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PLASTIC ARTERIAL GRAFTS

"New, man-made arteries, crimped to prevent kinking and forked to provide free blood-flow to both legs, now have been successfully installed in more than 200 persons--HAS CRIPPLES WALKING." Those are the headlines in the daily newspapers.

Indications for use of arterial grafts as well as problems in diagnosis and techniques of insertion are discussed in the following conditions:

- Arterial injuries
- Segmental arteriosclerotic obstruction
- Aortic and peripheral aneurysms
- Lesions of the thoracic aorta

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Springfield, Illinois

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Foreword

A GROWING appreciation of the segemental nature of arterial lesions, aneurysmal or obstructive, underlies modern advances in arterial surgery. It is axiomatic that restoration of full flow is the treatment of choice for arterial insufficiency. The limited success of measures designed to enhance collateral flow alone confirmed the axiom and lent clinical credence to the segmental nature of arterial obstructions. Angiography identified these segments and has focused attention on the aortic bifurcation, the iliofemoral segment, the femoropopliteal segment, the carotid bifurcation and the left coronary artery. Clinical definition of the problem turned attention to the design of arterial substitutes and the technics of their insertion. It was early realized that the supply of homografts was too limited to satisfy the clinical or investigative demands. Subsequent experience with homografts has suggested an undesirable vulnerability to sclerotic changes in atherogenic individuals.

Early in 1954, Mr. Pat Moore, an electrical engineer at Chemstrand Corporation in Decatur, Alabama, came to the University Medical Center in Birmingham for treatment of his aortic insufficiency. The ensuing considerations of valvular prosthesis awakened Mr. Moore's interest in an alliance in industry and medicine at the research level for the solution of clinically pertinent problems. Dr. James S. Tapp, of Chemstrand, and Dr. W. Sterling Edwards, of the Medical College of Alabama, happily accepted the challenge. It was their decision, promptly endorsed, to attempt primarily to prepare an acceptable prosthesis for arterial replacement. Although problems still remain, this monograph is testimony of considerable progress. Unfortunately, Mr. Moore was denied survival to realize the fulfillment of his vision, but there are now many surgeons and patients alike who feel that his efforts have made a significant contribution to the development of an acceptable arterial substitute.

Birmingham, Alabama

CHAMP LYONS, M.D.
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Introduction

AT THE invitation of Mr. Charles C Thomas, the author has undertaken the task of producing this monograph as a progress report on the rapidly developing changes in the field of arterial grafts. As in all new areas in research, new ideas soon become obsolete and old theories are changing frequently.

A large part of this monograph is devoted to the progress made in our laboratory in the development of a plastic arterial graft which has proved to be safe and practical. It is hoped that this will not be construed to mean that it is our feeling that the ultimate in synthetic grafts has been obtained or that no better prosthesis than this is likely to be developed. That is, of course, far from true and the purpose of this monograph is to stimulate others to continue work in this field so that the multiple problems remaining can be attacked from many angles; resulting in an earlier solution.

It is also hoped that this monograph will help those in smaller communities where homograft arterial banks are not available to have on hand a supply of safe and simple grafts for emergency replacement of diseased or damaged arteries.

The author wishes to take this opportunity to express his appreciation to Dr. Champ Lyons, Chairman of the Department of Surgery of the Medical College of Alabama for his continued encouragement and support in this project, and to acknowledge the technical assistance of Mr. Clarence Forrest and Mr. Paul Boyles. The photography has been painstakingly done by Mr. Joe Mineo of the Veteran's Hospital and by Gladys and Robin McQueen of the University Hospital. The drawings were done by Mr. John Desley and the manuscript prepared by Mrs. Dolly Walls. Most of all, the author would like to express his indebtedness to the Chemstrand Corporation for their whole-hearted co-operation in helping with a project from which they realized there could be little financial gain and especially to Dr. James S. Tapp, of the Research and Development Department of the Chemstrand Corporation without whose knowledge, imagination, and hard work this project could not have been accomplished.

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W. Sterling Edwards, M.D.

Contents

PLASTIC ARTERIAL GRAFTS

Chapter I

History of Arterial Grafts

SINCE THE turn of the Twentieth Century, surgeons and investigators have sought methods of replacing diseased arteries in animals and human beings. Alexis Carrel [9, 10] was one of the pioneers in this field. Working at the Rockefeller Institute in New York in the first decade of the century, this imaginative investigator carried out many studies on the replacement of the thoracic aorta in animals. His attempts to use paraffin lined glass and aluminum tubes met with early success, but the incidence of delayed thrombosis was high, leading to the death of the dogs. Many of these tubes produced erosion of the adjacent aorta at the point of the ligature which held the tube in the aorta and death followed from severe hemorrhage. A paraffin lining was chosen because of its quality of unwettability or water repellency which reduced the tendency of blood to clot.

A French physician, Tuffier [87, 88] also tried paraffin lined silver tubes in arterial injuries of World War I, but most of these occluded with clot in 4 days or less, although a few tubes remained patent as long as ten days. Makins [55] reported similar results in his own cases and in those of other surgeons. Murray and Janes [65] used glass tubes in dogs, but even with large doses of systemic heparin these remained patent only up to 72 hours.

More recently Blakemore and associates [3] tested vitallium tubes in 15 dogs with only one success in which the aortic replacement remained patent for 5 days. Attempts have been made to use very smooth and unwettable polyethylene tubes. H. D. Moore in Oxford, England [63] carried out a number of experiments in the thoracic aorta of rabbits, using polyethylene tubes of 2½ to 3 mm. internal diameter as a vascular bridge. These tubes were tied in place by a loose ligature at each end. The incidence of thrombosis was high and there were only 4 out of 20 that survived for any extended period of time. Several of the animals had late thrombosis as long as 3 or 4 months following placement. This investigator attempted the replacement of ten internal jugular veins in six rabbits and all were unsuccessful in spite of the use of heparin and of a silicone coating in these polyethylene tubes. Donovan [24] also investigated the replacement of the thoracic aorta in dogs with polyethylene tubes. A very small percentage of the 23 dogs reported maintained a long-term patent tube without evidence of thrombosis. His experiences in the replacement of the femoral artery of dogs were more discouraging; all thrombosed within 2 days. Lining polyethylene tubes with silicone and saturating them with heparin preoperatively did not increase the average duration of patency. In 2 of the cases of thoracic aortic replacement with polyethylene tubes Donovan had fatalities several months after surgery from mesenteric embolism.

A few attempts were made by surgeons in World War II to replace damaged arteries in injured soldiers by use of polyethylene tubes and these were almost uniformly unsuccessful.

In dogs Hufnagel [40, 42] studied specially polished methyl-methacrylate tubes with more encouraging results. These tubes bridging defects in the thoracic aorta were relatively large caliber vessels with an internal diameter of 10 to 13 mm. Methacrylate is hard and somewhat troublesome to insert. Despite the report of a low incidence of occlusive thrombosis in larger tubes of this material there is an occasional late embolus to the periphery.

The most important outgrowth of Hufnagel's work on rigid tubes was the development of the "multiple point fixation" principle which eliminated the danger of necrosis from tying a rigid tube in a vessel with a single ligature. This principle made possible the aortic ball valve for aortic insufficiency. This highly polished rigid plastic valve has had a low incidence of thrombotic occlusion but the incidence of distal embolus developing from the prosthesis itself has been somewhat troublesome.

It seems, therefore, that all of the impermeable plastic tubes no matter how smooth or unwettable the inside lining have had a discouraging history of a relatively high incidence of total or partial thrombosis either acutely or several months after implantation.

The next major step in the advance of arterial replacement was the use of autogenous veins. Pringle [73] and Gordon Murray [61] were among the first to attempt this technique in humans. Blakemore [4] developed a nonsuture technique of venous anastomosis to arteries using a cuff of vitallium to fold back the vein for insertion into the lumen of the patient's arteries. Vein grafts have had varying successes in the hands of different investigators and they certainly have a remaining place in present day surgical therapy. Veins can be used in peripheral artery replacement of short segments especially in areas of muscular support such as the middle of the thigh with very good long-term results. Experience from the Korean War as well as civilian reports [25] have shown long-term patency in autogenous venous replacement of arterial injuries.

Johnson and Kirby,[44-46] however, showed that autogenous veins could not be safely or satisfactorily used to replace unsupported large arteries such as the abdominal aorta. The difficulty here lies in distention of the unsupported vein graft with development of an aneurysm. Recently long venous autografts have been used in an effort to bypass arteriosclerotic femoral obstructions. A high incidence of late thrombosis (9 to 12 months) has been reported.[39, 81] This may not be the fault of the vein graft but of the progression of the patient's arteriosclerotic disease.

There remains, then, a place for the use of venous grafts in arterial injuries where no other replacement methods are available. The chief disadvantages of the use of veins in this application are, first, that separate incisions may be necessary to obtain the vein, the second, that acute venous spasm and size disproportion may make anastomosis difficult.

Arterial replacement surgery did not make significant progress until satisfactory methods of arterial homograft transplantation were developed. Again Alexis Carrel [11] pioneered this area in the early Twentieth Century, transplanting arteries from one animal to another with some success. Carrel [11] and Guthrie [33] studied fresh arterial homografts and heterografts with varying success. Their work was not followed up for 35 years (as is so often the case in basic discoveries). Gross and associates [30, 31] encountered several patients with coarctation of the thoracic aorta in which end-to-end anastomosis was impossible. This stimulated a renewed investigation of techniques of arterial transplantation and led to the development of a technique of short term preservation of living homologous arterial grafts in 10% homologous serum in a balanced salt solution. Arteries were obtained from fresh autopsy material under sterile conditions and immediately placed in nutrient media containing penicillin. These living grafts could be kept for several weeks without degeneration but their short term survival made the development of a large supply impractical.

The freeze-drying or lyophilization method of homograft preservation introduced in 1951 by Marrangoni and Cecchini,[56] and by Natellis and Visalli,[66] has made much more practical the development of arterial homograft banks. These investigators showed that human arteries, taken from young donors without any pre-existing arteriosclerosis, could be lyophilized and preserved in vacuum tubes for indefinite periods. Donor vessels were taken at first by sterile autopsy,[69] but various methods of sterilization have developed. These have included ethylene oxide; [41] beta-propiolactone,[86] and high voltage radiation [54, 59] either by cathode ray or cobalt bomb. Controversial evidence has been presented that these techniques of sterilization adversely effect the arteries and cause more rapid degeneration after these arteries have been reconstituted and implanted.[8, 76]

There is no question but that freeze-dried homograft banks have supplied a terrific stimulus to technical advances in aortic and peripheral vessel surgery. Even simpler methods of preserving arteries which may be equally satisfactory, such as preservation of arteries in 70% ethyl alcohol,[49] seem to offer equally satisfactory results clinically with the saving of a great deal of effort and expense.

Despite these advantages and despite the fact as pointed out recently by Creech and associates,[17] that a high percentage of satisfactory results can be expected using preserved homografts, several disadvantages should be considered. The rapid increase in indications for arterial replacement surgery have outstripped the supply of homografts in most localities in this country and abroad. It is especially difficult to obtain small caliber vessels such as long femoral homografts, because of resistance on the part of pathologists and undertakers to long incisions in the thighs. It is impractical for small community hospitals to keep on hand enough grafts to supply occasional needs in the case of injuries or ruptured aneurysms.

In addition to these problems of homograft availability, there is a more serious problem of late degeneration. The early 1- or 2-year results after homograft placement have been excellent in the majority of cases, but enough disruptions of these grafts have been reported to cause some concern.[7, 34, 35] A long-term animal study by Coleman and others[12, 47, 67] revealed a high incidence of graft degeneration in 3 or 4 years, which has been disturbing. Creech[20] has reported that the production of arteriosclerosis in dogs with aortic homografts results in a more serious degeneration of the homograft than of the animal's own vessels.

In an effort to provide more readily available grafts, studies on heterologous vessels have been undertaken by Creech[16] and Hufnagel.[41] Sheep and calf arteries were found by Creech to be too variable in thickness for practical use so most of the preliminary studies were carried out using hog vessels implanted in the dog. These arteries were preserved by: (1) freeze drying, and (2) fixation in 4% neutral formalin. Detailed histologic studies were carried out on all specimens and the authors observed that, in general, the fate of heterografts is that of gradual deterioration rather than replacement and restoration. Dilatation of the heterografts was seen in one-half of all those which were older than 18 months, and the rate of thrombosis was prohibitive, no matter which method of preservation was used. With these discouraging results, confirmed by others, heterologous vessels have been discarded as a source of available grafts.

These considerations have led to continuing efforts to develop more readily available and more permanently safe types of arterial replacement.

In 1952, Voorhees, Jaretzki and Blakemore[90] first reported the use of tubes constructed from synthetic fabric as a possible method of replacing blood vessels. This is a quotation from the introduction to their paper.

> It was observed in this laboratory that a single strand of silk suture transversing the chamber of the right ventricle of the heart of a dog became coated in a few months throughout its length by a glistening film free of microscopic thrombi. An an outgrowth of this observation, it was conceived that if arterial defects were bridged by a prosthesis constructed of fine mesh cloth, leakage through the walls of the prosthesis would be terminated by the formation of fibrin plugs, and would thus allow the cloth tubes to conduct arterial flow. In the absence of foreign body reaction it was anticipated that massive thrombosis would

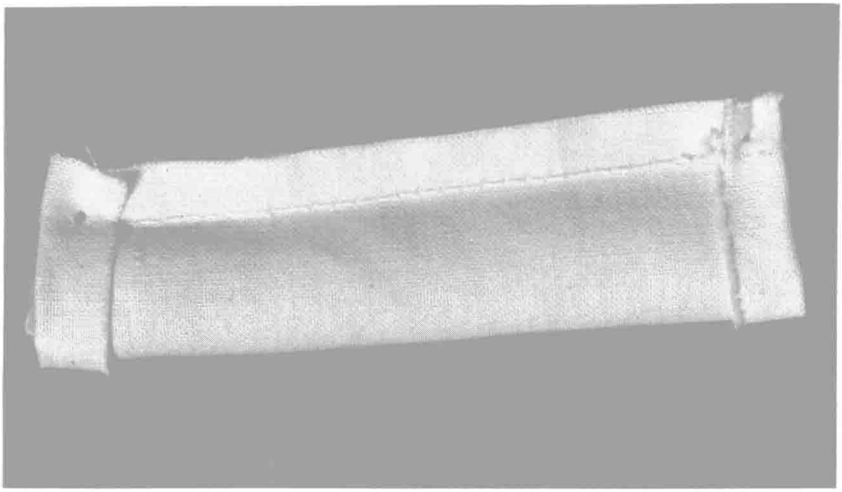

Figure 1. Original method of fashioning a tube of fabric by a longitudinal seam plus cuffing of both ends for ease of suturing. (From *Surgery*, courtesy of the C. V. Mosby Company.)

not occur, that fibroblasts would grow into the interstices of the mesh replacing the fibrin plugs, and that the fibroblasts would then serve as a basis for endothelial proliferation or undergo sufficient adaptation to form a functional intima.

The report which these authors presented consisted of the results of fifteen animal experiments in which tubes made of Vinyon "N" cloth were interpolated into the abdominal aorta. These cloth tubes were fashioned by folding a sheet of fabric and fashioning a tube by a longitudinal seam. In a majority of the animals a vitallium cuff technique was used for anastomosis. There were only three occlusions from thrombosis in this series of 11 dogs and many of these animals were followed for 3 to 6 months. With this encouraging success Blakemore and Voorhees[5] developed methods of cuffing back the ends of fabric tubes to prevent the fraying of the raw cloth so that a double layer of cloth would allow anastomosis by standard vascular techniques (Figure 1). A method of producing bifurcation tubes was developed by sewing two sheets of cloth together on a sewing machine to form a "Y" tube with cuffed ends. Clinical experiences with both straight and "Y" tubes of this type using Vinyon