AN INVESTIGATION OF A BONDING AGENT AND A STAPLING INSTRUMENT IN VASCULAR SURGERY

In Partial Fulfillment of the
Requirements for the Degree
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by

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GENERAL INTRODUCTION

It is difficult to discover who was the first surgeon to repair a blood vessel. Hopfner (1) in 1903 published a review of the literature, and he stated that Lambert of Newcastle was the first surgeon to write about vascular suture and that Hallowell, in 1795, was the first to perform it on a patient. He sutured a lateral defect in a brachial artery, the limb survived, but it is not certain whether the vessel remained patent or not. Probably the first end-to-end anastomoses were performed by Murphy in 1897 (2,3). Alexis Carrel (4) employed two or three stay sutures, then a continuous mattress or over and over suture, to enable accurate apposition of the intimal surfaces. His latter technique, which was developed in 1907, is essentially that used today.

The introduction of radiographic techniques for the visualization of arterial pathways by intraluminal injection of radio-opaque substances provided the valuable information that many vascular lesions, even in severe arteriosclerosis, were localized and therefore, amenable to direct surgery. Aortography was originated in 1929 by Dos Santos, Lamas and Caias (5). Its use in the United States was first described by Nelson (1942), (6), and subsequently by Doss and his co-workers (1942), (7,8), and Wagner (1946), (9). The introduction of Heparin in the field of vascular surgery by

Murray in 1940 (10) was another valuable contribution. Before this time the vascular surgeons had only liquid petrolatum to prevent thrombosis. They had to coat their sutures, graft and vessel ends with this material and, as a result, every needle hole was a site for potential bleeding.

The interest in vascular surgery to produce arterial and venous shunts stimulated the experimental evaluation of the relative merits of nonsuture and suture methods of blood vessel anastomoses. Blakemore and Lord (11) deserve much credit for stimulating surgeons in the practicability of blood vessel repair and anastomosis, utilizing the nonsuture vitallium tube method. However, the results from using it in battle injuries during World War II were not outstanding (12, 13, 14). The use of absorbable fibrin tubes instead of vitallium ones for vein graft was then advocated by Swenson and Gross; their reported experimental results were very good, thrombosis occurred in only one case out of 27 (15). Johns (16) compared the result of the suture and nonsuture methods for the anastomosis of veins in animals. He reported 90% functioning patent end-to-side splenorenal anastomoses and 73% end-to-end ones, utilizing the suture technique, whereas with the nonsuture vitallium tube method only 17% were patent in a group of end-to-end splenorenal anastomosis.

The next major step was the introduction of replacement

techniques for diseased or injured arterial and venous segments. These replacements consisted of venous autogenous grafts (17), arterial homografts (18,19), venous homografts (20,21), heterografts (22,23), vascular grafts from the rectus fascia (24), grafts made from split thickness skin (25), grafts from chamois (26), stainless steel wire (27) and the various synthetic fabrics - including nylon, ivalon, orlon, dacron and teflon (28,29,30,31).

Most of the early development of reconstructive arterial techniques were performed with arterial homografts. Such grafts have consequently been followed the longest, and there has been full opportunity to observe their behavior over an extended period postoperatively. Perhaps because of this, and because of greater ease and convenience of the plastic prostheses, the artery bank has largely become a thing of the past (32). Among the plastic prostheses, dacron and teflon tubes are at present, the generally accepted form of plastic arterial prostheses. The pore size of the fabric appears to be a factor determining the ultimate nature of the lining or "neo intima", since a tight weave inhibits vascularization and organization of the lining and leads to degenerative sequence (33). Degeneration of the lining and mural thrombosis in prostheses of small size accelerates their occlusion (34). Degenerative sequences have not been so important in tightly woven aortic grafts (35), and

such grafts are preferable in the thoracic aorta, where hemorrhage through a more porous prosthesis may be forbiddingly formidable, particularly in a heparinized patient. In vessels the size of common iliac artery, or larger, the plastic prostheses are generally considered to be satisfactory; however, failure of suture lines in the abdominal aorta, with false aneurysm formation and rupture into the gastro-intestinal tract, are beginning to make their appearance, one, two and three years after operation. The same sort of late suture line failure has been seen in small caliber prostheses in the extremities (36). Such suture line separation probably presents failure of a graft to establish a sufficiently firm fibrous tissue bond with the host artery and consequent sole dependence of the integrity of anastomosis on fine silk suture. Fine silk has been found to deteriorate rapidly after implantation in the body, losing up to 90% of its strength within six months to a year (37). For this reason, sutures of a stable material like dacron, must be used when long term dependence on the suture is required (38). Firm healing can only be expected when live tissue is sutured to live tissue. Some vascular surgeons are suspicious of the long term behavior of all small caliber plastic prostheses, and these doubts tend to be confirmed in the laboratory animals. The literature is consistent in reporting an unacceptably high rate of thrombosis when

plastic prostheses are used in the femoral or carotid artery of the dog, independent of the kind of prostheses used (34, 39, 40, 41). Results are somewhat better when porous fabric is used, but still range between 45 and 65% patency at one year, thrombosis occurring late in about half of the preparations.

PROBLEMS

The problems encountered in vascular anastomoses are usually in two areas; in the situations when speed is essential and in small vessels with an external diameter less than 4 mm.

The length of the time that a blood vessel may be occluded is sometimes quite critical. This is particularly true in regard to vessels supplying or draining a specific organ, such as renal, hepatic or carotid vessels. In whole organ transplantation, the multiple vascular anastomoses presents a problem and the need for rapid re-circulation of blood through the organ is obvious.

A persisting major problem in vascular surgery concerns vessels less than 4 mm. in diameter. Here early thrombosis and progressive narrowing have been so frequent as to cause some investigators to state that they are inevitable. The published results include the work of Schumacker and Lowenberg (42), who reported 65% thrombosis in arteries 4 mm. or less in diameter. Hurwitt and his associates (43), who had 50% thrombosis, and Thal and his

group (44), successfully anastomosed seven out of 17 arteries of 3 mm. in diameter. Urschel and Roth (45) reported the most promising results utilizing Heparin and local antispasmodic agents with a 93% patency rate in canine arteries 1.5-4 mm. in diameter, and 73% patency in arteries 1.5-2 mm. in diameter. Seidenberg et al reported excellent results by meticulous direct anastomosis of small arteries with sutures using 7-0 braided silk (46). Jacobson and his co-workers (47) were able to demonstrate a high degree of patency following a meticulous technique with fine suture material, using a dissecting microscope and specially designed surgical instruments. This method has not gained wide acceptance because it is cumbersome and requires the use of extra equipment in the operative field. The high rate of thrombosis in standard suture methods caused many of the investigators to revert to nonsuture methods. Carter and Roth (48), Rohman, Goetz and Dee (49), using a variety of fixed rings reported patency rates of 52 to 96% in small vessel anastomosis. The use of identical teflon rings for end-to-end anastomosis of 2-4 mm. arteries has been described by Holt and Lewis (50) with 100% patency. Urschel and Roth (51) reported 95% patency in nonsuture anastomosis in canine arteries by their ring method. These methods all require the permanent installation of a fixed ring at the points of anastomoses with its attendant

long term danger of hemodynamic and structural change. Vogelfanger and his co-workers (52,53), however, were able to report 70% complete patency and 10% partial patency in anastomoses of canine arteries of 2-3 mm. in diameter, using a stapler device which he developed in conjunction with the National Research Council of Canada.

OBJECT OF STUDY

This study was designed to investigate the efficacy of a nonsuture method and of a stapling technique in normal and in experimentally-produced atherosclerotic vessels, as compared to the conventional methods. A plastic adhesive (methyl-2-cyanoacrylate) was used for nonsuture techniques. The Vogelfanger stapler was employed for stapling technique. These were compared as to shortness of required operative time, the incidence of complications and general efficacy of methods.

Chapter I

PLASTICS

Definition:

Plastics form a group of materials which are commonly obtained by synthesis of one or more chemicals to form a polymer (54). By definition, the molecules of a polymer are composed of a large number of linked, similar molecules. This definition can be narrowed further to cover only those polymers which flow plastically at one stage or another of their fabrication. They are organic substances and in general, have interesting physical and chemical properties. When pure, containing no filler, reinforcement or pigment, they are naturally of low specific gravity (between 0.9 - 1.6), transparent, easily colored, excellent insulators to a vast range of conditions and reagents.

Classification:

Plastics are usually divided into two groups. The thermosetting types set hard on polymerization. They do not soften again on re-heating, but only degrade and char. The thermoplastics, on the other hand, soften on re-heating without loss of quality.

In these materials, the long chain-like molecules lie side by side, although coiled randomly like a caterpillar. In thermosets,

cross linking takes place between the atoms of the molecules at right angle to the main axis of the molecules, as the arms and legs of the caterpillar grasp each other. Thus, a thermosetting material has internally fewer degrees of freedom and therefore, is more rigid than a thermoplastic. It is also less elastic and although, generally, it can support greater stresses, if deformed too far it will break its molecular and atomic bonds irretrievably, rather than yield plastically, and thus it will be liable to shatter under shock. The unique properties or combinations of attributes have widened the use of plastics in surgery in the past few years. The best application requires that the materials are only selected after full consultation between the surgeon, the engineer and material specialists.

Mechanical Properties of the Plastics:

The designer can confidently expect the plastics to compare in strength with such materials as natural fibers, textiles, leather and rubber and indeed, to be superior under certain conditions than are the naturally occurring. Strength varies simultaneously with such properties as temperature, chemical environment, molecular weight, structure and the condition of polymer, and the type of loading and in the case of hygroscopic polymer with humidity.

Chemical Properties of Plastics:

Plastics are extremely resistant to inorganic media, but are

sensitive to attacks in particular cases by organic materials to a greater degree than are metals. They are usually far more resistant to attack than most natural fibrous materials and rubbers, but like them, they suffer weakening by the photochemical action of strong sunlight unless protected by dense pigments or other such means. Water has some effect on plastics, although relatively little. It must be emphasized that some plastics absorb chemical compounds if stored for long periods in antiseptics (Fishburn, 1953) (55), and this hazard must be determined for each substance.

The Use of Plastics in Vascular Surgery:

The plastic prostheses have been utilized in vascular surgery in a solid and rigid form or in a pliable porous state. The former was complicated by the development of progressive thrombosis at the anastomotic site, leading frequently to complete occlusion or even to peripheral embolization. The solid prostheses have been generally abandoned except as a rigid prosthesis to carry the prosthetic aortic valve, as recommended by Hufnagel in 1955 (56) for aortic incompetence.

On the other hand, a variety of pliable prosthetic materials have been developed. The first used was Vinyon N cloth in 1952 (57). A variety of other plastic materials, notably nylon, orlon, terylene or dacron and teflon have been used in various forms. At present,

dacron and teflon fabric tubes are the generally accepted form of arterial prostheses.

The use of plastic adhesives is a separate subject which will form the second chapter of this monograph.

Hazards of Plastics:

The carcinogenic potential of the plastic materials has been discussed extensively in the medical literature. The occurrence of malignant tumors in relation to implants of plastics in rat and mouse has been reported. In most cases these tumors have been fibrosarcomas. In man, no malignant tumors have yet been reported in relation to implants made of plastic materials. Turner (1942) (58), found that a fibrosarcoma may develop at the site of implantation of a phenol formaldehyde (Bakelite) disc, 18 mm. in diameter, 1.5 mm. in thickness, implanted subcutaneously in Wistar rats. But he found no tumor when squares of the same material (Bakelite), 10 mm. by 10 mm. by 1.5 mm. were implanted subcutaneously in the abdominal wall of 10 DBA strain mice. Oppenheimer, Oppenheimer and Stout (1948) (39), reported that sarcomas occurred in relation to regenerated cellulose film (Cellophane) wrapped around the kidneys of Sherman strain rats to produce hypertension. They followed up this observation by implanting regenerated cellulose film (Visking 5 HS-Cellulose sausage casing) into two groups of 55 rats.

In one group the left kidney of each rat was wrapped with the film, in the other group a piece of film, 2 - 3 cm. square was embedded subcutaneously in the anterior wall of the abdomen, the film being kept flat by catgut sutures passed through the corner of the film. Twenty-three rats with wrapped kidneys and 42 with subcutaneous implants survived more than 11 months, and of these, 35% in each group developed sarcomas. In some cases the tumors were transplanted to fifth generation. Laskin, Robinson and Weimann (1954) (60), Druckery and Schmahl (1952) (61), Oppenheimer and his colleagues (1955) (62), and Nothdurft (1956) (63), have found that with the rat or mouse or both, malignant changes occur in the capsule surrounding polymeric implants. In Oppenheimer's experiments (62), malignant tumors were induced in Wistar and Sherman strain rats and in the mice of Longacres, Paris and C. 57 strain by subcutaneous implantation of small squares or circles of the film, approximately 15 mm. in width, of cellophane, dacron, polyethylene, polyvinyl chloride, celastic, pliofilm, nylon, polymethyl metacrylate, polysterene, saran, ivalon, KEL-F, teflon and silk. Some of these materials were commercial products and their chemical composition is not stated. The thickness of the film varied from 0.01 mm. to 0.4 mm. Theyinvestigated the possibility of breakdown of the polymer by including radioactive labelled material (C14). It was

found that C14 could be recovered in the urine following the implantation of the labelled polythene and labelled polymethyl metacrylate after 26 and 54 weeks respectively. When the films were removed, urinary radioactivity disappeared. Nothdurft (1956) (63) implanted a variety of materials subcutaneously in Wistar rats in the following forms:

1. Non-perforated discs, 17 mm. in diameter.
2. Perforated discs, 17 mm. in diameter; the perforation being carried out by means of a hand sewing machine.
3. Powder.

He used gold, silver, ivory, platinum, polystyrene, cellophane and polyvinyl chloride for implantation. Three hundred and ninety-five of the 517 rats in Group 1 (non-perforated discs), 117 of 235 rats in Group 2, and only one rat of 112 in Group 3, developed tumors. Stinson (1964) (64) implanted the discs of approximately 18, 12 and 4 mm. in diameter of polymethyl metacrylate in the gluteal muscles of guinea pigs and rats. After prolonged implantation, malignant tumors occurred in the rats in relation to the large (18 mm.) and medium (12 mm.) discs. The material used in the guinea pigs was without carcinogenic activity.

Nothdurft believes that it is the physical form of the implant which is the deciding factor and that the chemical nature of the

implant is largely unimportant. It is impossible to find a common chemical agent in all the different materials used in the various published reports. Both Oppenheimer and Nothdurft showed that the tumor develops in the layer of the cells immediately adjacent to the implants. Malignant changes usually occur more than a year following the implantation of materials. Nothdurft found the highest incidence of tumors in relation to non-perforated discs between 12 - 18 mm. in diameter. He believes that with a non-perforated disc a relatively avascular capsule develops and the metabolic changes in the cells adjacent to the implant eventually cause tumor formation. He further states that the powdered implants have a good blood supply and that they do not show the hyaline changes which are seen in fibrocytes adjacent to non-perforated discs (65).

If a non-perforated disc of a biologically inert material is implanted in the tissues of the rat, a fibrous capsule develops. If the implant is of a critical size, cells in certain parts of the capsule, particularly in the layer adjacent to the implant, may have a reduced blood supply. It has been postulated that possibly, over a period of time, disturbances of the cellular metabolism lead to tumor formation. The implant might thus be termed a physical carcinogen, since in itself it does not provide a chemical carcinogen. The concept that dimension in relation to the blood supply is a critical factor

might explain why such a variety of organic materials can result in tumor formation.

There is one important aspect of this whole problem. The majority of the work has been confined to rats and mice. It may well be that the reactions of rats and mice have little bearing on what may occur in other animals, including man, although this can be decided in the course of time. The plastic materials have been used in man only during the past 30 years, and it may be that 30 or 40 years will have to elapse before any tumor develops. The few tumors that have been reported in relation to metallic implants (66,67,68,69,70), which are alloys and not pure elements, indicate the necessity for prolonged observation of patients in whom prostheses of any type have been used.

Chapter II

THE USE OF METHYL-2-CYANOACRYLATE IN VASCULAR SURGERY

Introduction:

Rapidly polymerizing adhesives which produce strong bonds upon setting and are easily applied have been recently developed by industry. The ability of these plastic adhesives to cement tissue surfaces together have aroused the interest of a number of investigators who are currently exploring the usefulness of these materials in various surgical applications. One of these adhesives, methyl-2-cyanoacrylate (Eastman 910), has been successfully used in the repair of arteries and veins (71,72,73,74,75,76,77,78,79,80,81), skin (79, 82,83), intestine (79,84,85,86), bronchi (87), trachea (88), nerves (89), nephrotomy (90), ophthalmological surgery (91), and in repair of extremity transection (92). It has been used with success as an adjunct to suture in anastomosis of blood vessels (93) and of esophagus (94). Further experimental applications include the treatment of fracture of the mandible (95), sealing of cut lung surfaces (96,97,98), production of pulmonary hypertension (99), use as a substitute of dura matter (100), as a parasitic diagnostic technique in dermatology (101), and as a hemostatic agent (102,103, 104, 105).

A. PROPERTIES OF METHYL-2-CYANOACRYLATE

Chemical Structure:

The monomer of methyl-2-cyanoacrylate is produced by condensing formaldehyde with an alkyl cyanoacetate in the presence of a basic catalyst to yield first a polyl (Alkyl Cyanoacrylate), the depolymerization of which yields the alkyl-2-cyanoacrylate. A thickening agent (to increase viscosity), a plasticizer (to prevent embrittlement) and an inhibitor (stabilizing agent) are added to give it viscosity and to overcome embrittlement of the bond during aging. The material forms strong, rapidly setting bonds with a wide range of adherent combinations. The bonding occurs through a mechanism of anionic polymerisation, catalysed by traces of water or other weak bases present on the surfaces to be bonded. The adhesive acts by its molecular attraction with smooth, dense surfaces (specific adhesion), and by the interlocking of set adhesive on irregular or porous surfaces (mechanical adhesion). The polymerized material can withstand temperature up to 165^{o}C., is resistant to chemicals except for mild weakening in acid, alkali and humid environment.

Toxicity of Methyl-2-Cyanoacrylate:

The effect of undiluted unpolymerized material was tested on rats, both by mouth and intraperitoneal injection. As was expected, the material became polymerized and solid upon injection. The

material was practically devoid of physiological actions other than those contributed to the mechanical action of the plastic which is formed under these circumstances. The ground polymerized material was suspended in corn oil and then administered as a suspension to rats by mouth and intraperitoneally. In this case the lethal dose was greater than 6400 mgm./kg. by mouth, and about 800 mgm./kg. by intraperitoneal injection. This would place the compound in the class of relatively non-toxic material as far as general toxicity is concerned.

Behavior of Methyl-2-Cyanoacrylate in Animal Tissues:

Fasset (107) applied a 10% solution of the monomer in acetone and olive oil to the depilated skin of the guinea pigs for a period of 24 hours. Doses up to 20 cc./kg. caused only very slight evidence of skin irritation. Further experiments revealed that the material could not be considered a potent skin sensitizer in guinea pigs.

Since it is slightly irritant to the eyes and nose, Fasset exposed rats to a vapor saturated by the material. Concentrations as high as 7.6 mgm./l. were obtained (1674 part/million). Three rats were exposed to this concentration for a period of six hours with no mortality. There was, however, evidence of nasal and upper respiratory irritation.

Subcutaneous injection of material by Fasset caused a

temporary foreign body reaction with subsequent diminution of cellular reaction. intense fibrosis did not result. Experience in our laboratory in dogs and rabbits corroborates the absence of excessive reaction of tissue.

Sterility of Methyl-2-Cyanoacrylate:

Cultures of the monomer of methyl-2-cyanoacrylate taken directly from original container have been sterile. Awe et al (103) showed that no growth was obtained in any of the media inoculated with the polymerised adhesive. Cultures of the adhesive in thioglycolate were all sterile. In the inhibition test they found that the adhesive inhibits the growth of all inoculated organisms tested. The degrees of inhibition of various organisms indicated by the size of the clear zone surrounding the drop of adhesive.

The researchers in the Microbiology Department of the Ethicon Company (108) intentionally contaminated specimens of methyl-2-cyanoacrylate monomer with a variety of spore formers which could be recovered after incubation periods up to 60 days. They found that one of these spore formers was not killed by the monomer and viable spores were incubated from specimens after periods of 7, 14, 21 and 60 days.

B. THE USE OF EASTMAN 910 IN NORMAL VESSELS

Materials and Methods:

Seventy-one procedures were performed on the aortas and femoral arteries of 42 mongrel dogs weighing 7 - 18 kg., anesthetized with pentobarbital 25 - 30 mgm./kg. The operations were performed under sterile conditions and the dogs were given penicillin and streptomycin during the immediate postoperative period. The femoral pulses were checked daily. The long-term survivors were housed in a dog farm in the country.

The bonding agent was applied to the exposed arteries directly from the polyethylene container, care being taken to avoid spillage into the lumen of the vessel and into the surrounding tissues.

a) Linear incision.

The femoral artery or aorta was occluded by arterial clamps proximal and distal to the site of arteriotomy and was denuded of adventitious tissue. A longitudinal incision was made 1 - 2 cm. in length. The lumen of the artery between the clamps was irrigated with Heparin-saline solution. The vessel was then elevated on a flat surface (knife handle) in such a manner that the edges of the incision were closely approximated. The vessel was sponged dry and one or two drops of plastic were placed on the surface of the vessel at the incision. A previously prepared patch (mersilene or

autogenous fascia) was used to cover the incision. It was held in place by finger pressure for one to two minutes. Then the clamps were removed.

b) Transection of the femoral artery.

The artery was clamped proximal and distal to the site of transection and a polyethylene tube was introduced into the vessel through an arteriotomy. The artery was transected around the polyethylene tube. The two ends of the artery were closely approximated over the tube. Two drops of plastic were placed on the incision line and it was wrapped with mersilene or fascia. The polyethylene tube was removed, the lumen of the artery was irrigated with Heparin-saline and the site of introduction of the tube was closed with 6-0 silk. Occluding clamps were then removed.

c) Defect of the arterial wall.

A defect of the arterial wall measuring approximately 10 mm. by 1.2 mm. was created in three femoral arteries, and these were patched using Eastman 910 by utilizing the same technique as for the closure of transection of the femoral artery.

d) Arteriotomy without closure.

The continuity following an arteriotomy may be re-established during the normal healing process, without closing the arterial defect (109,110). Accordingly, it was thought necessary to include a

small group of dogs in whom the femoral artery was incised and nothing further was done to the artery. The fascia and skin were closed as usual.

In the long-term survivors, arteriograms were performed prior to sacrifice. Hypaque (R) was injected through a polyethylene tube inserted through one femoral artery and roentgenograms were taken.

Results.

The results obtained in the various groups are summarized in Table I.

The four dogs which had an incision of the artery without an attempt at closure bled profusely and did not recover from the anesthesia. In the three dogs in which a longitudinal arteriotomy was closed with Eastman 910 alone, a delayed hemorrhage occurred on the 3nd and 5th postoperative day.

In the 16 dogs with a patched linear incision of the aorta, a hemorrhage occurred in two animals on the 7th and 14th postoperative day respectively. The others were sacrificed after intervals of 3 days to 7 months. In all cases the vessels were found to be patent.

Of 21 dogs in which the linear incision in the femoral artery was closed with plastic and patching as described, two bled 11

SUMMARY OF RESULTS OBTAINED IN VARIOUS GROUPS

Technique	No.	Complications: Hemorrhage	Complications: Thrombus	Remarks
Linear incision without closure of femoral artery	4	4 (extensive)		
Linear incision of femoral artery closed with bonding agent alone	3	3 (3-5 days postoperative)		
Linear incision of aorta closed with bonding agent and patching	16	2 (7-14 days postoperative)		14 were sacrificed 3 days - 7 months postoperatively. All vessels patent
Linear incision of femoral artery closed with patching and bonding agent	21	2 (11-12 days postoperative)		19 were sacrificed 3 days - 22 months postoperatively. All vessels patent
Linear incision of femoral artery closed with 6-0 silk	12			12 were sacrificed 8 days - 8 months postoperatively. All vessels patent
Transection of femoral aorta closed with bonding agent and wrapped with mersilene or fascia	12	3 (8-13 days postoperative)	1 (15 days postop.	9 were sacrificed 28 days - 12.5 mo. postoperatively. All vessels patent
Femoral defect closed with bonding agent and patching	3	1 (8 days postoperative)		2 were sacrificed 3 - 6.5 months postoperatively. Both vessels patent

and 12 days postoperatively, and the rest were sacrificed four days to 22 months postoperatively. All vessels were patent. In 12 of these dogs an identical incision had been made in both femoral arteries, one side was closed with a patch and the bonding agent as described, the other side was closed with a continuous suture of 6-0 silk. No postoperative bleeding or thrombosis occurred in this group and the animals were sacrificed four days to eight months after the procedure. All vessels were patent.

Following transection of the femoral artery and repair by Eastman 910 on 12 dogs, there were three instances of hemorrhage on the 9th to 13th day, and one thrombosis on the 15th day. The other nine animals were sacrificed after one to 13 months. Again, all these vessels were patent.

One of the three dogs with a patched defect of the femoral artery bled eight days postoperatively, and the other two were sacrificed three and six and one half months respectively following surgery. The arteries were patent, and the patches on gross and microscopic examination appeared to be satisfactory.

Discussion

In the evaluation of the results, particular attention was paid to the failures. Although the procedures were carried out with aseptic technique, gross infection at the operative site occurred in some of the

dogs. If the infection progressed to the formation of an abscess, a massive hemorrhage occurred seven to 14 days after the operation. In the presence of local edema and redness of the skin only, there were no failures.

Two of the delayed hemorrhages occurred without abscess formation. One dog with a patch over a linear incision of the femoral artery, was involved in a fight with another dog on the seventh post-operative day, resulting in severe and fatal bleeding. The other dog with a patch of fascia over an incision in the aorta, developed a false aneurysm which ruptured on the 14th day.

The high failure rate associated with gross infection indicated that chance of successful bonding is unlikely in an infected field.

No definite information was obtained regarding the fate of the bonding agent. In contrast to other plastic materials there was no evidence of double refractility and no specific tinctorial method could be evolved. The presence of Eastman 910 is suggested in the histological slides taken from specimens up to four months after the experiment. After that time it could not be demonstrated, although the presence of small amounts cannot be excluded. The mersilene could easily be seen, especially under polarizing illumination, and no change in the appearance was noticed in the long-term survivors.

In some of the dogs sacrificed within two weeks after the

experiment, varying minor degrees of intramural thrombus and intimal inflammation could be found at the operative site. In some of the specimens taken two months or longer following experimental surgery, the thrombus appeared to be organized and incorporated into the intima causing subintimal fibrosis.

In the animals sacrificed after an interval or two months or longer, there was a great variation in the amount of scar tissue present in the media and in the intima. In some specimens the original defect could not be identified at all, while in others, a separation of the elastic fibers was evident. In a few instances, thickening of the arterial wall at the site of the scar formation could be demonstrated. The amount of scarring appeared to be related to the efficiency and accuracy of the repair, rather than to the particular technique used. No definitive differences between mersilene patch and fascia patch were evident.

No definite conclusions could be drawn based on a comparison of the results obtained in the group of dogs in which one femoral artery was sutured, whereas a similar incision on the contralateral side was closed with bonding agent and patch. There appeared to be a higher degree of scar formation and tissue disorganization on the side which was sutured. The persistence of the suture material as contrasted to the apparent disappearance of the bonding agent is of

interest.

In this series of experiments, longitudinal incisions and transections of arteries were performed. Villegas et al (119), have shown that the stresses exerted on longitudinal incisions exceed those exerted on transverse incisions and accordingly the repair of a longitudinal incision would appear to be an adequate test for a method of arterial repair.

C. THE USE OF METHYL-2-CYANOACRYLATE IN ATHEROSCLEROTIC VESSELS

Introduction:

In 1904, Marchand (113) coined the term "Atherosclerosis" to designate the type of intimal arteriosclerosis due to amorphous lipid accumulation in the intima. The prefix "Athero" (Greek athre - meaning mush), was selected to designate the lipid accumulation in intima which is the hallmark of the developed lesion. At that time atherosclerosis had not yet been produced experimentally in any animal species. Experimental attempts with adrenaline, digitalis, barium chloride, pathogenic bacteria and other agents had produced arterial lesions, but not atherosclerosis. The changes in animal vessels resembled rather the Monckeberg type of arteriosclerosis (medial calcinosis, senile arteriosclerosis) of man (114, 115).

Experimental atherosclerosis was first produced by Ignat-

owsky (116) and Saltykow (117), by feeding rabbits a diet composed of meat, milk and eggs. In this feeding, it was not clear exactly what dietary factor was responsible for the production of the lesion. Stukkeu (118) and Wesselkin (119), soon demonstrated that only cholesterol containing foods were atherogenic. Anitschkow (120), Wacker and Hueck (121) induced typical lesions by giving rabbits pure cholesterol in oil. Early reviews of this pioneering work were assembled by Dewey (122), Bailey (123), Chuma (124) and Schonheimer (125).

The anatomical lesions in rabbits appear to be primarily due to the deposition of cholesterol within the intima of the blood vessels, and it would seem that these deposits are derived mainly from the circulating blood plasma and no antecedent endothelial damage is necessary.

Materials and Methods

Sixteen young male New Zealand albino rabbits were maintained with commercial rabbit chow food, enriched with 0.5 gm. of cholesterol per day for a period of four months. The serum cholesterol was determined at the commencement of the experiment and at 45 and 90 days following the start of the high cholesterol diet. The mean cholesterol level of serum rose from 36 mg./100 cc. to 485 mg./100 cc. The method of cholesterol determination was a modi-

fied Schonheimer technique adapted for use with 50 microliters of serum.

Two of these rabbits died 95 and 100 days respectively following the start of the diet. The remainder were subjected to surgery. They were anesthetized with pentobarbital, 30-40 mg./kg. The operation was performed under sterile conditions. The aortas were exposed through a midline incision. The diameter of the aortas was approximately 2 mm. Atherosclerotic plaques with various degrees of intensity could be observed. Each aorta was occluded by two bulldog clamps, proximal and distal to the site of the arteriotomy. It was then denuded from adventitious tissue. A longitudinal incision was made, about 5 - 6 mm. in length. The lumen of the aorta between the clamps was irrigated with Heparin-saline solution. The aorta was then elevated on the handle of a knife in such a manner that the edges of the incision were in close approximation. The aorta was then sponged dry and one or two drops of plastic were placed on the surface of the vessel at the incision line. A previously prepared piece of autogenous fascia was used to cover the incision and held in place with finger pressure. After two minutes the clamps were removed.

Results and Conclusions:

Two of the 14 rabbits died due to anesthesia. The rest of

them were sacrificed 48 hours to three and one half months post-operatively.

Grossly, there were marked atheromatous lesions in all the aortas. The atheromatous plaques were occasionally seen to involve the whole circumference of the aorta, but generally they involved only part of the vessel. There was no evidence of thrombosis at the operative site.

Microscopically, there was a great variation in the amount of scar tissue present in the media and intima. In some, the site of incision could hardly be identified, but in others a separation of the media was evident.

In atheromatous plaques, there were changes in subendothelial tissue, characterized by an increase in the intimal ground substances and the appearance of fine fat droplets in these foci. There was also proliferation of the connective tissue in these foci, usually most abundantly over the luminal aspect of the atheroma. The center of the plaques contained granular acidophilic, lipid-rich debris and crystalized, needle-like spicules of cholesterol.

Chapter III

THE USE OF THE VOGELFANGER STAPLING CLAMP IN VASCULAR SURGERY

Introduction:

A method based on the principle of application of a metallic suture with the help of a semi-automatic stapling device was independently described by Russian (126), Canadian (52, 53, 127), Japanese (128) and American (92, 129) workers. The prototype of the Canadian vascular stapler was developed in 1956 as a result of the combined efforts of Vogelfanger et al and the National Research Council of Canada. The original instrument was designed for the anastomosis of vessels ranging from 6 - 8 mm. in diameter, but since that time it has constantly been revised and after four modifications, it is now possible to anastomose vessels 2 - 5 mm. in diameter (Mark 4); the Mark 5 instrument being able to anastomose vessels 1 - 2 mm. in diameter.

Description of the Instrument:

The apparatus is composed of: (i) two hemostatic clamps, (ii) two universal handles, (iii) a series of paired bushings, (iv) a series of calibrated forks for the measurement of the external diameter of the vessels, and (v) an everter, a series of pins and rubber rings.

The key components of the instruments are the bushings which are of two types. The so-called 'stapling bushing' consists of a cylindrical member with circumferential grooves in which tiny U-shaped tantalum staples are located. The corresponding 'anvil bushing' has appropriately-shaped molding surfaces, against which the staples are driven and suitably bent in the form of a letter 'B'. The bushings are available in diameter of 1-5 mm. and are graded in steps of 0.25 mm. in those below 2 mm. (Mark 5), and in steps of 0.5 mm. in the larger size (Mark 4). These sizes are those of the pitch diameter of the staple slots corresponding to the external diameter of the vessel; thus, the bore of the bushing is smaller in diameter than the normal size of the vessel to which it is applied. Each bushing is split longitudinally into two segments, the end of which has a small lip to facilitate the retention of the blood vessel in place after eversion. Retention of the vessel end or cuff is effected by a ring of a soft, elastic material, e.g. rubber of suitable size, slipped over the everted vessel and bushing.

Handles, to which the bushings are fitted, are spring loaded and normally return to the closed position. The staple driving handle has a lever which, when pulled towards the back of the instrument, causes the staples to be driven out. There is another lever for approximation of the handles.

The hemostatic clamps used with this instrument are secured to the handles, and when the handles are opened the clamps are released. The staples are of the tantalum wire, 0.005 and 0.0045 inches in diameter, those for Mark 5 being 0.0025 inches.

Calibrated forks with notches in steps of 0.25 mm. are used for the measurement of the external diameter of the vessel. These gauges are not applied to the vessels but positioned adjacent to them, and sizes are compared by eye in order to prevent the spasm of the vessel.

The everting tool is comprised of a range of pins and matching cylindrical pieces, specially shaped rubber washers and a handle whereby the pin is spring mounted, permitting relative movement between the pin and cylinder when pressure is applied to the handle. The rubber washing mounted on the pin is then pushed over the blood vessel and the bushing.

A. THE USE OF STAPLERS IN NORMAL ARTERIES AND VEINS

Materials and Methods:

Sixty procedures were performed on the femoral arteries and veins of 23 mongrel dogs weighing 7 - 14 kg., anesthetized with pentobarbital, 25 - 30 mgm./kg. The surgery was performed under sterile conditions and the dogs were given antibiotics during the

immediate post-operative period. The femoral arteries were checked daily. The long term survivals were kept in a dog farm in the country.

The vessels were exposed and the following steps were taken:

1. The size of the vessel was measured. If the vessel was an even or half a millimeter in size, the same size of bushing was selected. If the vessel was not of a size corresponding to any of the bushings, the next size smaller bushing was used. This gave slight reduction to the size of the vessel at the line of the anastomosis, but eversion over a large bushing would be much more difficult.
2. The vessel was then denuded of adventitious tissue.
3. The bushings were fitted to the handles. (Great care was taken when fitting the bushings to avoid the application of levering action between the bushing and the housing by rocking the bushing holder. Such action may cause distortion or damage).
4. The corresponding size component (pin and rubber ring of everter) were selected.
5. The hemostatic clamps were then applied in such a manner that securing pins faced each other. The clamps were sufficiently wide apart to provide for the width of the instrument with bushings, plus the length of vessell required to turn the cuff.
6. The vessel was transected midway between the clamps and was

irrigated with saline-Heparin solution.

7. After making sure that the approximater lever was fully retracted (rearmost position), the staple driving half of the instrument was opened by squeezing the handle and was passed over the vessel which was steadied by means of the hemostatic clamp. The pressure was slowly released on the handle, making sure that the vessel was not nipped between the halves of the bushing.

8. The handle was then permitted to slide along the vessel to the hemostatic clamp. The clamp was pressed, locking the pin into the housing in the handle.

9. The vessel was then everted over the bushing, using the everter. (The rubber ring remained on the bushing to hold the cuff in place).

10. A similar procedure was then followed in regard to the application of the second handle to the other end of the vessel.

11. The two halves of the instrument were then brought together so that the cam of the anvil handle fitted into the recess of the staple driving handle; then the approximator lever was allowed to slide toward the bushings which caused the two halves to be drawn together.

12. The staples were driven by pulling gently but firmly on the staple driving lever towards the end of the instrument. The turning of the staple could usually be detected by the change in pressure

or by an audible click. Excessive pressure on the lever may damage the staple driving bushing.

13. The rubber rings were removed by stretching and cutting with scissors.

14. Then the cuff was turned from the staple driving bushing, back on the anvil bushing by pushing it gently with forceps. The approximator was retracted and the handle on the staple driving side of the instrument was removed. The double cuff, which was on the anvil side was then turned back onto the vessel on the other side of the suture, and the other handle was removed.

15. The hemostatic clamps were then removed (distal first). There was occasionally slight oozing following removal of vascular clamp, which could be controlled by application of gentle pressure.

The diameter of the arteries ranged from 2 - 3 1/2 mm. in diameter and those of the veins from 2 1/2 - 4 1/2 mm. in diameter. The average time for performance of anastomosis was between 3 and 5 minutes.

Results:

The dogs were sacrificed three weeks to six months post-operatively. Of 42 anastomosed femoral arteries, two developed thrombosis, three had narrowing at the site of anastomosis and the rest were patent without any evidence of narrowing or thrombosis.

All of the 18 anastomosed femoral veins were patent without any evidence of thrombosis.

Microscopically, the healing was complete with minimal scar formation. In one of the two thrombotic vessels, the thrombus was proximal to the line of anastomosis.

Discussion:

It should be stressed that the measurement of the vessels must be undertaken at the earliest point in the dissection and with minimal trauma to the vessels. If this precaution is ignored, the resulting spasm leads to a grossly inaccurate estimate of the diameter and consequently, may cause a permanent stenosis at the suture line, especially in small, muscular arteries. On the other hand, if the vessel is stretched to fit the appropriate bushing and is sutured with a roundly curved, everting mattress suture in a perfect circle with appropriate intersuture spaces, and with no foreign materials exposed in the lumen, it will create an ideal junction to ensure patency.

We anticipated many difficulties in the anastomosis of the small veins. However, the venous anastomoses were easier to perform and we were gratified with the results.

B. THE USE OF A STAPLER IN THE ATHEROSCLEROTIC AORTA

Materials and Methods:

Twenty-four young male, New Zealand albino rabbits were

divided into two groups: Group 1 consisted of 19 rabbits weighing 1500 - 2500 gms. and these were maintained on commercial rabbit chow food, enriched with one gram of cholesterol powder dissolved in cotton oil, per day. Group 2 consisted of five rabbits, maintained on the same diet but without cholesterol. Both groups were kept on this diet for 120 days.

The serum cholesterol was determined at the commencement of the experiment and at 30, 70 and 110 days following the start of the diet. The method of cholesterol determination was a modified Schonheimer technique adapted for use with 50 microliters of serum.

The mean cholesterol level of Group 1 rose from 51 mgr. /100 cc. to 2102 mgr./100 cc. of serum. That of Group 2 changed from 54 mgr./100 cc. to 57 mgr./100 cc.

Seven rabbits of Group 1 died four months following the start of the diet. The remainder were subjected to surgery. They were anesthetized with pentobarbital, 30-40 mgr./kg. The operation was performed under sterile conditions. The aorta was exposed through a midline incision. The diameter of the aorta was approximately 2 mm. Atherosclerotic plaques of various sizes could be observed in the aortas. Then an end-to-end anastomosis was done in the aorta utilizing the stapler clamp as described previously. The average time of clamping the aorta was about four to five minutes. All the Group 2

rabbits were sacrificed after four months. Their aortas were removed and opened. As well, the aortas of seven rabbits in Group 1, who had died prior to surgery, were removed and opened.

Results and Discussion:

The aortas of Group 2 rabbits were normal, without any evidence of atherosclerotic plaques, grossly or microscopically.

The 12 rabbits in Group 1, who had end-to-end anastomosis of the aorta, were sacrificed after intervals of two days to eight months post-operatively. All vessels were patent without any evidence of thrombosis.

Grossly, there were marked atheromatous lesions in all the aortas; the plaques occasionally involved the whole circumference of the aorta. The distribution of these atheromas was characteristically patchy and focal, and with particular predilection for points of maximal stress. Thus, the posterior wall of the aorta fixed to the prevertebral tissue, was more severely affected than the anterior and lateral walls. Some of the atheromas appeared as a fine, flat, flecking or streaking of the intima, from 2-4 mm. in diameter. In others, the yellow softness was replaced by a firmer, pale grey-white to yellow tissue, resulting in irregular narrowing of the lumen. In addition, small, elevated, pinhead-like nodules could be seen, particularly adjacent to the orifices of the aortic branches.

The healing of the anastomotic site was complete without any evidence of thrombosis or stricture.

Buck (130) and Parker (131) had demonstrated in their electron microscope studies, that the intima of the rabbit coronary and femoral artery consists solely of endothelial cells. The aortic intima was also found in their studies to be composed solely of a single layer of endothelial cells living directly upon the first elastic lamina, as Duff (132) had earlier observed. Frequently, even this single layer of cells was not observed.

Microscopically, the cholesterol-induced lesions in the aortas exhibited a variable appearance, depending on their stage of development and severity. Early lesions consisted of accumulations of large foam cells. These foam cells varied in amount from a single layer of cells to several layers. Oil red O staining demonstrated fatty material in abundance within the subendothelial foam cells. Under polarizing illumination, refractile, rod-like cholesterol crystals were seen filling these cells. At this stage there was no change in media and adventitia. These early lesions, which are called by Katz 'pure atheromas' (114), are apparently the initial lesions of cholesterol-induced atherosclerosis.

In some advanced lesions, fatty material could be seen in the media adjacent to the involved intima. The splitting of the

elastica could be demonstrated in some of the specimens.

There was some variation in the amount of scar tissue present at the site of anastomosis, but it was generally minimal.

DISCUSSION

It is obvious that the techniques described will not be expected to replace the conventional suturing methods in the foreseeable future.

In the field of small vessel anastomosis, the mechanical stapling device combines advantages of speed and high precision and eliminates much of the trauma associated with the usual surgical manipulation. Beattie and his group (133) found that it facilitated extensive organ transplantation procedures. Carrol (134) has recently described the anastomosis of internal mammary artery to circumflex coronary artery in less than two minutes. We successfully performed kidney and spleen transplantations within 10 to 12 minutes. This shortening of operative time may be extremely significant in the instances of mass casualties. Our 90% long term patency of femoral artery anastomoses and 100% success in femoral veins and atherosclerotic aortas of rabbits, were indeed gratifying. Unlike Vogelfanger (52), we irrigated the lumen of our transected vessels with Heparin-saline solution. The atherosclerotic vessels presented some technical difficulties during the eversion of the vessels. Accurate measurement, proper choice of bushing and gentle handling, contributed to smooth eversion. Increased familiarity with the instrument

helped us solve this problem, as well as any problems associated with working in deep wounds.

Our techniques for the repair of linear incision and transection of the arteries, using methyl-2-cyanoacrylate, were rather crude. Further progress in this field will depend on the development of the proper instruments, such as the one used by Healey and his group (76), which ensures proper intimal apposition of the ends of the transected vessels, and also prevents the spillage of adhesive into the lumen of the vessel. We could not reach any definitive conclusion as to the superiority of the non-suture anastomosis of vessels, using adhesive, in relation to the conventional suture technique. There was, however, less tissue disorganization in the glued vessels. The apparent disappearance of the adhesive is of great interest in a long follow-up of this kind of comparative study. We believe that, at present, the main use of adhesive is as an ancillary to suture and stapling techniques, as well as a hemostatic agent in cardiovascular surgery. The high failure rate associated with gross infection indicated that the chance of successful bonding is unlikely in an infected field.

SUMMARY

An experimental study has been carried out to investigate the use of a bonding agent (Methyl-2-cyanoacrylate) and a special metal stapling device (Vogelfanger stapler) in the surgery of normal and atherosclerotic vessels. It is anticipated that both of these methods will find a place in the armamenture of vascular surgeons, especially when speed is essential.

BIBLIOGRAPHY

1. Hopfner, E.: Arch. Klin. Chir., 71:417, 1903.

2. Murphy: Resection of arteries and veins injured in continuity, end to end suture. Medical Record, 1073, 1897.

3. Rob, C.G., Eastcott, H.H.G., and Owen, K.: The reconstruction of arteries. Brit. J. Surg., 43:499, 1955-1956.

4. Carrel, A.: The surgery of the blood vessels. Bull. Johns Hopk. Hosp., 18:18, 1907.

5. Dos Santos, R., Lamos, C., and Caldas, P.J.: L'arteriographie des membres de l'aorte et de ses branches abdominales. Med. Contempt. (Lisbon), 47:93, 1929.

6. Nelson, O.A.: Arteriography of abdominal organs by aortic injection. Surg. Gynec. & Obst., 74:655, 1942.

7. Doss, A.K., Thomas, H.C., and Bond, T.B.: Renal arteriography: its clinical value. Texas State J. Med., 388:277, 1942.

8. Doss, A.K.: Translumbar aortography: an apparatus for injecting the radiopaque media. Surgery, 16:42, 1944.

9. Wagner, F.B. Jr.: Arteriography in renal diagnosis, preliminary report and critical evaluation. J. Urol. 56:623, 1946.

10. Murray, G.: Heparine in surgical treatment of the blood vessels. Arch. Surg., 40:307, 1940.

11. Blakemore, A.H., and Lord, J.W. Jr.: Nonsuture method of blood vessel anastomosis, experimental and clinical study. J.A.M.A., 127:655, 748, 1945.

12. DeBakey, M.E., and Simeone, F.A.: Battle injuries of arteries in World War II: Analysis of 2471 cases. Ann. Surg., 123:534, 1946.

13. Ross, C.A., Hess, O.W., and Welch, C.S.: Vascular injuries of extremities in battle casualties. Ann. Surg., 123:161, 1946.

14. Stewart, C.F.: War experiences with nonsuture technic of anastomosis in primary arterial injuries. Ann. Surg., 125: 157, 1947.

15. Swenson, O., and Gross, R.E.: Absorbable fibrin tubes for vein anastomoses. Surgery 22:127, 1947.

16. Johns, T.N.P.: Comparison of suture and nonsuture methods for anastomosis of veins. Surg. Gynec. & Obst., 24:79, 1948.

17. Jones, T., and Dale, W.A.: Study of peripheral autogenous vein grafts. Arch. Surg., 76:294, 1958.

18. Linton, R.R.: Peripheral vascular disease. New Eng. J. Med., 240:645, 1949.

19. Linton, R.R.: Peripheral vascular diseases. New Eng. J. Med., 260:272, 322 and 370. 1959.

20. Kunlin, J.: Le traitement de l'ischemie arteretique par la greffe veineuse longue. Rev. Chir., 70:206, 1951.

21. Dye, W.S., Grove, W.J., Olwin, J.H., and Julian, O.C.: Two to four years behavior of vein grafts in lower extremities. Arch. Surg., 72:64, 1956.

22. Inhara, T., Menendez, C.V., Shaw, R.S., and Linton, R.R.: Frozen irradiated heterografts. Surgery 42:705, 1957.

23. Rosenberg, N., Henderson, J., Lord, G.H., Gaugharn, E.R.L., and Douglas, J.F.: Use of enzyme-digested heterografts as segmental arterial substitute. Arch. Surg.,76:275, 1958.

24. Kehne, J.H., and Sensenig, D.M.: Arterial replacement with rectus fascia. Arch. Surg., 72:516, 1956.

25. Wagner, M., Benjamin, H.B., Zeit, W., and Kusma, J.F.: Autoplastic cutis vascular graft. Arch. Surg.77:652, 1958.

26. Kittle, C.F., and Taquechel, C.: Preliminary investigation of dermal heterografts (leather) as prostheses for vascular defects. Arch. Surg., 72:69, 1956.

27. Lary, B.G., Meine, E.L., Jr., and deTakats, G.: Experimental use of steel mesh tubes for replacement of the arterial segment. Arch. Surg., 72:69, 1956.

28. Hardin, C.A.: Orlon and nylon prosthesis for abdominal aneurysms and a five years observation on experimental homografts. Ann. Surg., 146:78, 1957.

29. Cockett, F.B., and Norman, A.G.: Late result of direct surgery of aortic bifurcation and its major branches. Brit. Med. J., 1:727, 1958.

30. Szilagyi, D.E., France, L.C., Smith, R.F., and Whitcomb, J.H.: Clinical use of elastic dacron prosthesis. Arch. Surg., 77:538, 1958.

31. Merendino, K.A., Girvin, G.W., and Thomas, G.I.: Clinical use of teflon tubes as vascular substitute for major arteries. Surgery, 43:959, 1958.

32. Shaw, R.S.: Reconstructive vascular surgery. New Eng. J. Med., 266:339, 392, 1962.

33. Harrison, J.H., and Davalos, P.A.: Influence of porosity on synthetic grafts: fate in animals. Arch. Surg., 82:8, 1961.

34. Phillips, C.E., De Weese, J.A., and Campeti, F.L.: Comparison of peripheral arterial grafts: Experimental observation of hemodynamic changes using cineangiography. Arch. Surg., 82:38, 1961.

35. Harrison, J.H.: Synthetic materials as vascular prostheses. III. Long term studies of grafts of nylon, dacron, orlon and teflon replacing large blood vessels. Surg. Gynec. & Obst., 108:433, 1959.

36. Smith, R.F., and Szilagyi, D.E.: Healing complications with plastic arterial implants. Arch. Surg., 82:14, 1961.

37. Britt, C.I., Miller, E.M. Jr., Felder, M.E., and Sirak, H.D.: Comparative reaction of mersilene and silk suture implanted within heart. Ann. Surg., 153:52, 1961.

38. Dettinger, G.B., and Bowers, W.F.: Tissue response to orlon and dacron sutures: Comparison with nylon, cotton and silk. Surgery, 42:325, 1957.

39. Harrison, J.H.: Synthetic materials as vascular prostheses. I. Comparative study in small vessels of nylon, dacron, orlon, ivalon sponge and teflon. Amer. J. Surg., 95:3, 1958.

40. Harrison, J.H.: II. Comparative study in small vessels of nylon, dacron, orlon, ivalon sponge and teflon in large blood vessels with tensile strength studies. Am. J. Surg.,95:16, 1958.

41. Brown, R.B., Koth, D.R., Urschel, H.C. Jr., and Roth, E.G.: Further studies of small vessel anastomosis and replacement in dogs. I. Plastic prostheses. II. Unidentifiable host variable affecting results. Surgery, 47:987, 1960.

42. Schumacker, H.B. Jr., and Lowenberg, R.I.: Experimental studies in vascular repair. Surgery, 24:79, 1948.

43. Hurwitt, E.S., Altman, S., Borow, M., and Rosenblatt, M.: Intra-abdominal anastomoses. Surgery, 34:1043, 1953.

44. Thal, A., Perry, J.F., Miller, F.M., and Wangesteen, O.H.: Direct suture anastomosis of the coronary arteries in the dog. Surgery, 40:1023, 1956.

45. Urschel, H.C., and Roth, E.J.: Small arterial anastomosis. II. Suture. Ann. Surg., 153:611, 1961.

46. Seidenberg, B., Hurwitt, E.S., and Carton, C.A.: The technique of anastomosing the small arteries. Surg. Gynec. & Obst., 106:743, 1958.

47. Jacobson, J.H., and Suarez, E.L.: Microsurgery in anastomosis of small vessels. Surg. Forum, 11:236, 1960.

48. Carter, E.L., and Roth, E.J.: Direct non-suture coronary artery anastomosis in the dog. Ann. Surg., 148:212, 1958.

49. Rohman, M., Goetz, R.H., and Dee, R.: Double coronary artery - internal mammary artery anastomosis, tantalum ring technique. Surg. Forum, XI: 236, 1960.

50. Holt, G.P., and Lewis, F J.: A new technique for end to end anastomosis of small arteries. Surg. Forum, 11:242, 1960.

51. Urschel, H.C. Jr., and Roth, E.J.: Small arterial anastomosis. I. Non suture. Ann. Surg., 153:699, 1961.

52. Vogelfanger, I.J., Beattie, W.G., Brown, F.N., Devitt, J.E., Scobie, T.K., and Scobie, D.H.: The problem of small vessel anastomosis. Surgery, 52:354, 1962.

53. Vogelfanger, I.J., and Beattie, W.G.: A concept of automation in vascular surgery: A preliminary report on a mechanical instrument for arterial anastomosis. Canadian J. Surg., 1: 262, 1957.

54. Keenaway, A.: General Introduction ot Plastic. Modern Trends in Surgical Material. Butterworth & Co., 43, 1958.

55. Fishburn, A.G.: Symposium: Products containing plastics. British Pharmaceutical Conference, 1955.

56. Hufnagel, C.A.: The use of rigid and flexible prostheses for arterial replacement. Surgery, 37:165, 1955.

57. Voorhees, A.B., Jarentzki, A.H., and Blakemore, A.H.: The use of tubes constructed from Vinyon 'N' Cloth in bridging arterial defects. Ann. Surg., 135:332, 1952.

58. Turner, F.C.: Sarcomas at sites of subcutaneously implanted Bakelite discs in rats. J. Nat. Cancer Inst., 3:81, (1941-1943).

59. Oppenheimer, B.S., Oppenheimer, E.T., and Stout, A.P.: Sarcomas induced in rats by implanting cellophane. Proc. Soc. Exp. Biol., N.Y., 67:33, 1948.

60. Laskin, D.M., Robinson, I.B., and Weinmann, J.P.: Experimental production of sarcomas by methyl-metacrylate. Proc. Soc. Exp. Biol., N.Y., 87:329, 1954.

61. Druckrey, H., and Schmahl, D.: Fschr. Naturforscher, 76:353, 1952.

62. Oppenheimer, B.S., Oppenheimer, E.T., Stout, A.P., Danishefsky, I., and Eirich, F.R.: Further studies of polymers as carcinogenic agents in animals. Cancer Res., 15: 333, 1955.

65. Nothdurft, H.: Strahlentherapie, 100:192, 1956.

64. Stinson, N E.: The tissue reaction induced in rats and guinea pigs by polymethyl metacrylate and stainless steel (18/8/Mo). Brit. J. Exp. Path., 45:21, 1964.

65. Seale, J.T.: Biological and mechanical factors in prosthetic surgery. Modern Trends in Surgical Material, page 70, 1956.

66. Siddons, A.H M , and MacArthur, A.M.: Carcinomata developing at the site of foreign bodies in the lung. Brit. J. Surg., 39:542, 1952.

67. Hueper, W.C.: Experimental studies in metal carcinogenesis. Texas Rep. Biol. Med., 10:167, 1952.

68. Penn, J., and Epstein, E.: Notes on a case of carcinoma following shell-wound of the face. Plast. Reconstr. Surg., 12: 148, 1953.

69. Heath, J.C.: The production of malignant tumors by cobalt in rats. Brit. J Cancer, 10:668, 1956.

70. McDougall, J.: Malignant tumor in site of bone plating. J. Bone Jt. Surg., 38:B, 709, 1956.

71. Ballinger, H. W.F., Fineberg, C., and Figlio, D.: Repair of small blood vessels with minimal interruption of flow. J. Surg. Res., 3:475, 1963.

72. Carton, C.A., Kessler, L.A., Seidenberg, B., and Hurwitt, E.S.: A plastic adhesive method of small blood vessel surgery. World Neurol., 1:356, 1960.

73. Carton, C.A., Kessler, L.A., Seidenberg, B., and Hurwitt, E.S.: Experimental studies in surgery of small blood vessels. II. Patching of arteriotomy using a plastic adhesive. J. Neurosurg., 18: 188, 1961.

74. Carton, C.A., Heifetz, M.D., and Kessler, L.A.,: Patching of intracranial internal carotid artery in man using a plastic adhesive (Eastman 910 Adhesive). J. Neurosurg. 19:867, 1962.

75. Healey, J.E. Jr., Brooks, B.J., Gallager, H.S., Moore, E.B., and Sheena, K.S.: A technique for nonsuture repair of veins. J. Surg. Res., 1:267, 1961.

76. Healey, J.E. Jr., Moore, E.B., Brooks, B.J., and Sheena, K.S.: A vascular clamp for circumferential repair of blood vessels. Surgery 51:452, 1962.

77. Healey, J.E. Jr., Clark, R.L., Gallager, H.S., O'Neill, P., and Sheena, K.S.: Nonsuture repair of the blood vessels. Ann. Surg., 155:817, 1962.

78. Hosbein, D.J., and Blumenstock, D.A.: Anastomosis of small arteries using a tissue adhesive. Surg. Gynec. & Obst., 118:112, 1964.

79. Inou, T., Yoshimura, K., Furukawa, T., Koike, T., Hino, K., Mizuno, K., Ota, K., Wada, T., and Kimoto, S.: Studies of surgical use of plastic adhesive. Cohesive News, 1: November, 1961.

80. Kessler, L.A., and Carton, C.A.: Experimental studies in surgery of small blood vessels with use of plastic adhesive. III. Prevention of aneurysmal dilatation. Surg. Forum, XI: 403, 1960.

81. Nathan, H., Nachlas, M.M., Solomon, R.D., Halpern, B.D., and Seligman, A.M.: Nonsuture closure of arterial incision using a rapidly polymerizing adhesive. Ann. Surg., 152: 648, 1960.

82. Ashley, F.L., Falak, T., and Berman, O.D.: Nonsuture closure of skin lacerations and nonsuture grafting of skin with a rapidly polymerizing adhesive. Quart. Bull. Northwest. Univ. Med. Sch., Fall, 1962.

83. Fischl, R.A.: An adhesive for primary closure of skin incisions. Plas. Reconstr. Surg., 30:607, 1962.

84. Inou, T.: Studies on the surgical use of plastic adhesive. Amer. J. Proctl., 156: 3, 1962.

85. O'Neill, P., Healey, J.E. Jr., Clark, R.L., and Gallager, H.S.: Nonsuture intestinal anastomosis. Amer. J. Surg., 104: 761, 1962.

86. Seidenberg, B., Garrow, E., Pimental, R., and Hurwitt, E. S.: Studies on the use of plastic adhesive in gastrointestinal surgery. Ann. Surg. 158:721, 1963.

87. Healey, J.E. Jr , Sheena, K.S., Gallager, H.S., Clark, R.L., and O'Neill, P.: The use of a plastic adhesive in the technique of bronchial closure. Surg. Forum, 13:153, 1962.

88. Shaff, S.I.: A plastic adhesive for nonsuture repair of tracheal wounds. J. Amer. Vet. Med. Ass., 143:138, 1963.

89. Johnson, G.W., and Smith, G.W.: Effect of Methyl-2-Cyanoacrylate on the central nervous system. A preliminary evaluation in nerve anastomosis. Surg. Forum, XIV:414, 1963.

90. Mathes, G.L., and Terry, J.W. Jr: Nonsuture closure of nephrotomy. J. Urol., 89:122, 1963.

91. Bloomfield, S., Barnert, A.H., and Kanter, P.: The use of Eastman 910 monomer as an adhesive in ocular surgery. Amer. J. Ophthal., 55:946, 1963.

92. MacDonald, G.L. Jr., Tose, L., and Deterling, R.A. Jr.: A technique for reimplantation of dog limb involving the use of a mechanical stapling device and polymerizing adhesive. Surg. Forum, XIII: 68, 1962.

93. Manax, G.W., Bloch, J.H., Longerbeam, J.K., and Lillehei, R.C.: Plastic adhesive as an adjunct in suture anastomoses of small blood vessels. Surgery, 54:863, 1963.

94. Strahan, R.W., Sajedee, M., and DuVal, M.K. Jr.: The leaking esophageal suture line. A new method of repair using Eastman 910. Amer. J. Surg., 106:570, 1963.

95. Lighterman, I., and Farrel, J.J.: Treatment of experimentally induced mandibular fracture with plastic polymers. Surg. Forum, XIII: 466, 1962.

96. Sawyer, J.L., and Vasco, J.: Sealing cut lung surfaces with plastic adhesive. J. Thorac. Cardio. Surg., 46:826, 1963.

97. Thomas, P.A., Jr., Nims, R.M., Hunt, R.D., and Aronstam, E.M.: Experimental observations with a plastic adhesive, Methyl-2-Cyanoacrylate, as a sealing agent in pulmonary and bronchial surgery. Cohesive News, 3: May, 1963.

98. Wilder, R.J., Playforth, H., Bryant, M., and Ravitch, M.M.: The use of plastic adhesive in pulmonary surgery. J. Thorac. Cardio. Surg., 46:576, 1963.

99. Awe, W.C., Braunwald, N.S., and duPlessis, L.A.: A new method for the experimental production of pulmonary hypertension. Surg. Forum, XIII:150, 1962.

100. Albin, M.S., D'Agostino, A.N., White, R., and Grindlay, J.H.: Nonsuture sealing of a dural substitute utilizing a plastic adhesive, Methyl-2-Cyanoacrylate. J. Neurosurg., 19:545, 1962.

101. Keddie, F., Shadomy, J., Shadomy, S., and Barfatani, M.: Intrafollicular Tenia Versicolor demonstrated on monomer plastic strips. J. Invest. Derm., 41:103, 1963.

102. Awe, W.C., Roberts, W., and Braunwald, N.S.: Rapidly polymerizing adhesive as a hemostatic agent: Study of tissue response and bacteriological properties. Surgery, 54:322, 1963.

103. Braunwald, N.S., and Awe, W.C.: Control of hemorrhage from the heart and aorta utilizing a plastic adhesive. Surgery, 51:786, 1962.

104. Garret, H.E., and Law, S.W.: Control of vascular anastomotic hemorrhage in Heparinized dogs with a rapidly polymerizing adhesive. Surg. Forum, XII:254, 1961.

105. Marable, S.A., and Wagner, D.E.: The use of rapidly polymerizing adhesive in massive liver resection. Surg. Forum, XIII: 264, 1962.

106. Coover, H.W. Jr., Joyner, F.B., Shearer, N.H. Jr., and Wicker, T.H. Jr.: Chemistry and performance of Cyanoacrylate adhesive. Soc. Plastics Engrs.J., 15:413, 1959.

107. Fasset, D.W.: Personal communication from the laboratory of Industrial Medicine, Eastman Kodak Company, Rochester, N.Y.

108. Semple, J.R.: Personal communication, February 4, 1964.

109. Douglas, B., and Foster, J.H.: Union of severed arterial trunk and canalization without suture or prosthesis. Ann. Surg., 157:944, 1963.

110. Lambert, P.B., Frank, H.A., Bellman, S., and Friedman, E.: Observations on the recovery of continuity of divided arteries and veins. Angiology, 14:121, 1963.

111. Duguid, J.B.: Pathogenesis of arteriosclerosis. Lancet 2:925, 1949.

112. Villegas, A.H., Toll, G., and Shaw, R.S.: Comparison of the rate of healing in transverse and longitudinal aortomies. J. Thorac. Cardio. Surg., 45:233, 1963.

113. Marchand, F.: Uber Arteriosklerose (Athero-Sklerose), Verhandl. d. 21. Kong. f. inn. Med., 21:23, 1904.

114. Katz, L.M., and Stamler, J.: Experimental atherosclerosis. Charles C. Thomas, Publisher, 1953.

115. Klotz, O: Experimental production of arteriosclerosis. Brit. Med. J., 2:1767, 1908.

116. Ignatowski, A.: Uber die Wirkung des tierischen Eiweisses auf die Aorta und die parenchymatosen Orange der Kaninchen. Virchows Arch. f.path. Anat., 198:248, 1909.

117. Saltykow, S.: Arterienveranderungen (Atherosklerose und verwandte Krankheiten des Menschen). Centralb. f. allg. Path. u. path. Anat., 19:321, 1908.

118. Stukkeu, N.V.: Uber die Veranderungen der Kaninchenaorta bei Futterung mit verscheidenen Fettsotten. Centralb. f. allg. Path. u. path. Anat., 23:910, 1912.

119. Wesselkin, N.W.: Uber die Ablagerung von fettartigen Stoffen in den Organen. Virchows Arch. f. Path. Anat., 212:225, 1913.

120. Anitschkow, N., and Chalatow, S.: Uber experimentelle cholesterinsteatose und ihre bedeutung fur die entstehung einiger pathologischer prozesse. Centralab. f. allg. Path. u. path. Anat., 24:1, 1913.

121. Wacker, I., and Hueck, W.: Uber Experimentelle Atherosklerose und Cholesterinamie. Munchen. Med. Wchnschr. 60:2097, 1913.

122. Dewey, K.: Experimental hypercholesterolemia. Arch. Int. Med., 17: 757, 1916.

123. Bailey, C.H.: Atheroma and other lesions produced in rabbits by cholesterol feeding. J. Exper. Med., 23:69, 1916.

124. Chuma, M.: Uber Organveranderungen nach Lanolinfutterung beim Kaninchen. Virchows Arch. f. Path. Anat., 242:275, 1923.

125. Schonheimer, R.: Uber die Experimentelle Cholesterinkrankheit der Kaninchen. Virchows Arch. f. Path. Anat., 249:1, 1924.

126. Androsov, P.I.: New method of surgical treatment of blood vessel lesions. A.M.A. Arch. Surg., 73:902, 1956.

127. Smialowski, A.J., and Connock, S.H.G.: A vascular suturing instrument. Mechanical Engineering Report MI-827.

128. Inokuchi, K.: A new type of vessel suturing apparatus. A.M.A. Arch. Surg., 77:954, 1958.

129. Cooper, P., and Christie, S.G.: Trans. N.Y. Acad. Sci., 25:365, 1963.

130. Buck, R.C.: The fine structure of the aortic endothelial lesions in experimental cholesterol atherosclerosis of rabbits. Amer. J. Path., 34:897, 1958.

131. Parker, F.: An electron microscopic study of experimental atherosclerosis. Amer. J. Path., 36:19, 1960.

132. Duff, G.L.: Experimental cholesterol arteriosclerosis and its relationship to human arteriosclerosis. Arch. Path., 20:81, 1935.

133. Beattie, W.G., Brown, F.N., Devitt, J.E., and Vogelfanger, I.J.: In press. Can. J. Surg.

134. Carrol, S.E.: In press. Can. J. Surg.

APPENDIX

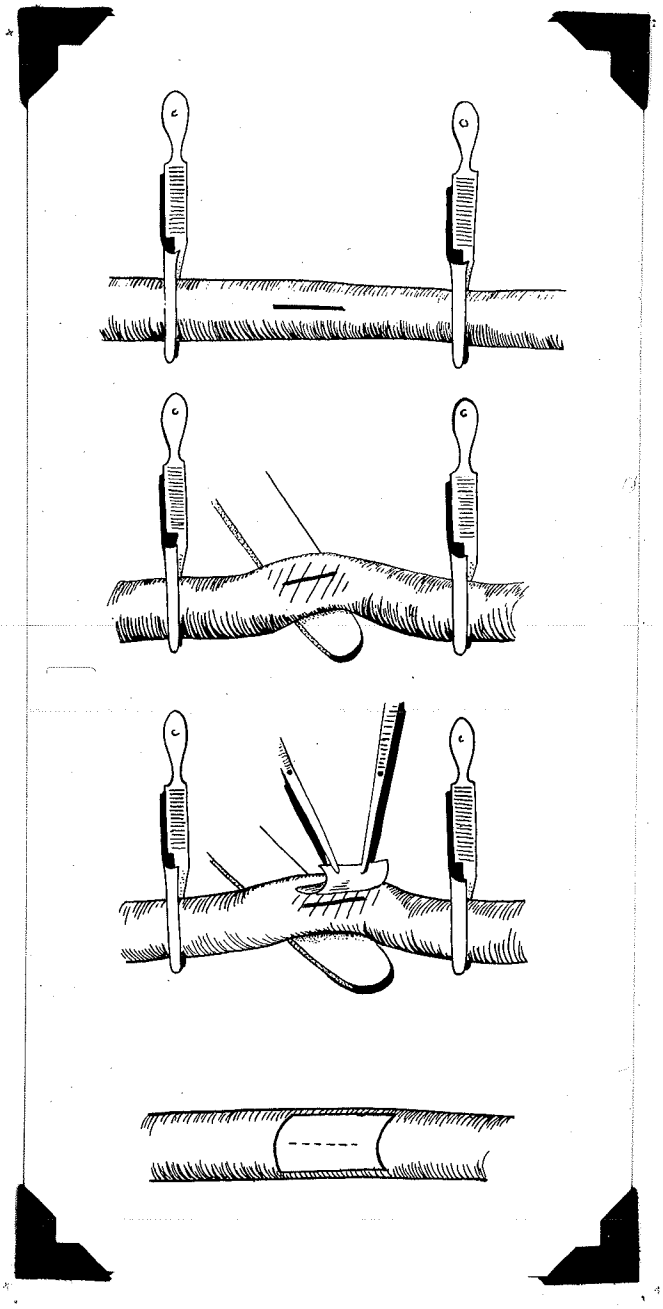

Figure 1. Diagram of the technique of closure of longitudinal incision of artery, utilizing adhesive and patching.

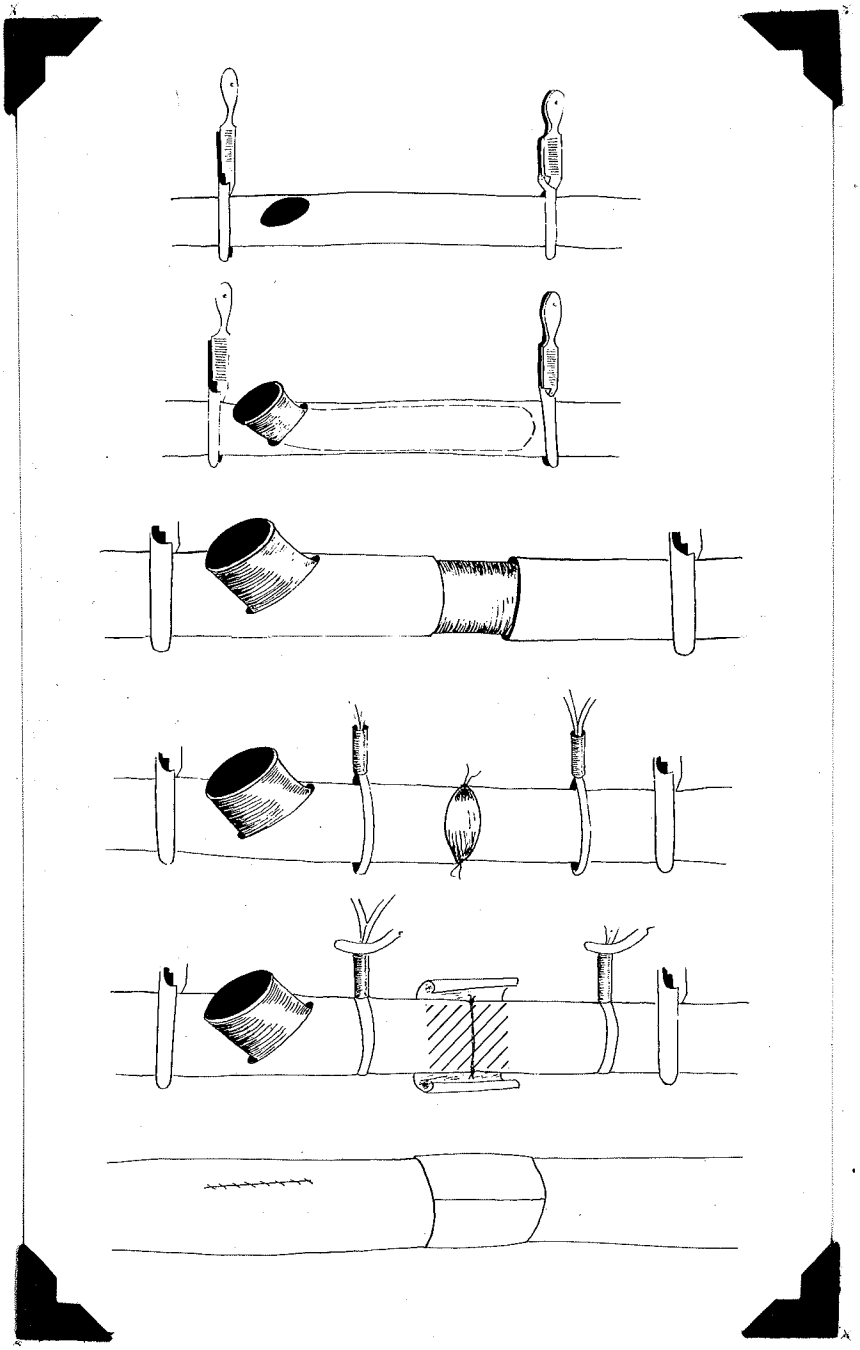

Figure 2. Diagram of the technique of end-to-end anastomosis, utilizing adhesive and wrapping.

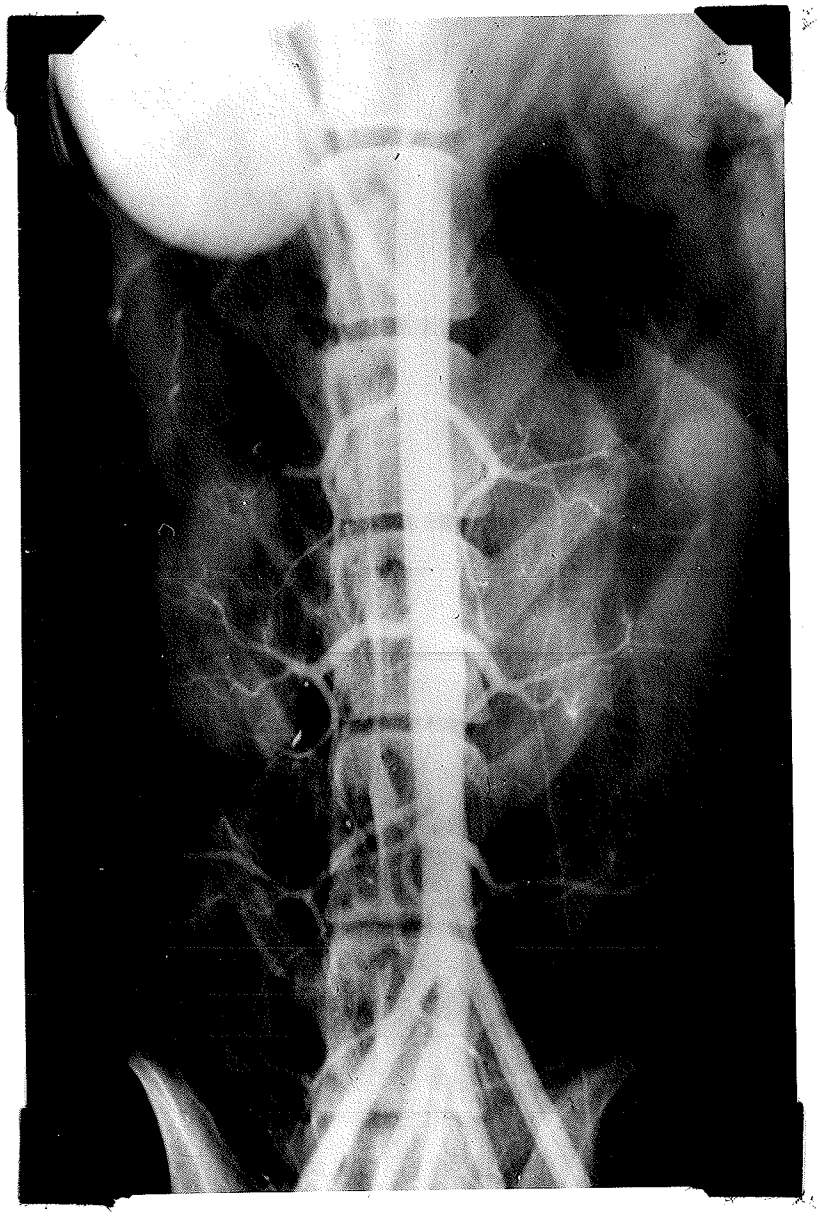

Figure 3. Aortogram of a dog taken six months following closure of a longitudinal incision with adhesive and Mersilene patch.

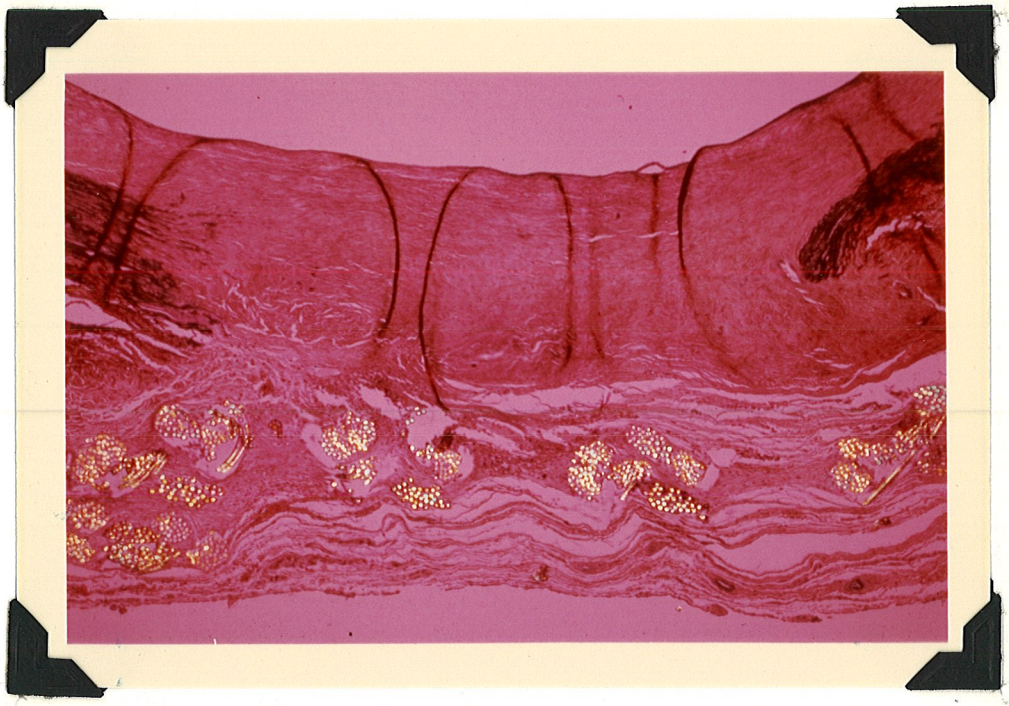

Figure 4. Microscopic section of the wall of a dog aorta, five months postoperatively. Longitudinal incision closed with adhesive and Mersilene patch. Mersilene is seen under polarizing illumination. Elastic stain X. 20.

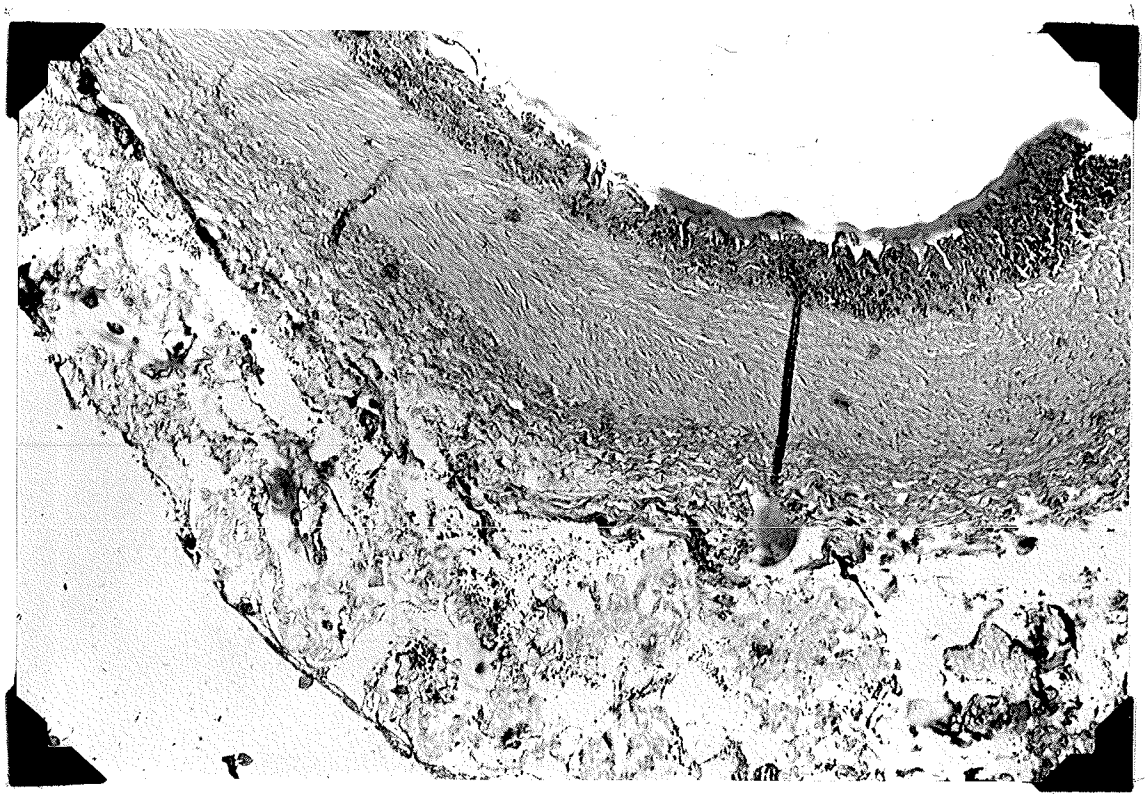

Figure 5. Microscopic section of the wall of a dog aorta, two weeks postoperatively, showing moderately active intimitis at the site of arteriotomy. Longitudinal incision closed with adhesive and Mersilene patch. H & E stain X.50.

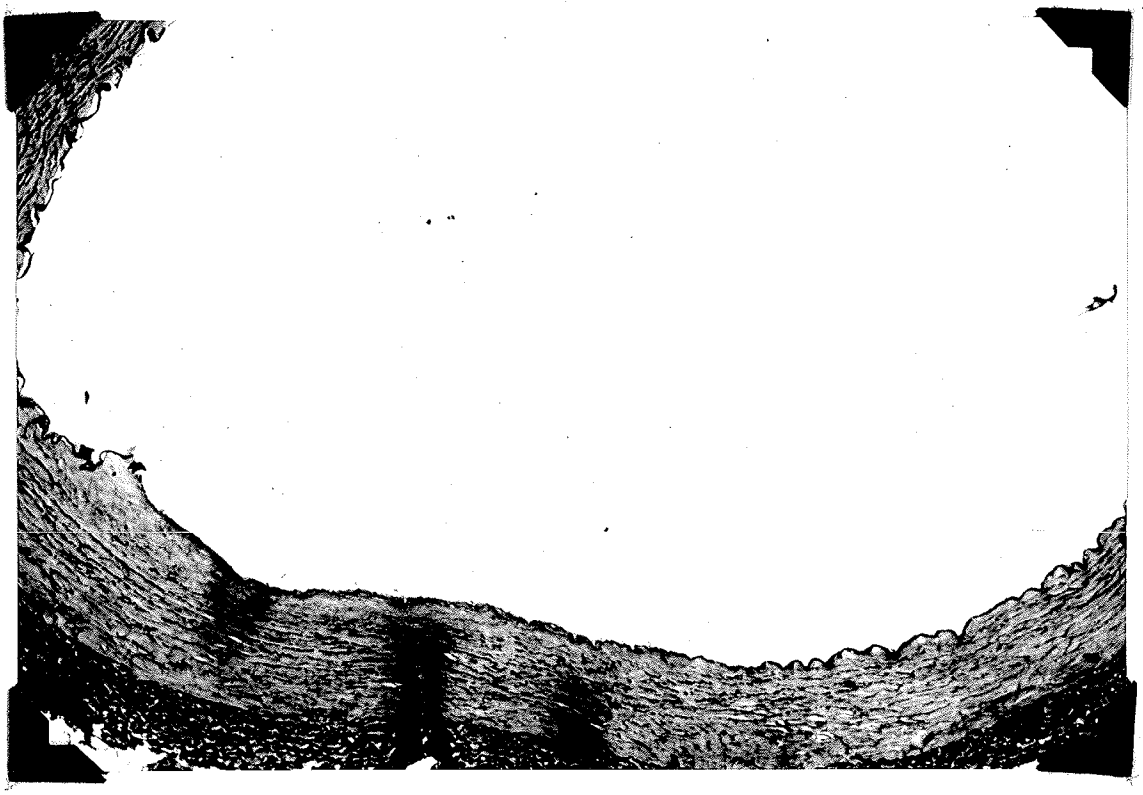

Figure 6. Femoral artery of a dog four months postoperatively. Only evidence of arteriotomy is loss of the internal elastic lamina at the site of the incision. Longitudinal incision closed with adhesive and fascia patch.
Elastic stain X. 50.

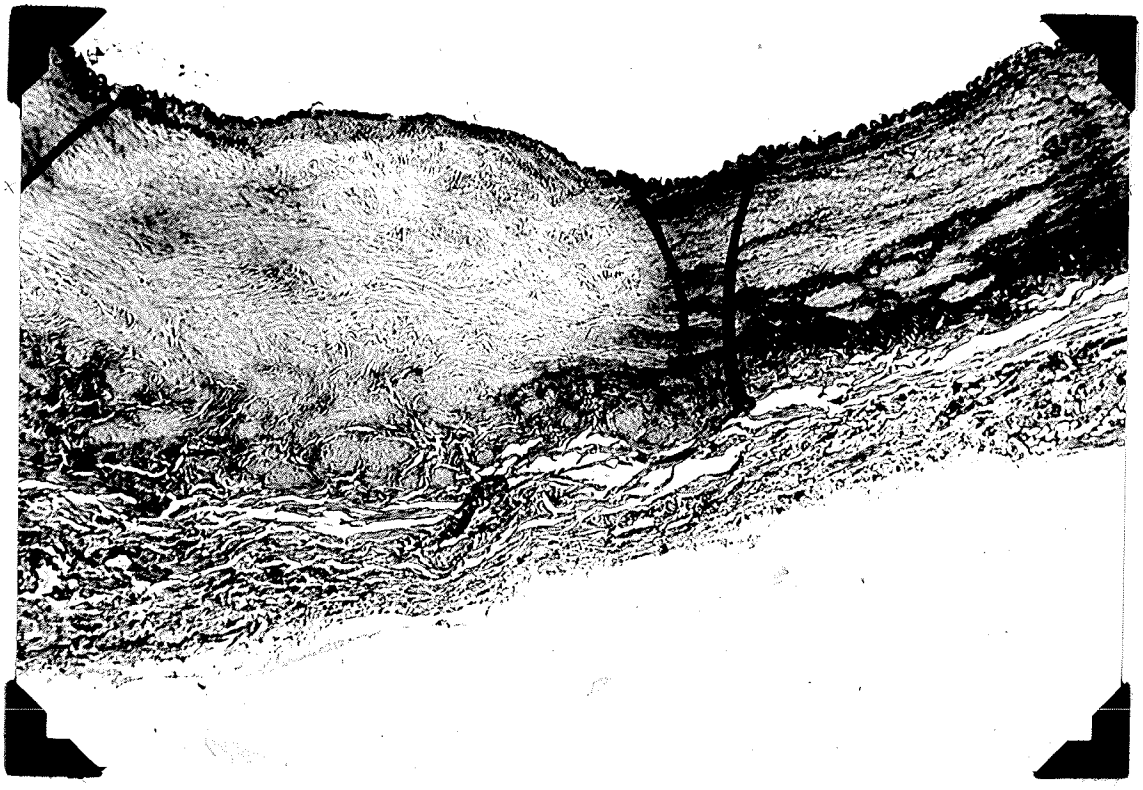

Figure 7. Aorta of a dog seven months postoperatively. Well healed scar in media and intima. Internal elastic lamina is preserved. Longitudinal incision closed with adhesive and Mersilene.
Elastic stain X. 20.

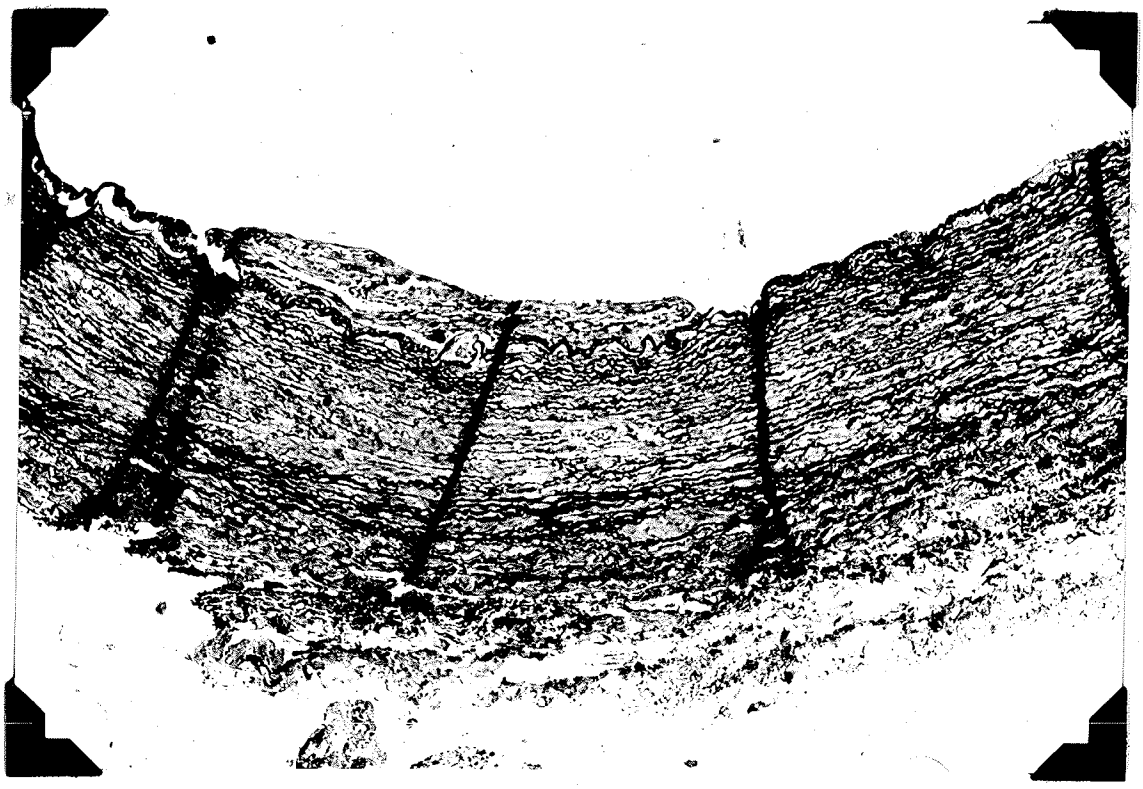

Figure 8. Aorta five months postoperatively. Only evidence of incision is small, organized mural thrombosis. Longitudinal incision closed with adhesive and Mersilene patch. Elastic stain X. 20

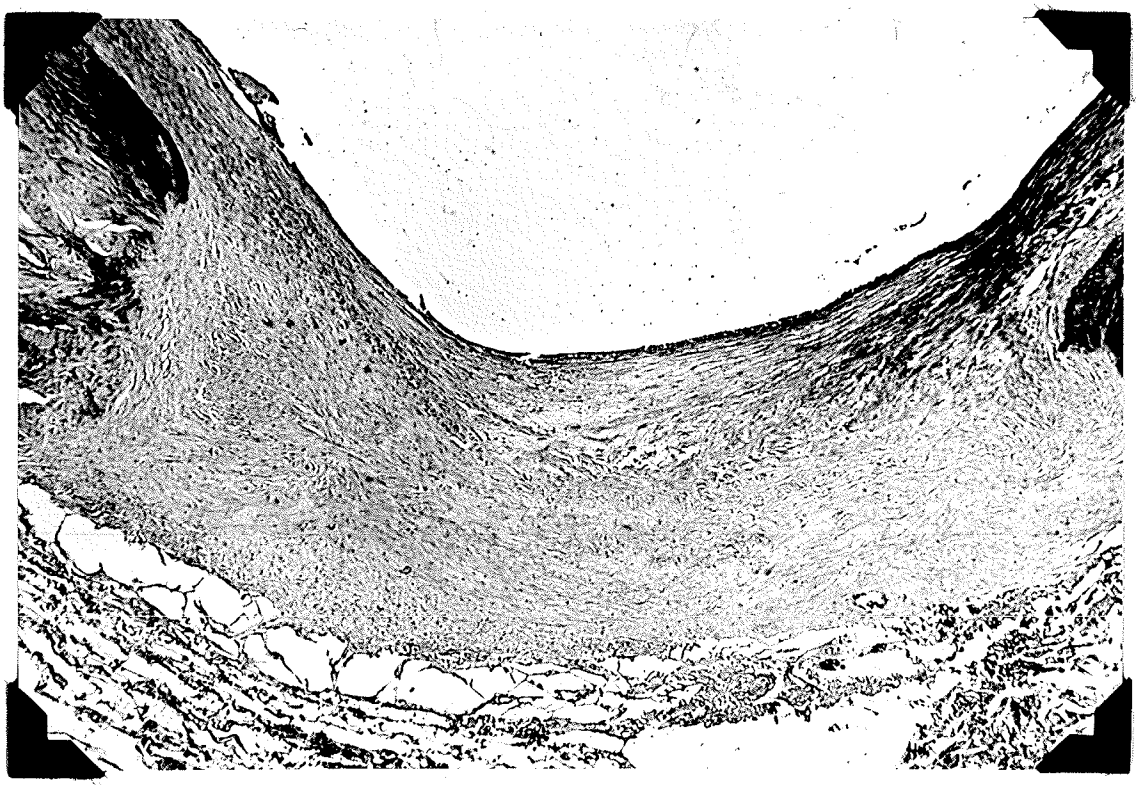

Figure 9. Aorta five months postoperatively showed the most extensive scar formation in the group of aortas studied. Longitudinal incision closed with adhesive and Mersilene patch.
Elastic stain X. 20.

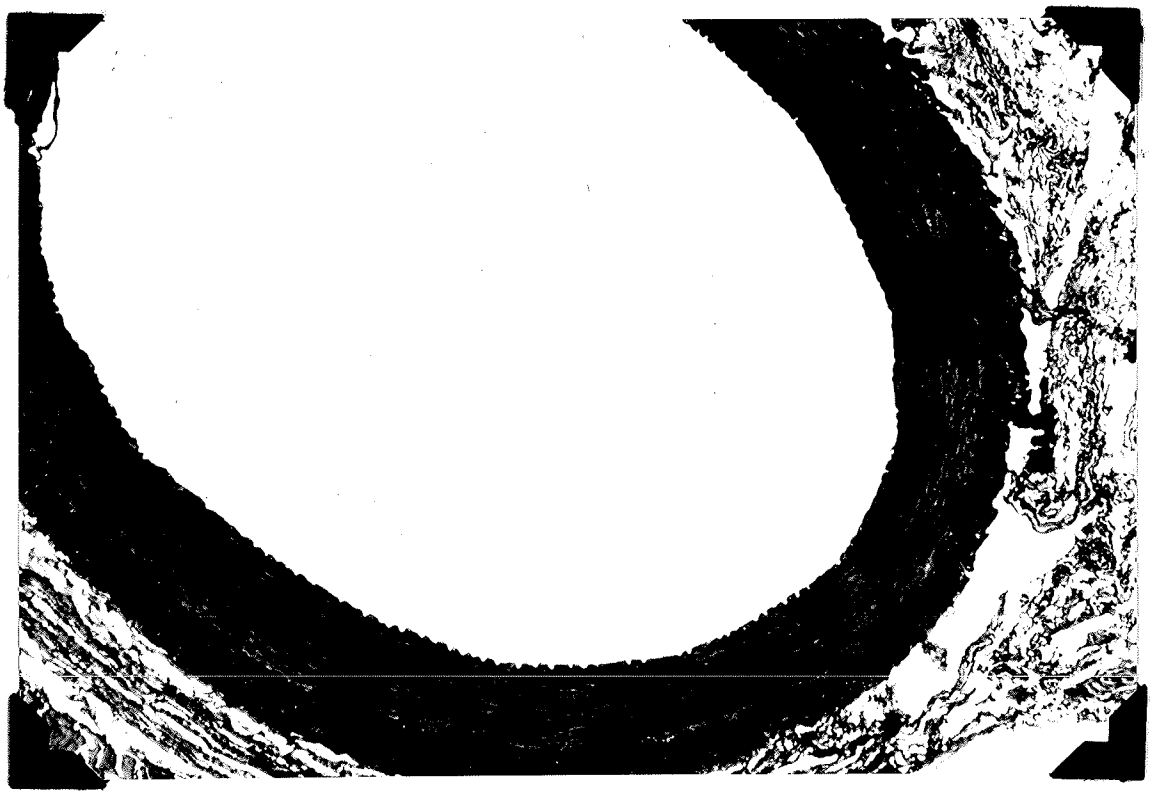

Figure 10. Femoral artery eight months postoperatively. The scar is hardly visible. Longitudinal incision closed with adhesive and fascia patch.
H & E stain X. 20.

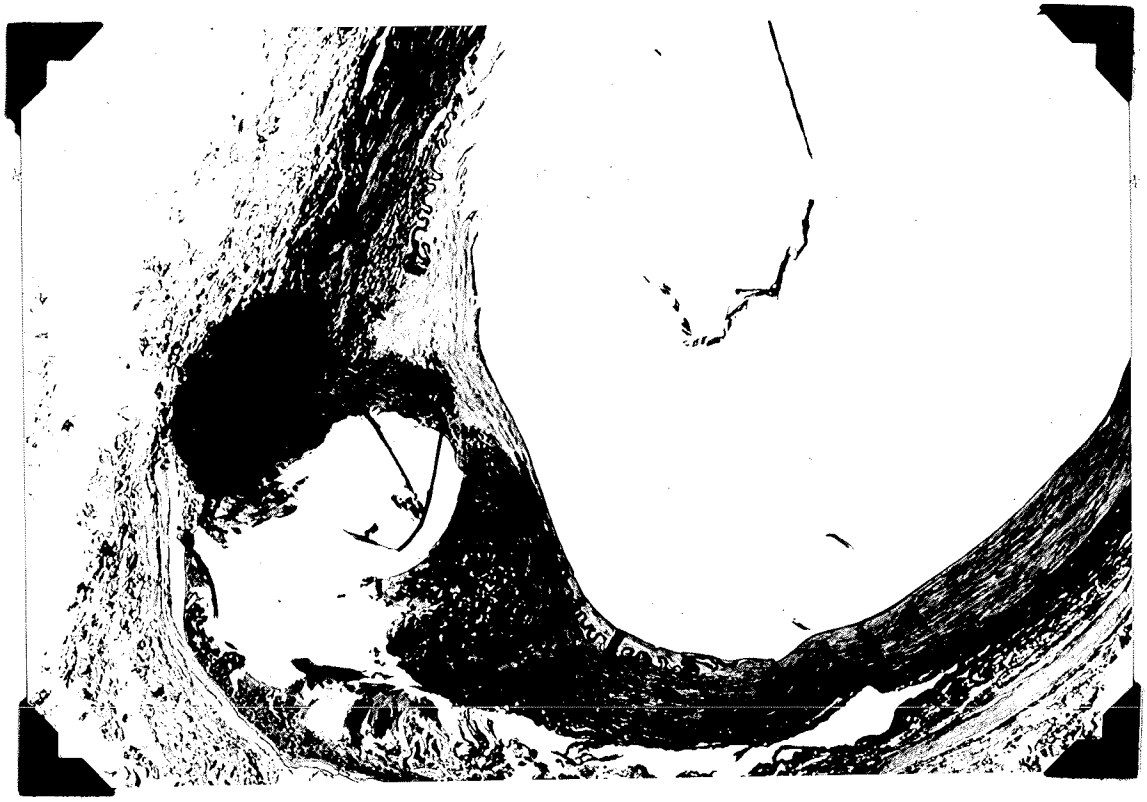

Figure 11. Femoral artery eight months postoperatively following suture with 6-0 silk. Disorganization of the media in the region of the suture and fibrosis of intima in the region of scar is apparent.
H & E X.20.

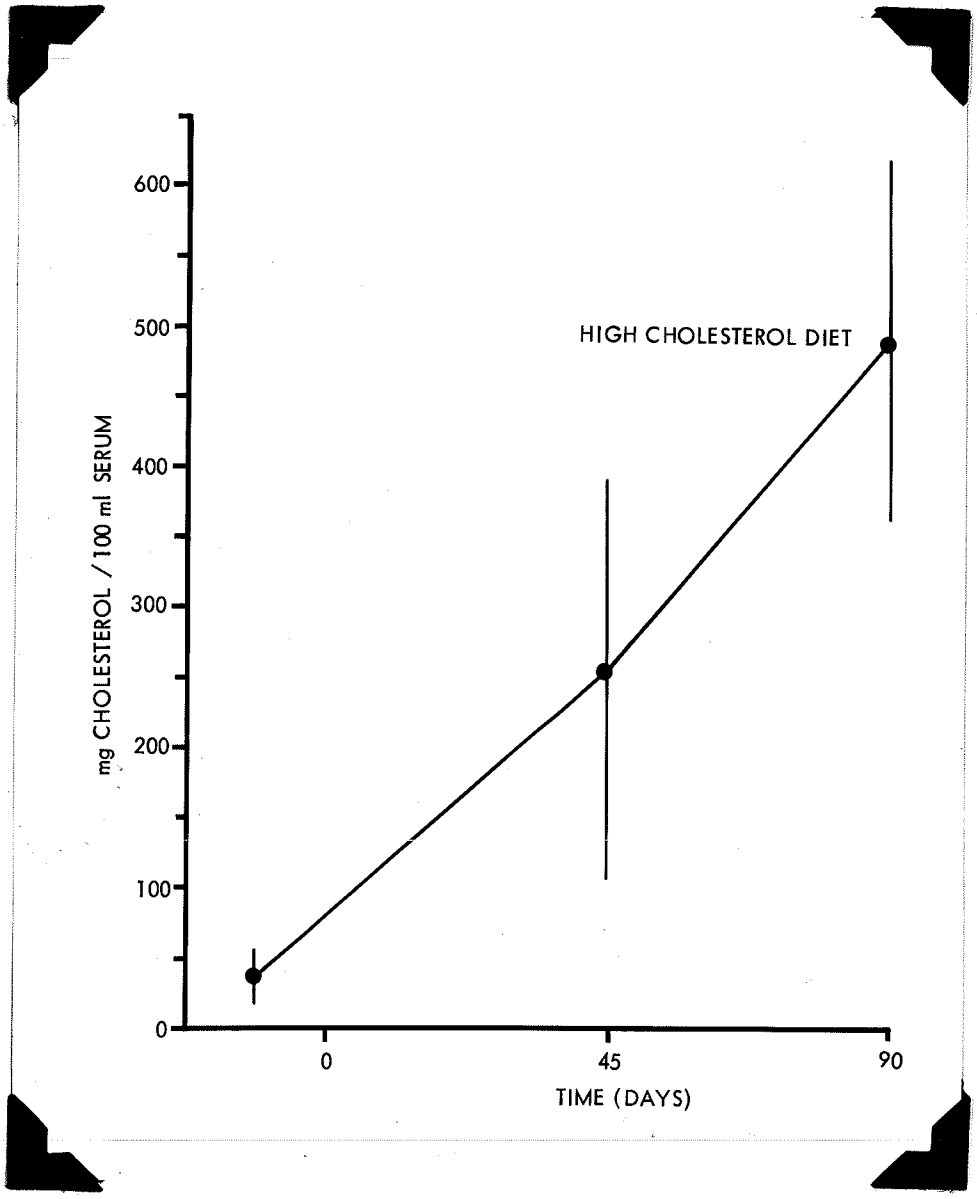

Figure 12. Blood cholesterol of 16 rabbits treated with 0.5 gm. cholesterol daily (means and standard deviation).

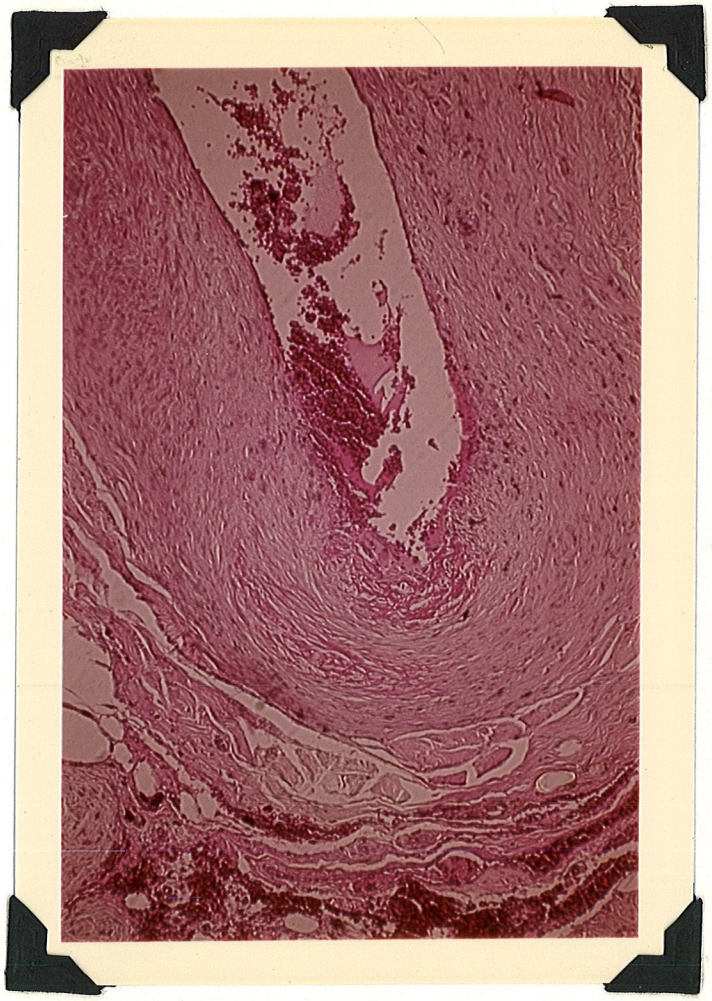

Figure 13. Microscopic section of the wall of an atherosclerotic aorta from a rabbit, three months postoperatively. Longitudinal incision was closed with adhesive and fascia. It shows complete healing and there is some evidence of the presence of adhesive in the section.
H & E stain X. 75.

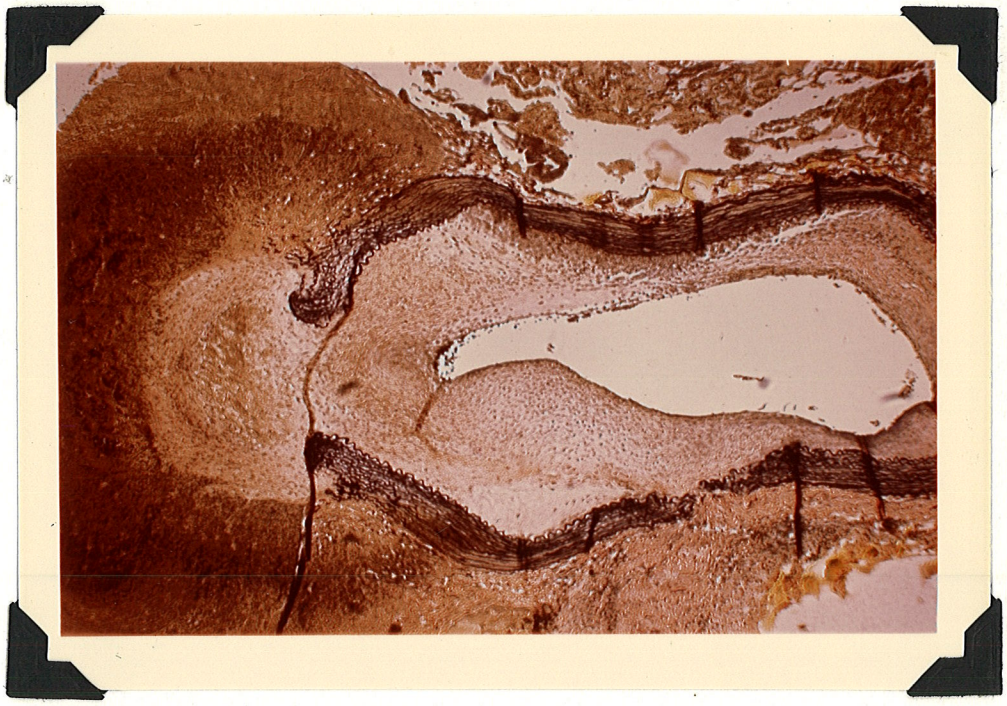

Figure 14. Atherosclerotic aorta of a rabbit three and one half months postoperatively, showing scar formation and separation of media.
Elastic stain X. 75.

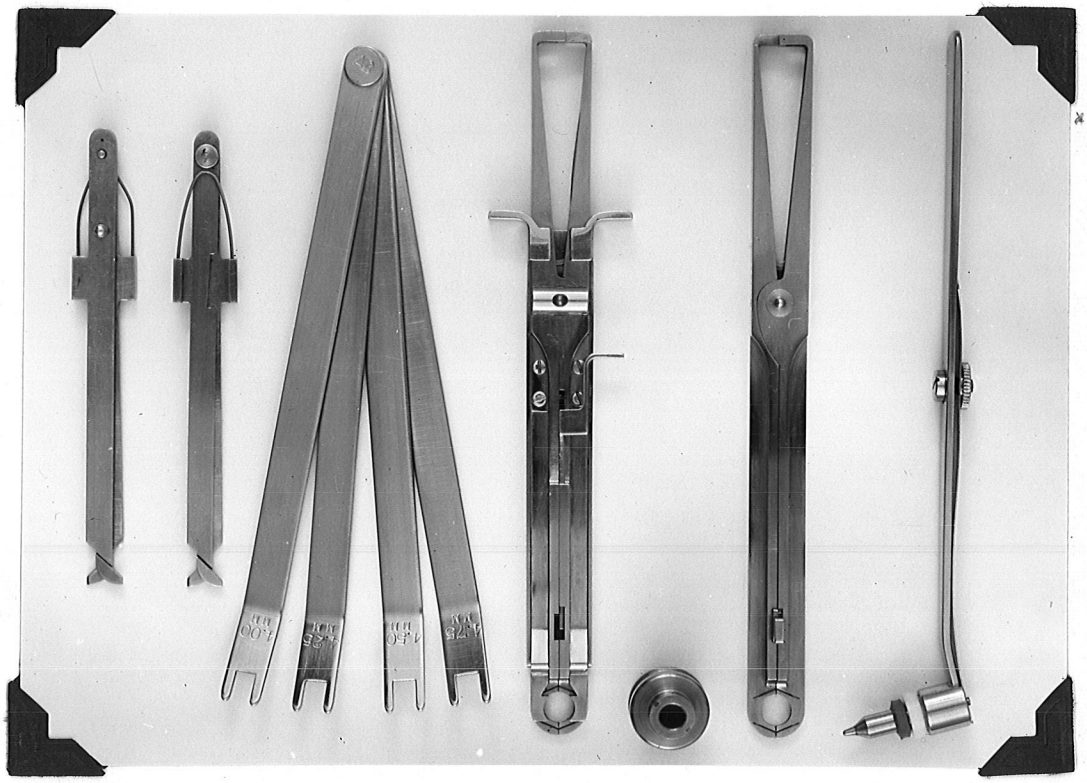

Figure 15. Vogelfanger's stapler set.

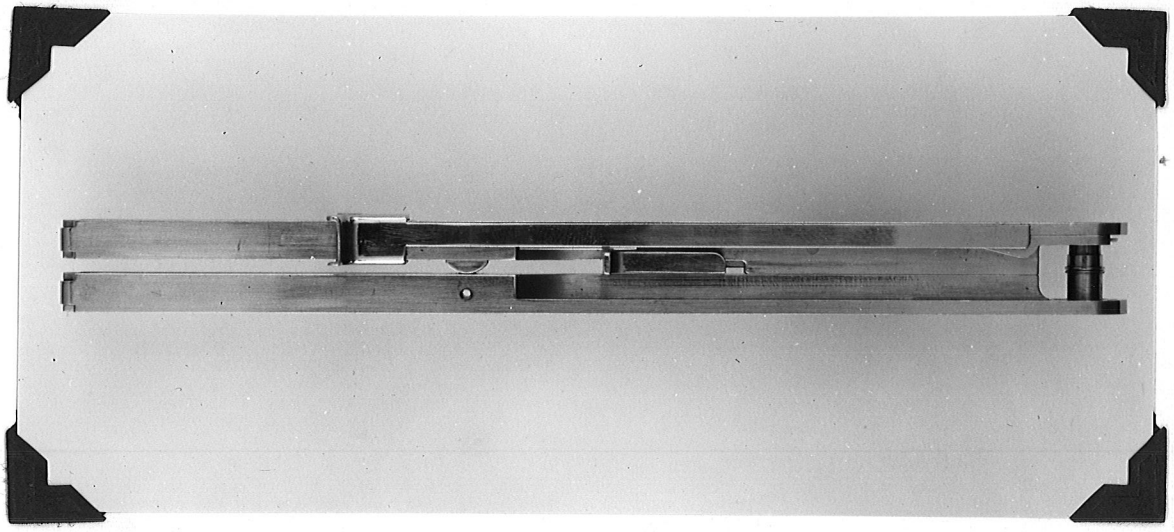

Figure 16. Assembled vascular stapler set Mark 4.

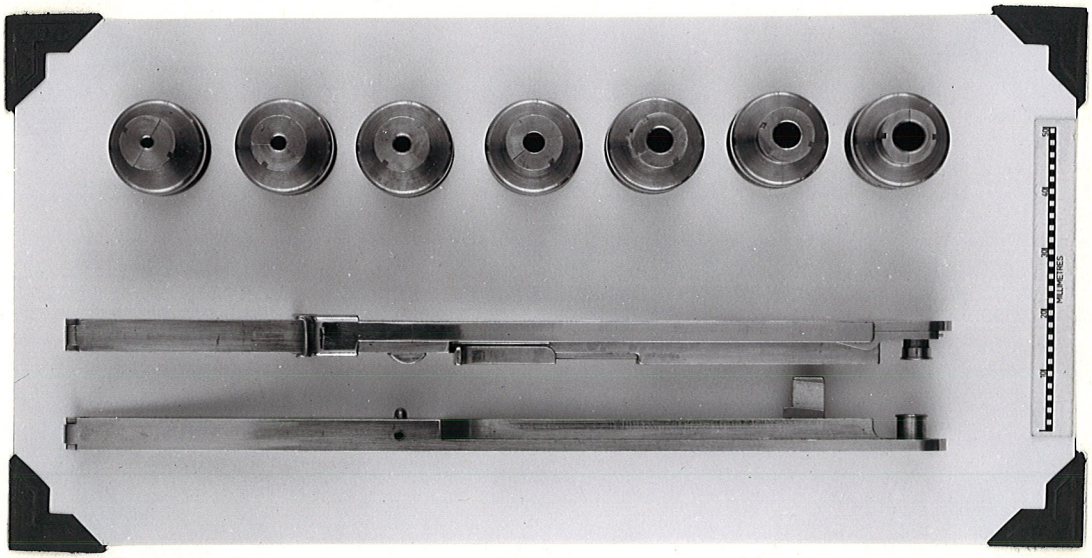

Figure 17. Vascular Stapler (handles and a set of bushings.

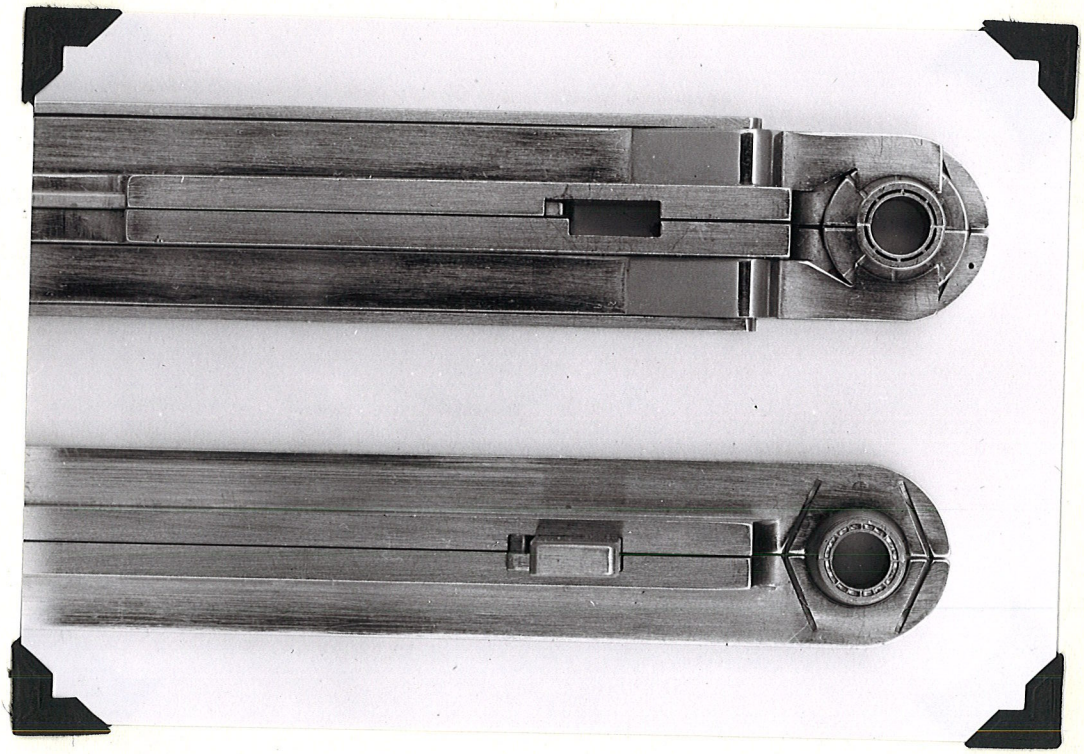

Figure 18. Close view of handles, bushings in situ.

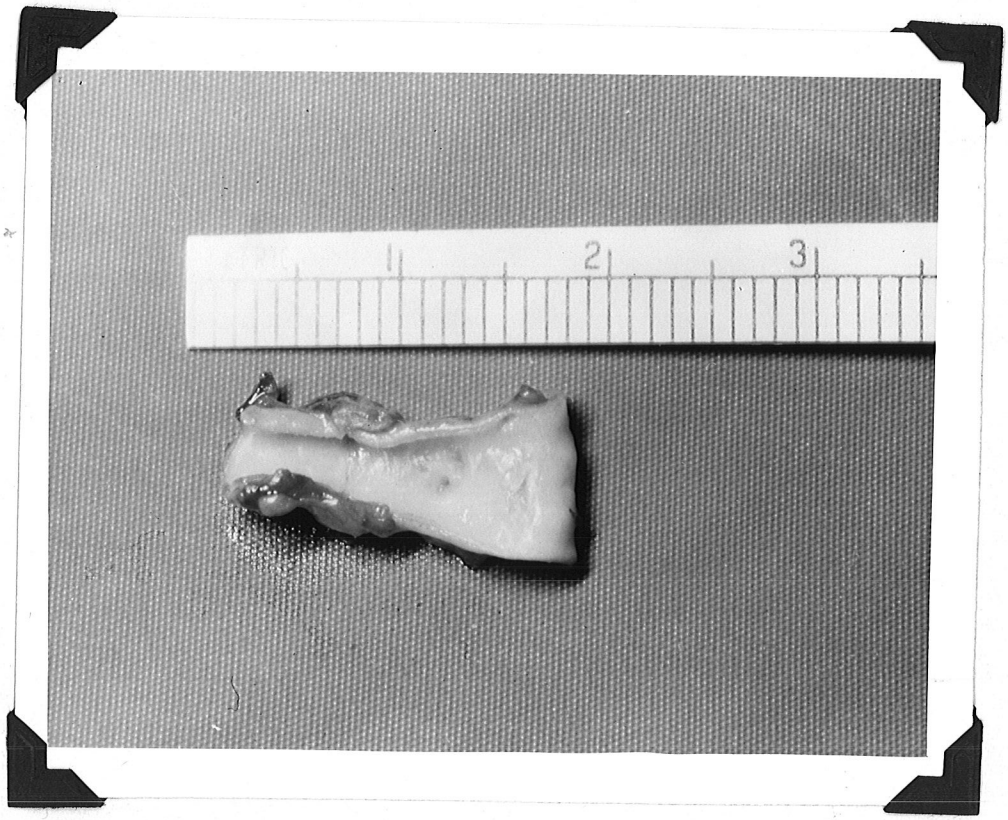

Figure 19. Gross specimen of the femoral artery of a dog six months postoperatively, using stapler for end-to-end anastomosis.

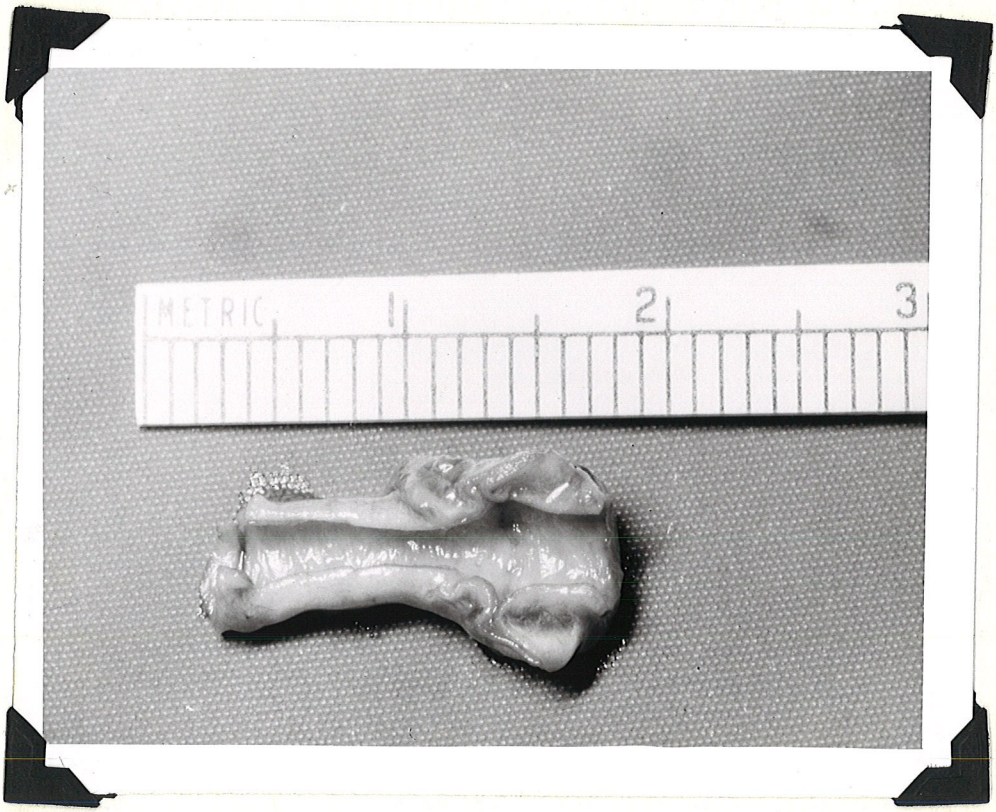

Figure 20. Gross specimen of the femoral artery of a dog four months postoperatively, using stapler for end-to-end anastomosis.

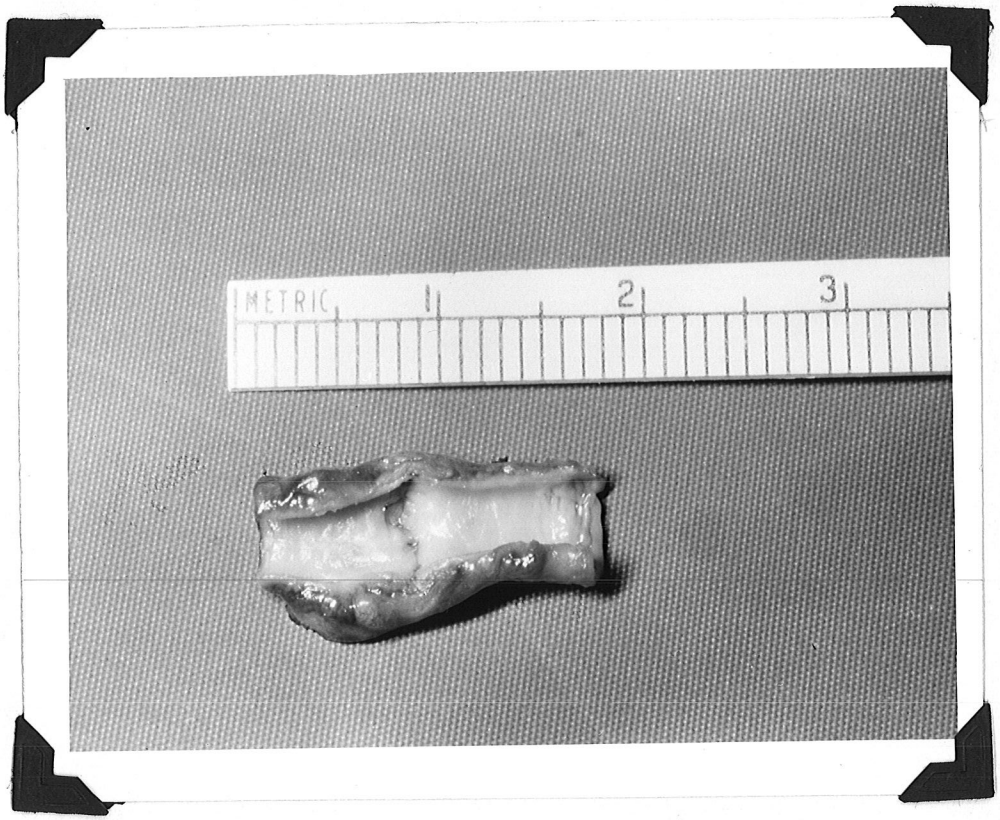

Figure 21. Gross specimen of the femoral artery of a dog three months postoperatively, using stapler for end-to-end anastomosis.

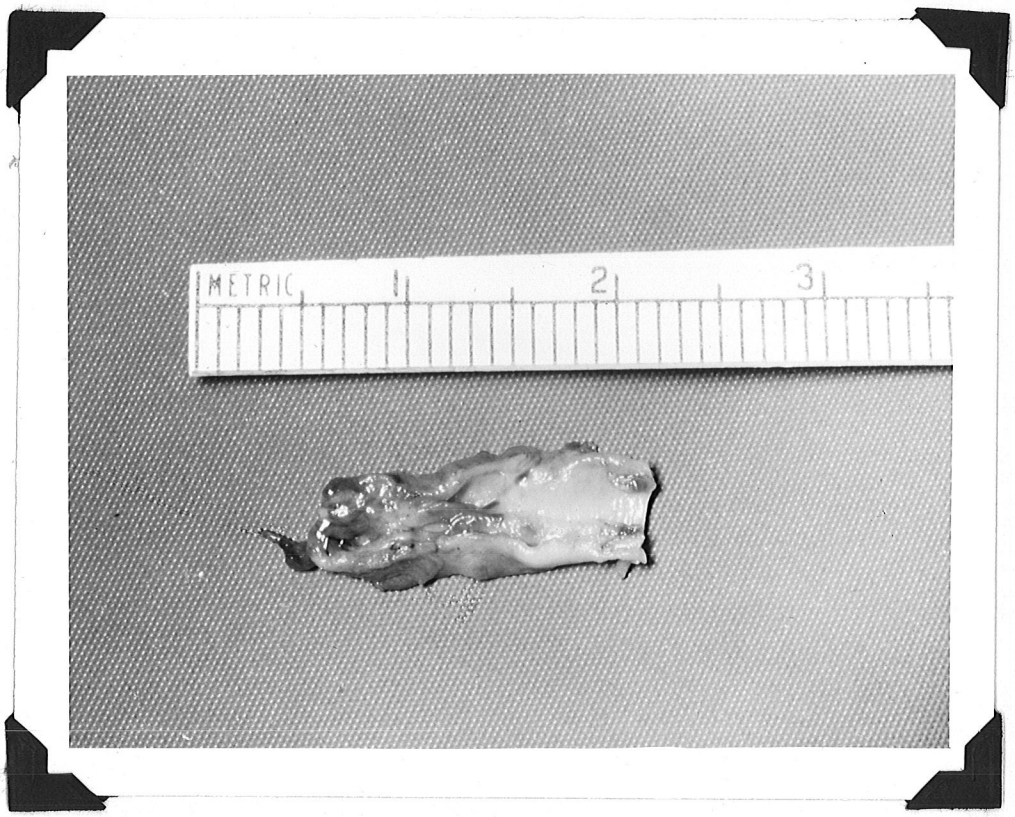

Figure 22. Gross specimen of the femoral artery of a dog, using stapler for end-to-end anastomosis. There is a large organized thrombus at the anastomotic site.

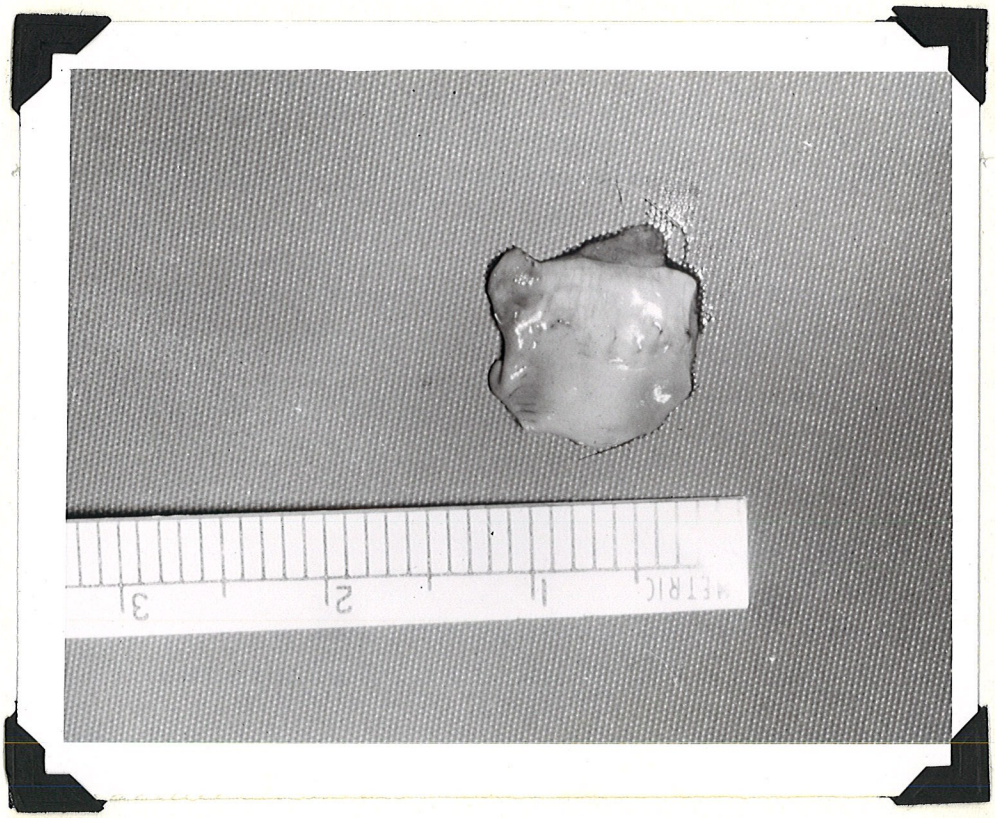

Figure 33. Gross specimen of femoral vein of a dog six months postoperatively, using the stapler for end-to-end anastomosis.

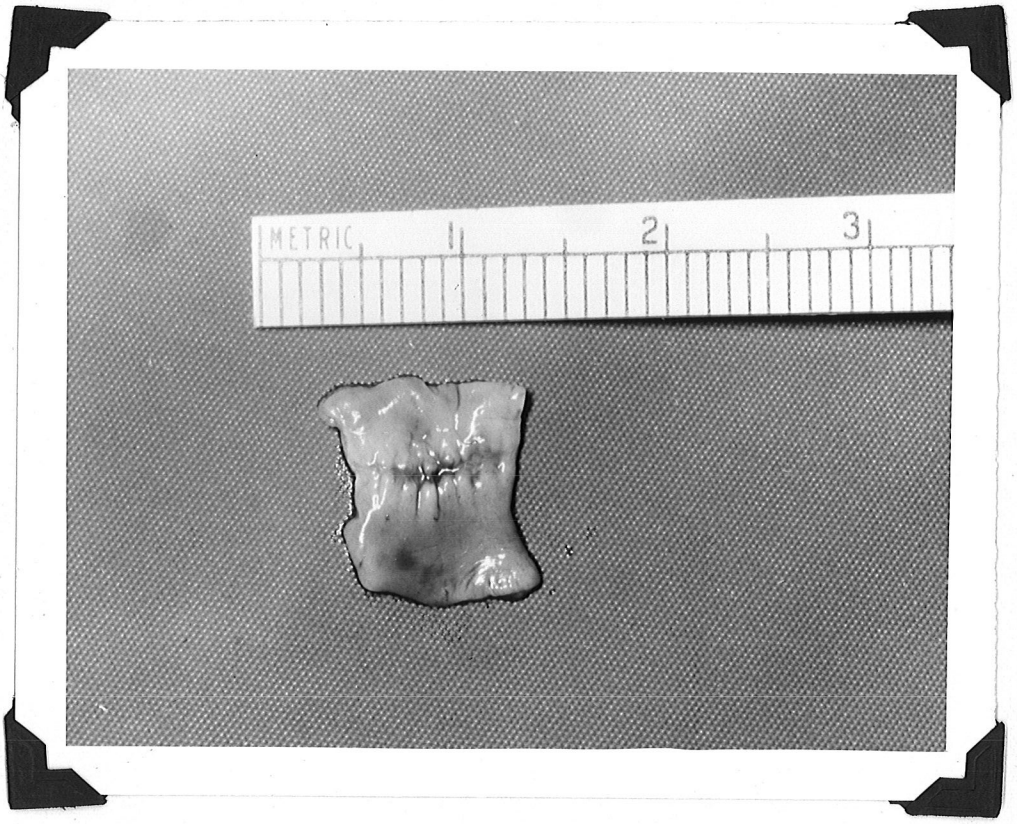

Figure 24. Gross specimen of femoral vein of a dog three months postoperatively, using the stapler for end-to-end anastomosis.

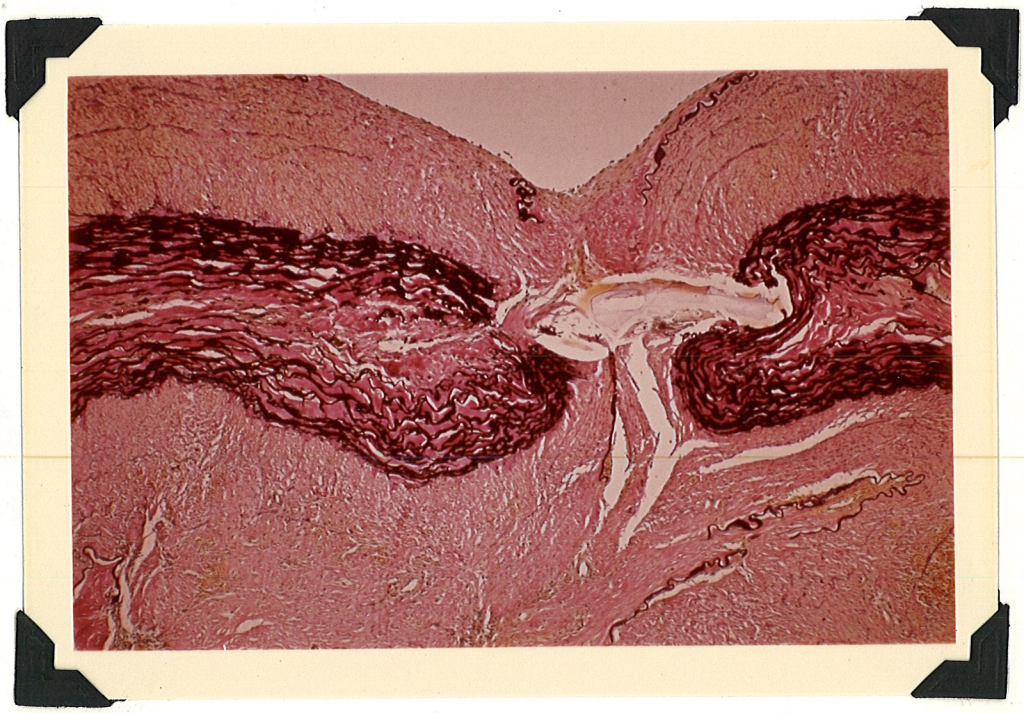

Figure 25. Histological section through the anastomotic area of the femoral artery of a dog six months postoperatively, showing the interruption of elastica, but satisfactory healing.
Elastic stain X. 50.

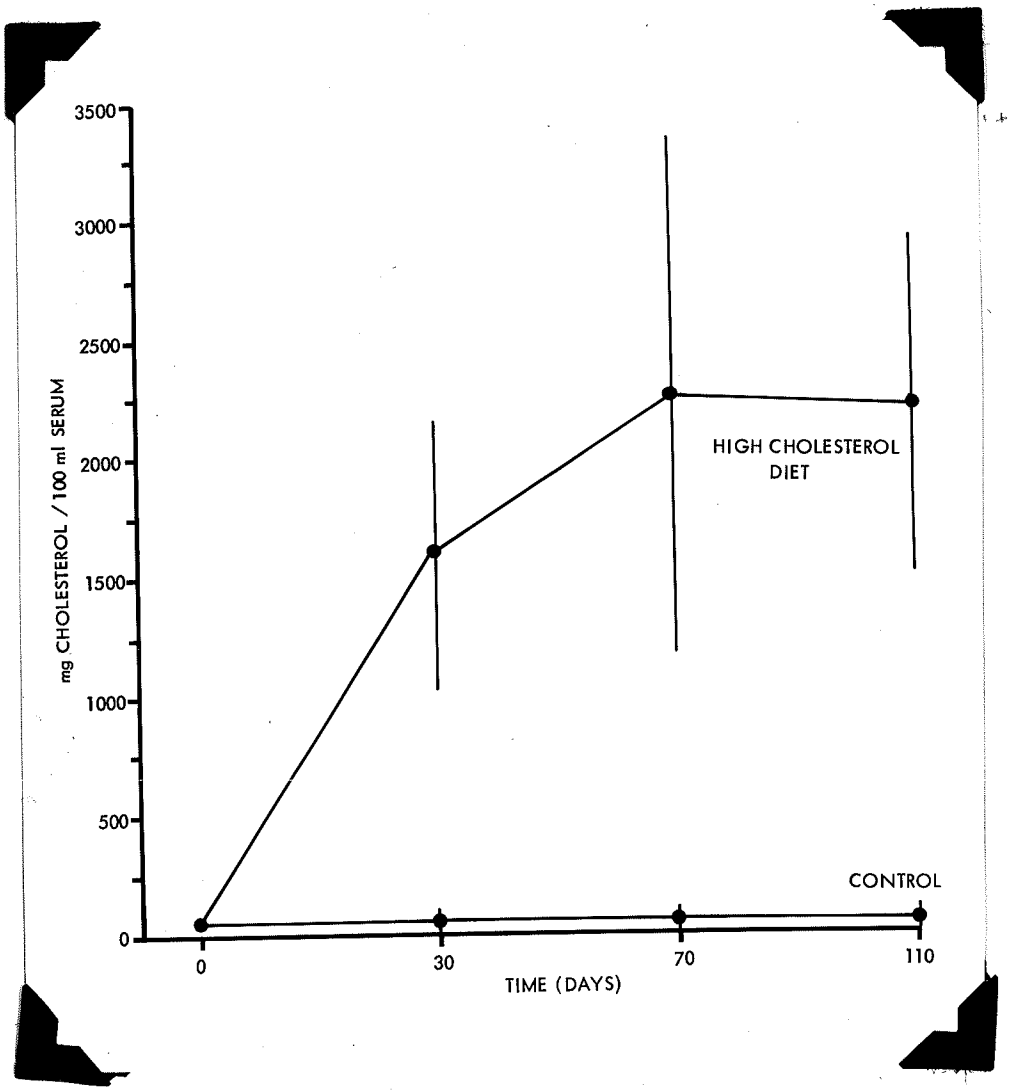

Figure 26. Blood cholesterol of 19 rabbits treated with one gram cholesterol daily and the control group (5 rabbits) maintained on the same diet without cholesterol. (Means and standard deviation).

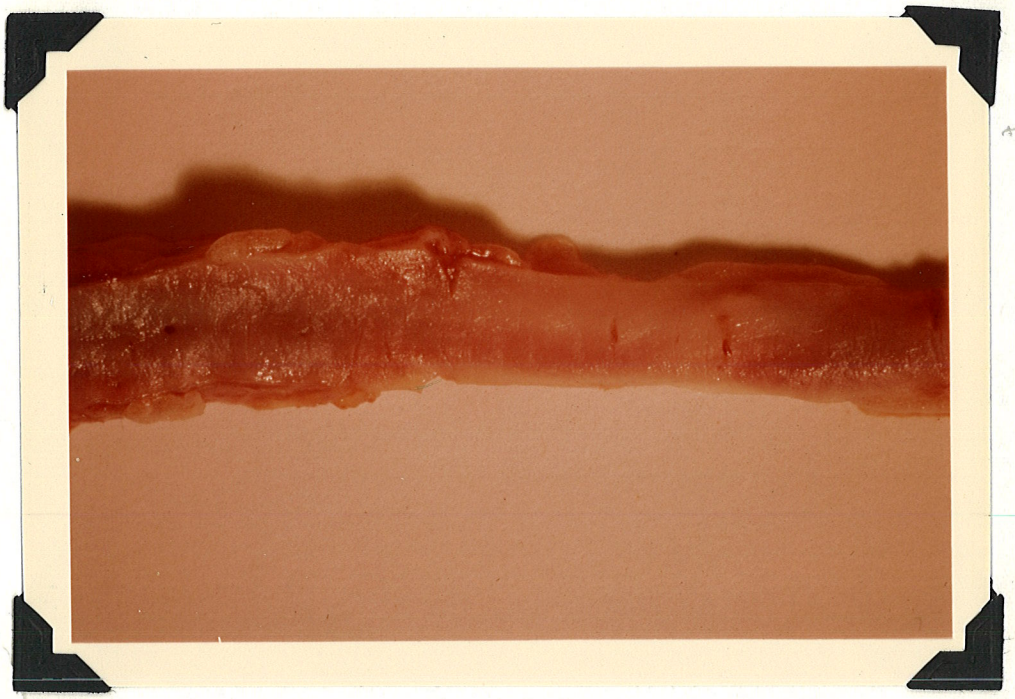

Figure 27. Gross specimen of the aorta of one of the rabbits in the control group.

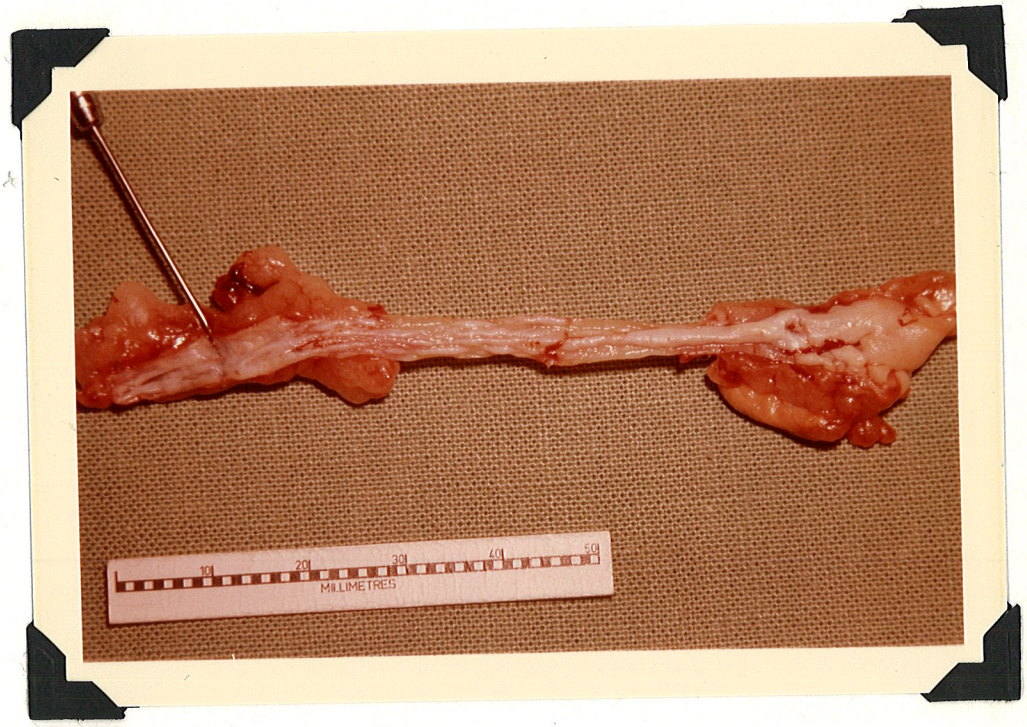

Figure 28. Gross specimen of the atherosclerotic aorta of a rabbit eight months postoperatively, using stapler for end-to-end anastomosis. The atherosclerotic plaques are well demonstrated. The needle is pointing to anastomotic site.

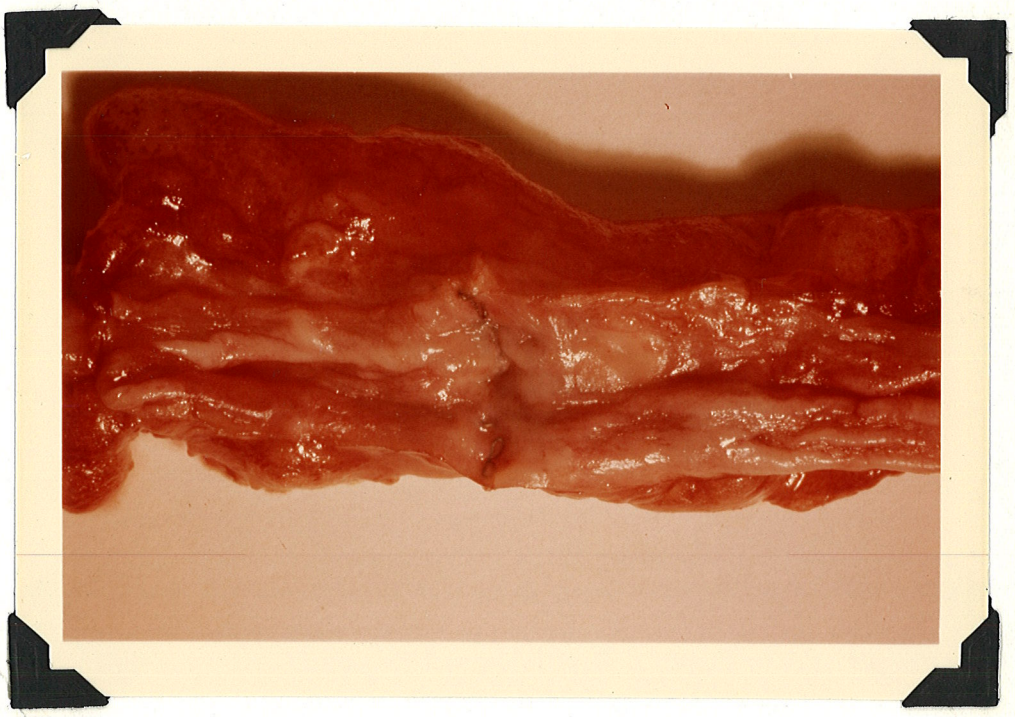

Figure 29. Close up view of a gross specimen of the atherosclerotic aorta of a rabbit eight months postoperatively, using the stapler for anastomosis.

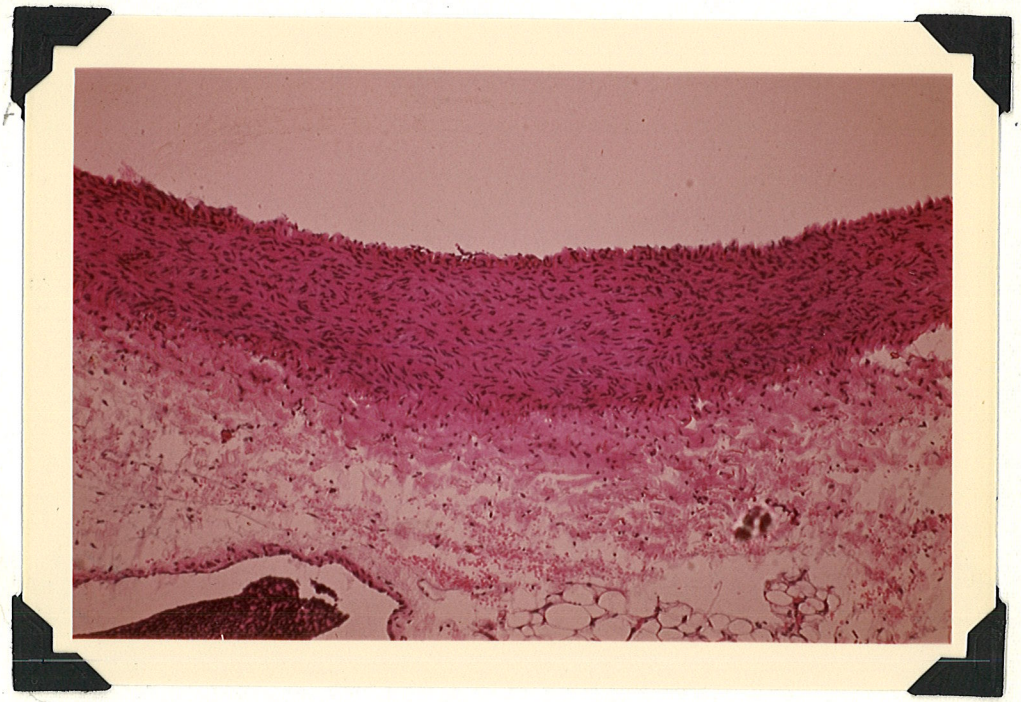

Figure 30. Microscopic section of the aorta of one of the rabbits in the control group, showing normal aorta.
H & E stain X. 75.

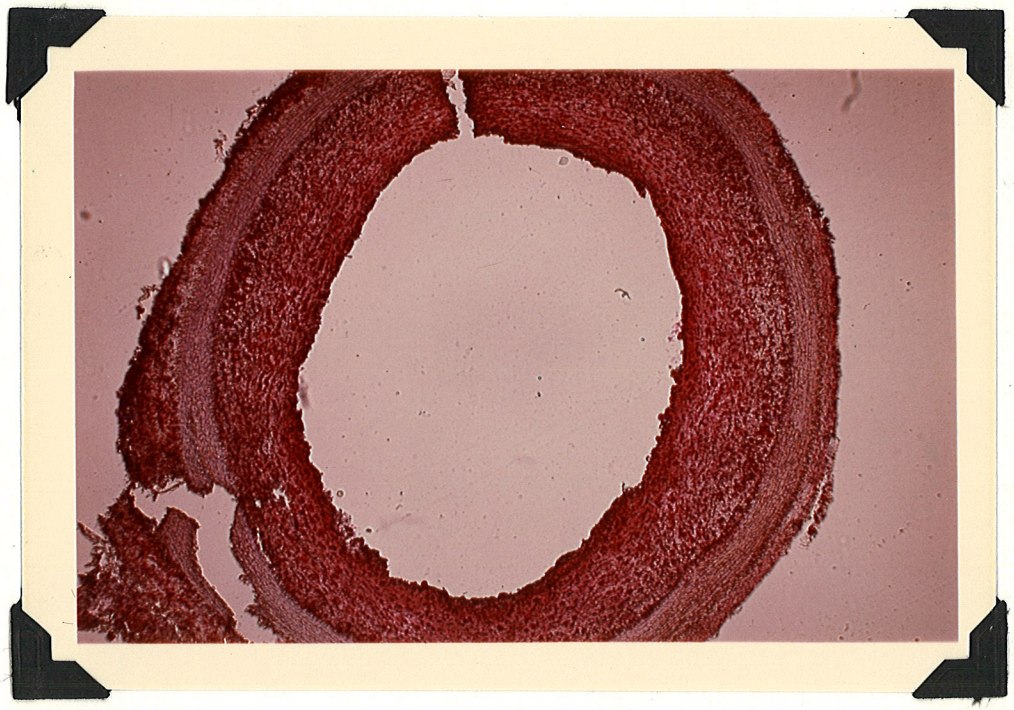

Figure 31. Microscopic section of the aorta of one of the rabbits in the high cholesterol diet, showing atherosclerotic plaque involving the whole circumference of the lumen. Oil Red O stain X. 40.

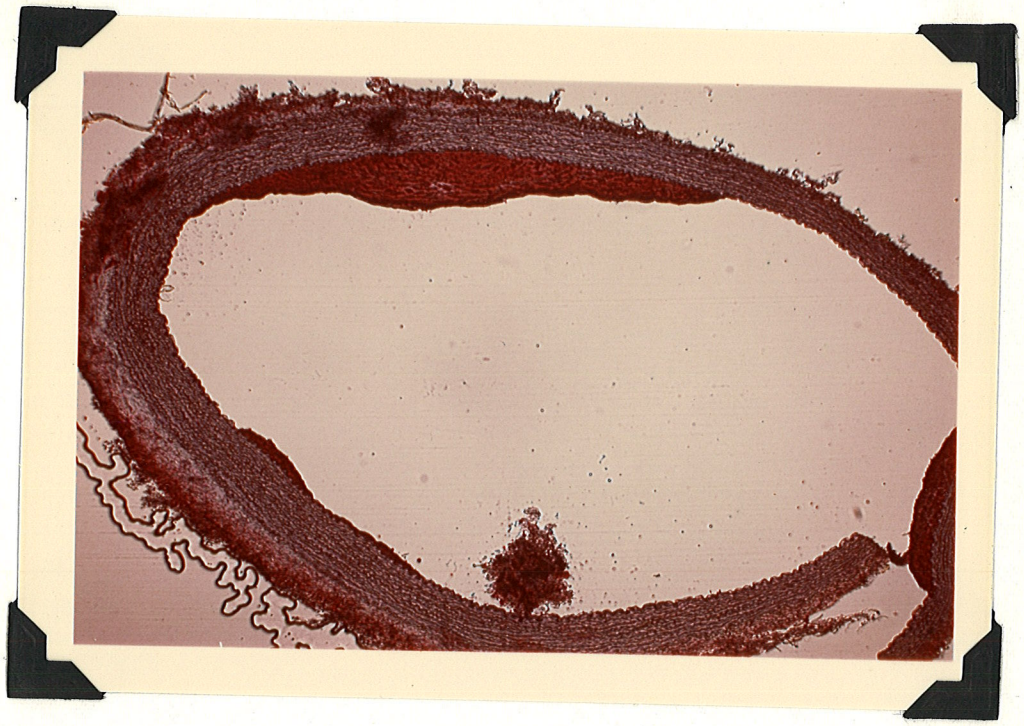

Figure 32. Microscopic section of the aorta of a rabbit showing several atherosclerotic plaques in different stages of development.
Oil Red O stain X. 40.

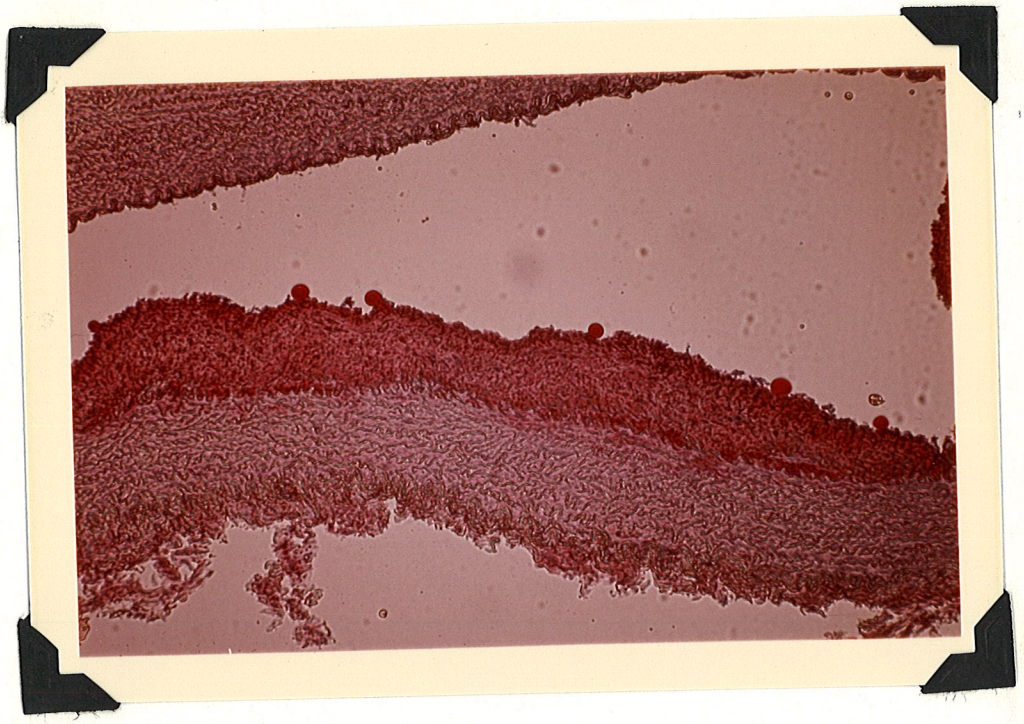

Figure 33. Microscopic section of the aorta showing an atherosclerotic plaque. There is evidence of cholesterol deposition in the media. Oil Red O stain X. 100.

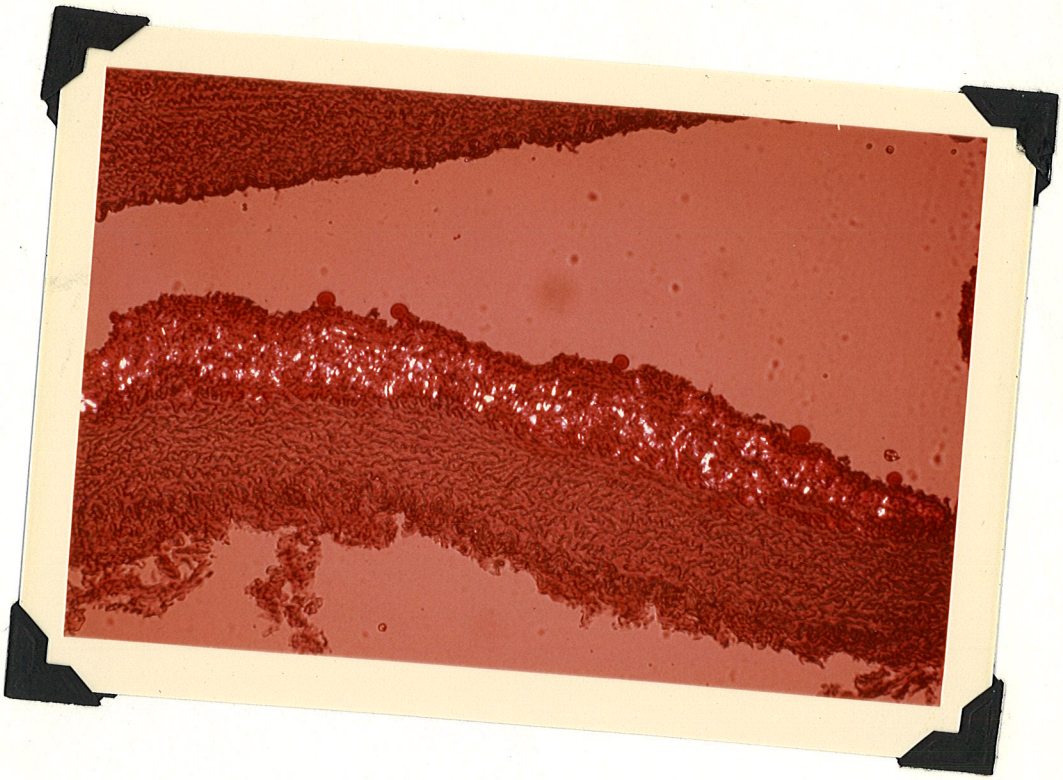

Figure 34. An atherosclerotic plaque under polarizing illumination, showing crystals of cholesterol.
Oil Red O stain X. 75.