosslinked by an aldehyde solution. This is essentially the same as the "biolization process," and better blood compatibility can be expected, as was shown by our blood pump studies.

Various types of allergic or anaphylactogenic reactions have been reported after the use of cellulosic membrane dialyzers. The repeated exposure of a foreign surface to blood during chronic hemodialysis produces acute immunolog-

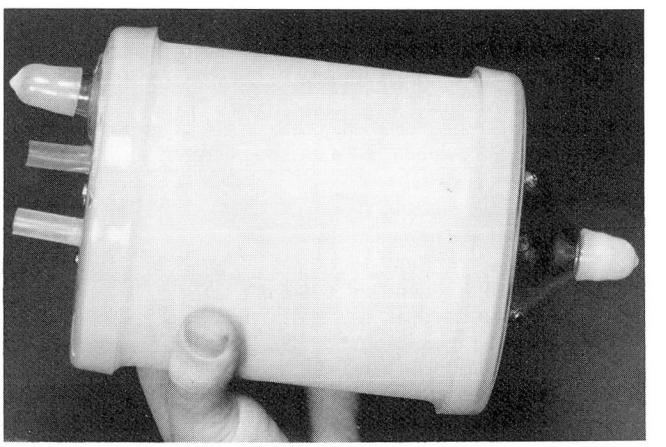

Fig. 10. Hand-held coil membrane oxygenator developed by the Cleveland Clinic.

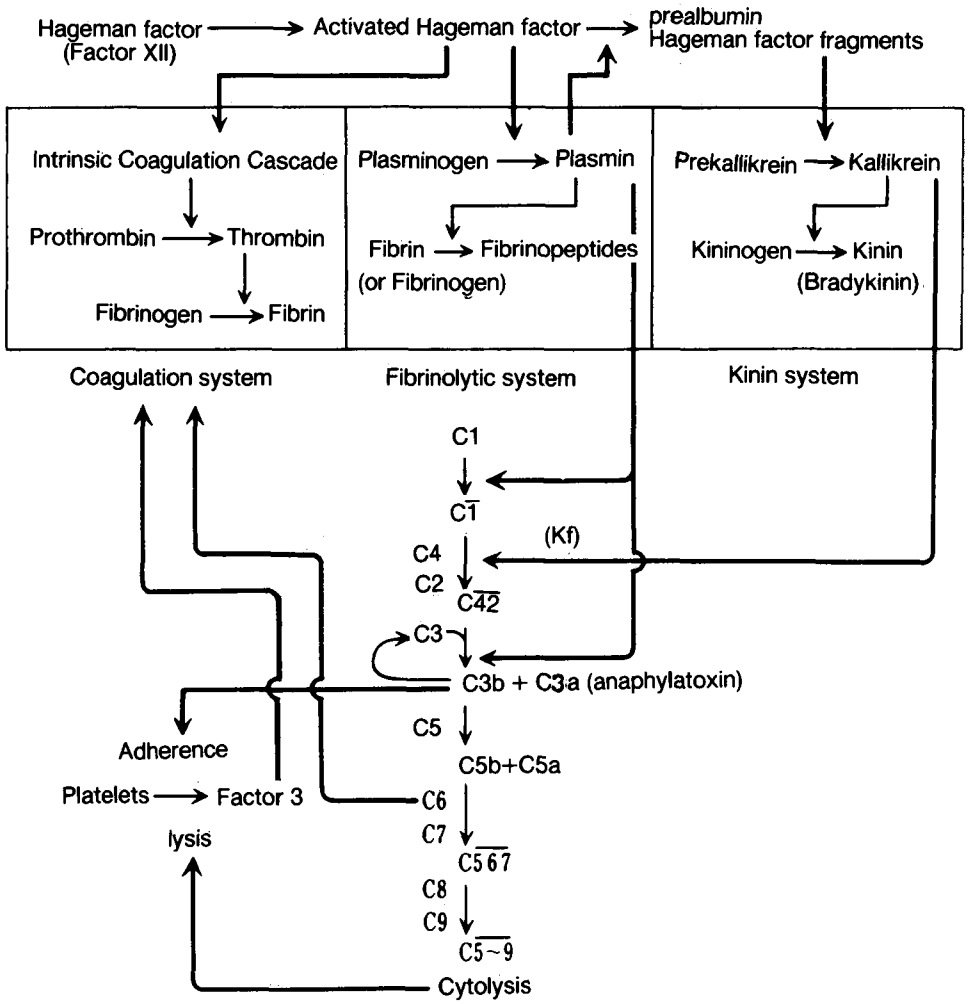

Fig. 11. The interrelation of the coagulation, complement, fibrinolytic, and kinin systems. (From Kokichi Kikuchi ed. Medical Immunology, Nankodo: Tokyo, 1980, p 109.)

ical reactions if the dialyzer membrane is not biocompatible. Even though severe acute reactions are few, such as 3.5/100,000 dialyses,[34] minor allergic reactions occur in about 1% of the patient population, and more than 10% of the patients show transient cardiopulmonary function derangement. Transient hypotension and transient hypoxia are the most notable symptoms. This type of complication may be related somewhat to the compatibility of dialyzers. There is an indication of a close correlation between pulmonary hypertension and transient reduction of leukocytes in sheep as acute immunological complications. Chronic immunological complications of hemodialysis should not be overlooked. Since there is a high incidence of atherosclerosis, cancer, and infection among hemodialysis patients, multiple immunological challenges should be avoided (*Table 7*).[35,36]

Table 7. Effects of biocompatibility of materials used for hemodialyzers

I.	Immunologically mediated acute complications
	Hypersensitivity
	Allergic reaction
	Anaphylactic shock
	Pyrogen reaction
	Transient reduction of leukocytes
	Transient hypoxia
	Transient hypotension*
II.	Immunologically mediated chronic complications
	Atherosclerosis
	Infection
	Immune deficiencies
	Malignant tumor

* Sodium and fluid depletion may also cause this.

Heparin is routinely used for extracorporeal circulation. The effects of its repeated use have been overlooked. However, our recent studies indicate there is a relationship between heparin and the transient reduction of leukocytes. The

compatibility of biomaterials cannot be interpreted only by the complement system. Our studies indicate that there is no direct or close correlation between leukocyte reduction and complement system alone. The interrelation of the coagulation, complement, fibrinolytic, and kinin systems is shown in *Figure 11*. The Department plans further studies to introduce methods and devices to reduce acute and chronic immunological complications for the patient requiring repeated extracorporeal therapies. Cryofiltration removes activated complements and does not produce as many acute complications as hemodialysis. Better polymeric membranes are becoming available. In addition, immunomodulation is possible, thus assuring a better-planned treatment system in the future.

Skeletomuscular assist program

Although various types of orthopaedic prostheses are widely used, further improvement and development of new types of joints and bones are critically needed. The Department of Orthopaedic Surgery has been active in developing new and refined skeletomuscular assist prostheses, and in studying the biomechanical aspects of bones, joints, and muscles. Further study of the biomaterial aspects of these implants is warranted. The skeletomusclar assist program is in the process of being integrated into the artificial organs program at the Cleveland Clinic.

Conclusion

The introduction and institution of new types of therapeutic artificial organs should reduce the number of end-stage organ failure patients. For example, the etiology of end-stage renal failure is largely of immunological origin, whereas end-stage heart failure patients who are candidates for cardiac prostheses have either artherosclerotic coronary disease or cardiomyopathy, both of which are autoimmunological diseases. Plasma treatment of these diseases during the early stages could prevent further progression. This would reduce the need for artificial organs. However, we believe the best medicine is prevention, which will afford longer life of better quality. It is my hope that, ultimately, there will be no need for artificial kidneys or hearts.

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