THE USES OF PLASTIC TUBES IN THE REPARATIVE SURGERY OF BATTLE INJURIES TO ARTERIES WITH AND WITHOUT INTRA-ARTERIAL HEPARIN ADMINISTRATION*

THOMAS J. DONOVAN, M.D.

FROM THE NAVAL MEDICAL RESEARCH INSTITUTE, BETHESDA, MARYLAND

BACKGROUND

DEBAKEY AND SIMEONE in an excellent review article[1] point out that 68.6 per cent of over 3000 amputations performed in two theaters of operation in World War II were necessitated by tissue loss alone, 19.5 per cent were due to arterial injuries *per se,* and 11.9 per cent were caused by gas gangrene and other infections. They indicate that the tremendous amount of tissue destruction caused by the speed and multiplicity of modern war missiles and the time lag between injury and treatment decide the fate of the majority of limbs before reparative surgery can be undertaken. It is possible, however, that in the event of another war the increasing number of civilian casualties from air raids may reduce this interval between injury and treatment. Furthermore, the enormous tissue destruction and loss of collateral circulation show clearly that the only hope for avoiding gangrene with these injuries lies in maintaining patency of the main artery to the limb—at least until post-traumatic edema subsides and collateral circulation becomes re-established.

The best methods for repairing these arteries are unfortunately impractical under battle conditions. The suture technics of Carrel and Guthrie will not bridge the gaps left by the loss of arterial substance. The technic of Blakemore[2] using venous-lined vitallium tubes preserves the principle of intima-to-intima coaptation, but is usually too time-consuming and complex for use under battle conditions by the average military surgeon. A simple reparative technic using lucite tubes was introduced toward the end of the last war. The method was not properly evaluated because of the unfavorable conditions during battle for making follow up observations and controlling the important variables. This investigation was undertaken to determine how well plastic tubes bridge gaps in arteries and the reasons for their relative success or failure. The ideal reparative technic for arteries ablated in battle should be simple, avoid thrombosis effectively, and use materials well tolerated in tissues.

Lucite, a methyl methacrylate polymer, has been shown to be relatively well tolerated in animal and human tissues. Polyethylene,† another synthetic plastic, is made by polymerizing ethylene under heat and pressure to hydro-

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* The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large. Submitted for publication January, 1949.

† The polyethylene tubing used in these studies was of formulation PHF, purchased from Surprenant Mfg. Co., 199 Washington Street, Boston, Mass.

carbon chains somewhat longer than those of paraffin. In addition to its chemical similarity to paraffin, polyethylene has the advantage of being flexible without plasticizers and in this respect is more suitable for replacing segments of arteries near joints.

TABLE I.—*The Coagulation Time (Minutes) of Blood in Contact with Various Surfaces*

Series	Polyethylene	Lucite	Glass	Paraffin	Collodion	No. of Comparisons	End Point	Diam. of Tubes (mm.)	Blood Used
Authors	11.5	—	5.3	12.4	12.5	30	Earliest sign of clotting	5	Canine
Hirschboeck	—	13.9	6.2	18.3	—	10	Complete clotting	10	Human

Ingraham, *et al.*[3] have reported that pure polyethylene caused minimal foreign body reaction and gliosis when implanted in the cerebral cortex of animals. They stressed the importance of using pure polyethylene, however, because any traces of the antioxidants or plasticizers used commercially to enhance its insulating or flexible properties have incited marked fibrosis and foreign body reaction. To establish the purity of the polyethylene used and to study its reaction in tissues, small pieces of polyethylene and lucite were inserted subcutaneously in the backs of 30 rats at the outset of this study. The animals were sacrificed at intervals postoperatively and the tissues surrounding the plastic studied histologically. Figure 1 shows that the tissue reaction at three months to pure polyethylene resembles that caused by the relatively well-tolerated lucite.

Clotting times were then performed under controlled conditions in glass and polyethylene tubes and in glass tubes lined with paraffin and collodion. The *in vitro* capacity of polyethylene for delaying coagulation is similar to that of lucite (Table I), being about twice that of glass and nearly as great as paraffin and collodion.[4] Surface tension studies (Table II) indicate that

TABLE II.—*The Values (Gm/cm.) for the Adhesive Force Between Water and the Surfaces of Polyethylene and Glass. These Figures Are Compared with Hirschboeck's Values for Glass, Lucite, Paraffin and Collodion*[5] *and the Established Value for Glass.*[6]

Series	Polyethylene	Lucite	Glass	Paraffin	Collodion
Authors	+0.034	—	+0.073	—	—
Hirschboeck	—	+0.038	+0.053	−0.037	+0.034
Harkins and Brown	—	—	+0.0736	—	—

polyethylene, like lucite, follows Lampert's rule that the capacity of a surface for delaying coagulation is inversely proportional to its "wettability."[4-7]

With this background polyethylene tubes were first tested by bridging gaps in the aorta of dogs with a technic similar to that of Hufnagel, who reported permanent anastomosis of the thoracic aorta of dogs using lucite tubes.[8]

FIG. 1A

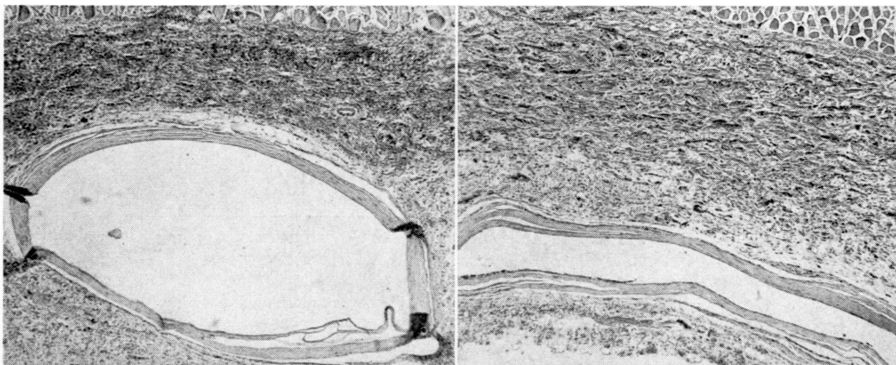
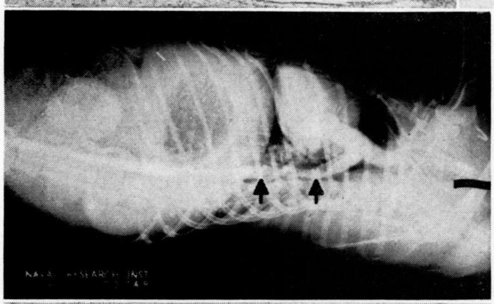


FIG. 1B

FIG. 2



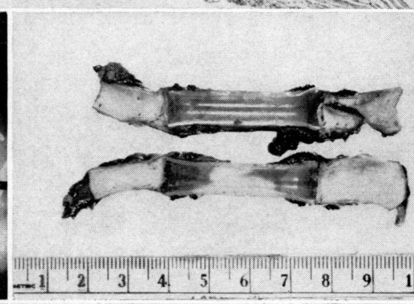
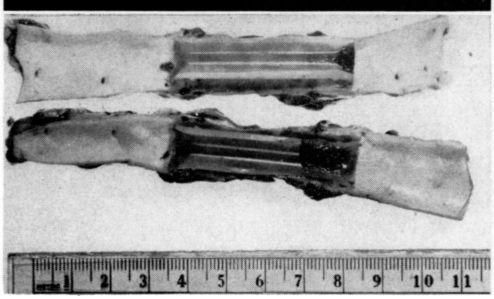


FIG. 3

FIG. 4



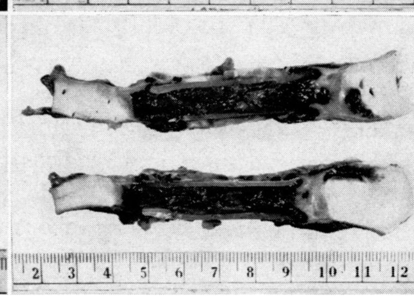


FIG. 5

FIG. 1.—The tissue reaction to polyethlene (A) and lucite (B) three months after subcutaneous insertion into rats. The fibrous capsule surrounds the space from which the plastics were removed during fixation. The width of each piece of plastic represented by the diameter of the capsule was about 2 mm. while the length approximated 1 cm.

FIG. 2.—Roentgen ray of the thoracic aorta 12 months after anastomosis with a polyethylene tube of 5 mm i.d. Arrows indicate the ends of the tube.

FIG. 3.—The aorta and tube of the animal in Figure 2, showing the tissue proliferation bridging over the vulnerable tube-vessel junction, thus inhibiting thrombosis.

FIG. 4.—An aorta and tube partially thrombosed nine months postoperatively.

FIG. 5.—A completely thrombosed aortic intubation in a dog sacrificed six months postoperatively. Both ends of the clot are almost completely covered with endothelium.

I. Aortic Intubations

MATERIALS AND METHODS

Description of the polyethylene tubes. Stock polyethylene tubing of 5.5 and 7.5 mm. i.d. was divided into lengths of 4 to 4.5 cm. and turned to a wall thickness of about 1 mm. The internal diameters were chosen to stimulate the size of the human femoral artery. Holding ridges of 1 mm. width and height were left about 5 mm. from each end of the tube. The ends of the tube were turned almost to knife-edge thinness and then flared by slowly inserting a smooth metal die heated to the softening temperature of the polyethylene. If any flaw was found on any part of the tube, it was discarded. The tubes were sterilized in 70 per cent alcohol or 1 to 1000 zephiran for 18 hours prior to operation.

Operative technic. The animals were premedicated with 0.25 grain of morphine, 0.01 grain of atropine and anesthetized with 6 per cent nembutal (1 cc. per 5 pounds body weight). Supplementary doses of nembutal were given later as needed through a plastic tube introduced into the vein of the front leg after the method of Zimmermann.[9] Positive pressure oxygen was given during the operation through an intratracheal tube of Koroseal by a mechanical respirator.

The seventh rib was resected and the pleural cavity entered through its bed. Five pairs of intercostal arteries were ligated and divided to make patency of the anastomosis more critical to the animal's survival. Division of these intercostal arteries probably eliminated the intercostal-to-intercostal collateral routes and impeded the subscapular-intercostal and internal mammary-intercostal anastomoses. It did not, however, interfere with the internal mammary-inferior epigastric pathways of collaterial circulation. The aorta was then freed from the thoracic duct and vagus nerve and the Gross aortic clamps applied for hemostasis.[10] The aorta was then divided or a short segment excised and the Hufnagel aorta spreader introduced distally to facilitate the atraumatic insertion of the polyethylene tube.[11] The limited excision was done in this study in an effort to reduce the strain on the ligatures and avoid subsequent aortic rupture from this cause. The tube was ligated in place with large braids of No. 2 silk strands, as suggested by Hufnagel,[8] to give multiple point fixation of the aortic wall and prevent its necrosis and rupture. The ligature behind the holding ridge was applied tightly while the one nearest the flare was tied more lightly. The tube and vessel were irrigated with saline and the proximal end inserted and ligated in a similar manner. The distal clamp was then removed and the proximal clamp released gradually while the animal was placed in a moderate Trendelenburg position. This obviated the hypotensive effect of splanchnic pooling so that usually only slight tachycardia was noted on release of the clamps.[12] The period of aortic occlusion rarely exceeded ten minutes and no paraplegia from this cause occurred. The aorta was repleuralized and the chest closed with chromic pericostal and interrupted cotton sutures.

Penicillin in saline solution (500 units/cc.) was used to irrigate the pleura periodically during the operation and penicillin in oil was given intramuscularly for several days postoperatively. No heparin or other anticoagulants were given at any time to these animals.

Postoperative observations. The anastomoses were studied postoperatively by observations on the oscillations,* strength, and warmth of the hind quarters. Absence of paraplegia is good evidence of patency during the immediate postoperative period. Later in the postoperative course the development of collateral circulation makes this a less reliable sign. At about three months postoperatively, roentgenograms of the aorta were taken using thorotrast or 70 per cent diodrast intravenously and repeated just prior to sacrifice from 6 to 12 months postoperatively, when pathologic studies were made.

RESULTS

A. *Initial group.* In the initial group of 14 aortic anastomoses, six dogs died on an average of ten days postoperatively from aortic rupture associated with clotting in the polyethylene tube. In four of the six aortic ruptures the tubes were too large, causing intimal trauma at the time of insertion and subsequent pressure necrosis of the aortic wall. Three animals developed thrombosis and paraplegia and were sacrificed. Some of the thromboses in this initial group were due to intimal damage during insertion and/or roughness and asymmetry of the tube. The anastomoses in two animals, one weighing 9 Kg. with a tube of 5.5 mm. i.d. and a 21 Kg. dog with a tube of 7.5 mm. i.d., remained open permanently. These animals were sacrificed 12 and nine months postoperatively.

B. *Second series.* Table III shows the results of a series of anastomoses with tubes of 7.5 mm. i.d. without the above-mentioned technical flaws. Two of the nine anastomoses remained permanently functional. Three of the fatalities were from hemorrhage and three from mesenteric embolism, two of the latter following large doses of intravenous thorotrast. The average length of survival in the fatal anastomoses was 51 days.

Pleural adhesions of varying density were found in all the animals autopsied more than three months postoperatively. Repleuralization of the tube and aorta did not completely prevent the adherence of pleura to the tube and adjacent tissues. The ends of the aorta, separated by the tube, were united in a few weeks by a neomembrane composed largely of fibrous tissue completely enveloping the tube. The chromic pericostal sutures and the intrapleural penicillin could not be incriminated in the fibrotic reaction, since the

* Oscillometry was recorded as 4 plus, maximal; 3 plus, moderate; 2 plus, decreased; 1 plus, minimal; and 0, absent. From 2 to 4 plus is considered normal range while 1 plus or 0 usually means decreased blood flow to the limb from thrombosis, embolism, or other causes. Oscillometric studies are valuable as corroborative data when trends and not individual observations are considered, but they do not compare with angiography for accuracy and amount of information given.

animals autopsied up to three weeks postoperatively were free of adhesions and widespread inflammatory reactions. In none of these animals was there any evidence of pleural sepsis.

C. *Permanent intubations.* Of the four permanent intubations, one was completely free of clots, two were partially thrombosed and one was completely thrombosed. Figure 2 shows a roentgenogram of the completely patent anastomosis 12 months postoperatively. Oscillations remained normal throughout the postoperative course. Figure 3 shows the appearance of the tube and aorta at the time of sacrifice. The tissue proliferation (connective tissue lined with endothelium) characteristic of the permanent intubations can be seen at both ends of the tube bridging over the vulnerable tube-vessel junctions, thus inhibiting thrombosis.

TABLE III.—*Results of Anastomoses of the Thoracic Aorta in Dogs with Polyethylene Tubes*

No.	Weight in Kg.	Time of Survival	Cause of Death	Condition of Tube	Comment
1	18	8 months	Sacrificed	Small clot in tube	Roentgen ray showed patency
2	18	18 days	Mesenteric embolism	Partial thrombosis at distal tube-vessel junction	
3	18	3 months	Mesenteric embolism	Small clots at tube-vessel junctions	Oscillations disappeared after 40 cc. thorotrast and returned after embolus
4	16	4 hours	Massive hemothorax	Fibrin deposition in tube and at proximal tube vessel junction	
5	21	4 months	Mesenteric embolism	Partial thrombosis at proximal tube-vessel junction	Embolism followed 40 cc thorotrast and recurred
6	21	11 days	Aortic aneurysm with leakage	Small clots at tube-vessel junctions	
7	21	4 days	Thrombosis of tube	Complete thrombosis of proximal end of tube	
8	19	6 months	Sacrificed	Complete thrombosis of long duration	Marked collateral circulation by roentgen ray
9	21	4 months	Massive hemothorax	Complete thrombosis of recent origin	Aortic rupture high above tube; marked cardiac hypertrophy

The two permanent intubations with small intraluminal clots had one to two plus oscillations during most of their postoperative course. The tubes in the aortograms were less clearly defined, also indicating partial thrombosis. Figure 4 shows one of these partially thrombosed tubes at autopsy.

Roentgen ray studies of the animal with complete thrombosis of the tube showed the complete blockage and marked dilatation of the collateral channels. The internal mammary arteries, greatly enlarged and tortuous, anastomosed with equally large inferior epigastric arteries, but no notching of the ribs was apparent. The subscapular arteries were also moderately expanded, but the lowermost intercostals were not visible. Oscillations were moderate the first month in this animal, slight during the second month and absent there-after despite normal function of the hind legs. Figure 5 shows this tube and aorta at the time of sacrifice.

COMMENT

Hufnagel's five permanent anastomoses of the aorta with lucite tubes in a series of 15 intubations were notable for the complete absence of clot formation. Nine of the ten fatal intubations were also free of clots.[8] These results contrast sharply with the prevalence of clotting in this study of polyethylene and suggest that lucite tubes are superior to those of polyethylene in respect to the avoidance of thrombosis. The larger sizes of the lucite tubes and aortas, however, must be considered as contributing to the superior results. The significance of this size factor will be discussed in the next section dealing with intubations of the femoral artery.

II. Intubations of the Femoral Artery

MATERIALS AND METHODS

Description of the polyethylene tubes. Polyethylene tubing of 2.7 mm. i.d. and 3.5 mm. o.d. was cut into lengths of 2 to 2.3 cm. The ends were flared with a hot die. Holding ridges were placed around the tubes by applying melted polyethylene about 3 mm. from each end of the tube. Some of these tubes were soaked in heparin (sodium heparin, Lederle, 10 mg. per cc.) for one month before operation. This was done because surface tension studies with polyethylene tubing indicated that the polyethylene absorbed water over a period of days and therefore might absorb aqueous heparin.[4] Other tubes were lined with silicone film,* which inhibits blood coagulation, by filling their lumina with silicone and silicone diluted with toluene to concentrations of 1/100 and 1/200. The toluene was baked off and the tubes rinsed for several hours in distilled water.

Description of the lucite tubes. Lucite tubes, 2 to 2.3 cm. long, were turned from stock tubing of 3 mm. i.d. with ridges about 3 mm. from each end. The ends were flared with a warm die, making them similar in shape to the polyethylene tubes but slightly larger in internal diameter. At no time was the inner surface of the tubes scratched or handled roughly. All tubes were carefully inspected for flaws and discarded if any irregularity or asymmetry was found.

Operative technic. The femoral artery was exposed from just below the groin to just above the knee. The long saphenous artery, which arises medially from the femoral artery about 5 cm. below the inguinal ligament, was freed and its branches divided. A polyethylene side tube about 60 cm. long, 1 mm. o.d. and 0.4 mm. i.d., was threaded into the long saphenous artery for about 1 cm. and held in place with four cotton ligatures. The other end of this tube

* The silicone was General Electric's Dri Film 9987 usually used on glass surfaces. The silicone for plastic surfaces was not available.

was led with a long flexible needle subcutaneously and dorsally through the skin of the costovertebral area, a location inaccessible to the animal's teeth. Through this tube 35 per cent diodrast was injected at 24-hour intervals postoperatively and the distal femoral artery visualized by arteriography (Fig. 6). A stylet was placed in the end of the tube between injections to prevent retrograde bleeding and clotting in this side tube.

The branches of the femoral artery were ligated and divided from above this long saphenous artery to the bifurcation of the femoral into anterior tibial and popliteal arteries. Bull dog clamps were applied, the femoral artery divided, and the adventitia retracted from the cut ends of the vessel. After the ends of the artery were irrigated with saline the plastic tube was inserted, using a new instrument designed to retract the arterial walls. The tube was

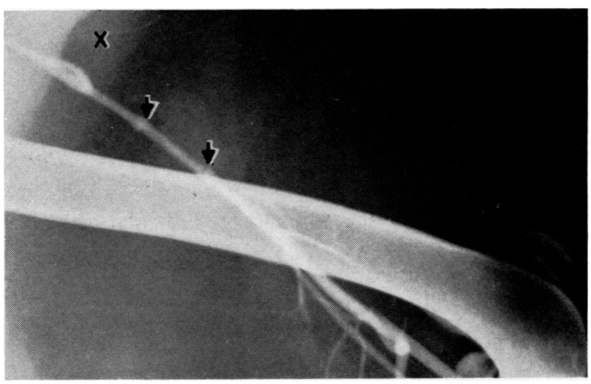


FIG. 6.—A polyethylene tube bridging a gap in the femoral artery of a dog two days postoperatively. Arrows mark the ends of the tube (note increased capacity) and X, indicates the small polyethylene side tube in a branch of the femoral artery proximal to the anastomosis.

ligated in place with No. 20 cotton ligatures on each side of the holding ridges and the adventitia replaced over the ends of the tube.

The instrument used to retract the vessel walls was constructed by attaching semicircular steel rockers to the tips of an outside caliper by means of a steel pivot (Fig. 7). Four barbless hooks were connected by silk suture material to the ends of the rockers. By adjusting the screwlock on the caliper, vessels of various sizes could be spread in the form of a square larger than their internal diameter (Fig. 7). This instrument has facilitated the insertion of these artificial tubes and minimized intimal damage during insertion, thus obviating subsequent thrombosis from this cause.[13]

In two animals with otherwise identical technic the ends of the divided artery were ligated. In one animal circular ligatures were used and in the other the Poppen type of suture ligature was employed, which invaginates the arterial wall and apposes the intima.[14]

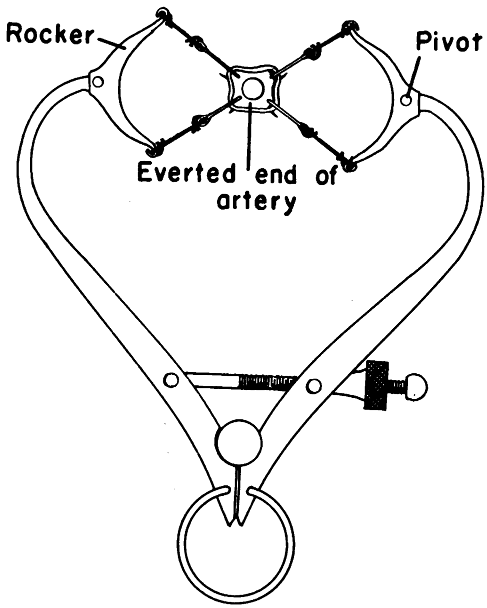


FIG. 7.—Diagram showing vessel spreader. Lower portion represents a four-inch caliper with screw-lock and spring. At the upper ends are the rockers attached with steel pivots. Four silk threads are shown leading to the hooks which retract the vessel walls.

Intima coaptation technics were also studied, *e.g.*, suture anastomosis and polyethylene tubes lined with veins after the method of Blakemore, *et al.*[2] (Fig. 8).

Postoperative observations. These anastomoses were studied postoperatively by daily arteriograms as described previously. In addition, observations on the oscillations, strength, and warmth of the extremities were made three times daily and the artery examined under anesthesia just prior to sacrifice.

RESULTS

A. Anastomoses with plastic tubes.

Duration of patency. Table IV shows a summary of the results in typical series of polyethylene and lucite intubations of the femoral

TABLE IV.—*Results of Anastomoses of Femoral Arteries of Dogs with Polyethylene and Lucite Tubes*

Dog No.	Weight in Kg.	Artery	Tube	Roentgen Ray Study of Course in Hours: Patent	Thrombosed	Duration of Patency in Days
1	28	Right	Polyethylene	48	72	2
		Left	Polyethylene	48	60	2
2	29	Right	Polyethylene	48	72	2
		Left	Polyethylene	72	80	3
3	23	Right	Polyethylene	10	24	½
		Left	Polyethylene	10	24	½
4	33	Right	Polyethylene	48	72	2
		Left	Polyethylene	48	72	2
	Average 28					Average 1.8
1	42	Right	Lucite	96	Dog sacrificed*	4
		Left	Lucite	24	48	1
2	35	Right	Lucite	72	96	3
		Left	Lucite	120	Dog sacrificed*	5
3	28	Right	Lucite	96	120	4
		Left	Lucite	48	72	2
4	35	Right	Lucite	72	96	3
		Left	Lucite	72	96	3
	Average 35					Average .13

* Dogs sacrificed to establish patency, as leakage from side tube prevented roentgen ray visualization.

artery. Six out of eight anastomoses with polyethylene tubes were open on the second day on roentgen ray study with an average duration of patency of slightly less than two days. The lucite tubes showed an average duration of patency of slightly over three days with six out of eight intubations open on the third day. The average period of patency of the six anastomoses using silicone-lined tubes or the four heparin-soaked tubes was not longer than with the untreated polyethylene tubes. Figure 6 shows a polyethylene tube in dog No. 4 on the second postoperative day.

Clot formation. Figures 9, 10 and 11 show the development of collateral circulation following thrombosis of the lucite tubes in dog No. 7. These

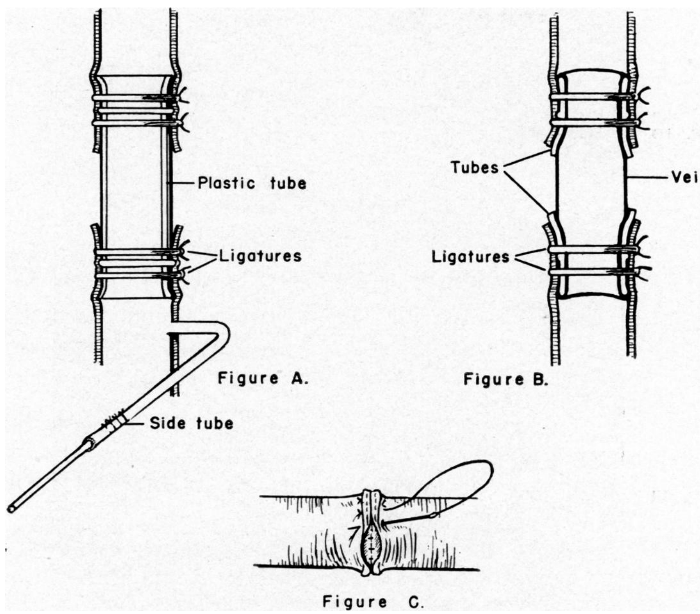


FIG. 8.—Three technics for reconstructing vessels. A. Plastic tube anastomosis. Note polyethylene side tube in a branch of the femoral artery. B. Venous-lined tubes, reproduced from Blakemore.[2] C. Suture anastomosis redrawn from Gross and Hufnagel.[10]

roentgen ray films are typical of others showing the same process occurring with polyethylene intubations. Following thrombosis the oscillations dropped to 1 plus or zero, but the hind legs never felt significantly cooler than the front legs. Emboli were seen in several roentgenograms, partially or wholly blocking the flow in the femoral, anterior tibial, or popliteal arteries (Fig. 9). In some instances their origin could be traced to the tube anastomosis by serial films. No appreciable difference was noted in the process of clot formation and extension or the development of collateral circulation in these siliconed, heparin-soaked and untreated polyethylene tubes.

Reaction to the lucite and polyethylene tubes. The adjacent tissues adhered

FIG. 9

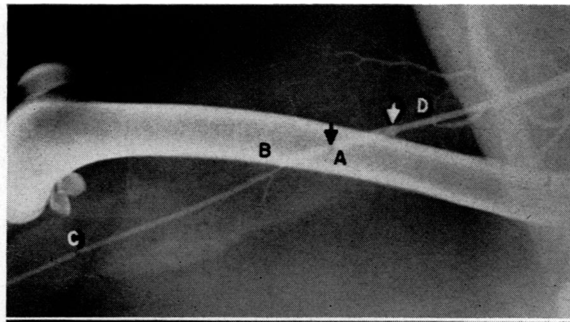


FIG. 10

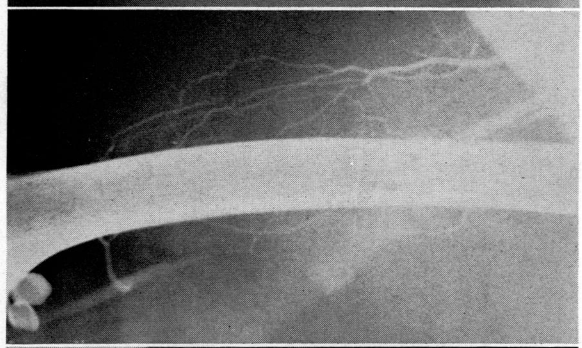


FIG. 11

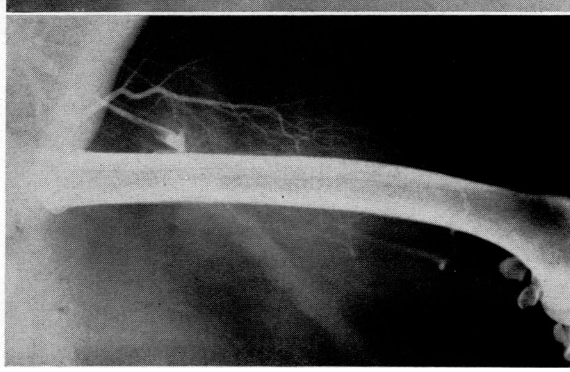


FIG. 9.—A lucite tube in the femoral artery on the fourth postoperative day. The arrows indicate the extent of the tube. (A) Demonstrates the clot almost completely occluding the distal end of the tube. (B) Shows an embolus at the bifurcation of the femoral artery completely blocking the anterior tibial artery and protruding into the popliteal artery. (C) Another small embolus in the popliteal artery. (D) Shows the narrowing of the femoral artery proximal to the tube and the development of collateral circulation which follows thrombosis of these tubes.

FIG. 10.—The lucite tube in Figure 9, 24 hours later showing complete thrombosis and further development of collateral circulation.

FIG. 11.—The other leg of the animal in Figures 9 and 10 showing the collateral circulation 48 hours after complete thrombosis of the tube.

to and enveloped the plastic tubes in a fibrous sheath of slight to moderate thickness with no discernible difference between the two plastics used.

B. Arterial ligations.

With the same operative destruction of collateral circulation as in the intubation technics, the two animals with femoral artery ligation had cold legs for about 24 hours and negative oscillations for about two weeks. After the 24-hour period following operation the collateral circulation developed as with the arterial intubations. Propagation of clots in the first few postoperative days was negligible with both ligation and intubation technics, but with the passage of weeks propagation from the tube thrombi seemed to be somewhat greater than following either type of arterial ligation.

C. Intima coaptation technics.

Examination of a suture anastomosis of the femoral artery at the end of a week showed complete patency with no fibrin deposition or clotting and the beginning of intima-to-intima union. In an anastomosis using venous-lined polyethylene tubes, roentgenograms showed patency at the end of a week. At the end of three weeks the tube was free of clots and the union between venous and arterial intima was complete. Reaction to the polyethylene tube, however, had thickened the venous wall and nearly occluded the lumen at the proximal tube-vessel junction.

DISCUSSION

The fact that some aortic intubations remain patent permanently whereas all femoral intubations clot about the third day may be explained in several ways. The pattern of blood flow in the aorta depends among other things upon the diameter of the vessel and the velocity of flow. Both of these factors vary in systole and diastole. The density and absolute viscosity of the blood, which also influence flow patterns, may or may not be constant. In spite of these variables, numerical values have been substituted in the formula for the Reynold's number.* The figure obtained for the Reynold's number during systole in the thoracic aorta of dogs is well above 2000, the critical level where laminar or viscous flow becomes turbulent in smooth pipes. The irregularity at the tube-vessel junctions further predisposes to turbulence.[15-17] Assuming that the values are correct, the significance of this higher velocity and possible turbulence in the aorta, as opposed to the femoral artery and smaller vessels, lies in the concomitant increase in the erosive power of the blood stream on freshly formed clots, since the shearing stress between circulating blood and vessel wall varies with the velocity and is much greater for turbulent than for laminar flow.†[16] Another of the possible explanations is that the large volume flow in

* The Reynold's number equals the velocity of flow multiplied by the diameter of the vessel and divided by the kinematic viscosity of the circulating fluid. Kinematic viscosity equals the absolute viscosity divided by the density of the fluid.[15]

† The fact that the shearing stress also varies inversely with the diameter of the vessel is of less importance in this range of velocities and Reynold's numbers.

the aorta may dilute or remove more effectively the locally liberated substances which promote clotting.

These considerations may explain the embolic phenomena observed frequently following the aortic anastomoses with polyethylene tubes as well as the capacity of these anastomoses for remaining open permanently. They also emphasize the important influence of the vessel size on the duration of patency of an anastomosis and qualify the apparent superiority of the larger lucite tubes over the smaller polyethylene tubes in the aortic and arterial anastomoses. In addition, these concepts modify the predictions of efficacy of these femoral intubations in the larger arteries of humans. This does not mean, however, that the results in the aortas of dogs can be extrapolated to the similar sized femoral arteries of man, since the pressure gradients (and hence velocities) are different in central and peripheral vessels.

Besides the arterial size, other technical factors which influence the duration of patency are: (1) The inner smoothness, over-all symmetry, and suitable size of the tube, (2) the intrinsic capacity of the tube for repelling water and delaying coagulation and (3) the amount of trauma to the arterial intima during insertion.

Although fatal hemothorax was a common complication in the aortic intubations, secondary hemorrhage following intubations of the femoral artery was a rare complication and usually due to tubes excessively large for the artery under repair. The greater retraction of the elastic tissue in the wall of the aorta and the higher pressures in the upper aorta (especially with a thrombus occluding the tube) probably increased the strain on the ligatures and contributed to the aortic ruptures.

Although the plastic tubes in the femoral arteries were thrombosed after two days, their gradual occlusion stimulated collateral circulation and avoided the temporary period of acute ischemia which followed arterial ligation. The marked stimulus to collateral circulation of the tube anastomoses was also demonstrated by the animal with an aortic anastomosis which maintained blood supply to the abdominal aorta sufficient to sustain normal function despite complete thrombosis of the tube and extensive operative destruction of collateral circulation.

The greatly prolonged durations of patency of the suture anastomosis and venous-lined polyethylene tubes show the superiority of these methods over the plastic tube anastomoses with respect to avoidance of thrombosis. Experienced vascular surgeons can obtain about 50 per cent permanent patencies with suture anastomoses of the dog's femoral artery. Blakemore has reported that his nonsuture method using venous-lined vitallium tubes is 85 per cent successful in day-old contaminated wounds in dogs, as compared with 40 per cent patency following suture anastomosis under these conditions.[2]

These facts plus the high percentage of thromboses which followed the Blakemore reparative technic in arterial injuries of the last war point up the difference between the results of intubations done under the ideal circumstances of the experimental laboratory and those done under battle conditions. In battle injuries to arteries repaired with plastic tubes, assurance of patency of the anastomoses beyond the period of post-traumatic edema would seem, from these considerations, to require supplementary anticoagulant therapy.

III. Intra-Arterial Heparin Administration

MATERIALS AND METHODS

Description of the tubes. The polyethylene tubes and the intubations of the femoral arteries were the same as described in the preceding section.

Heparinization. Intra-arterial heparin was infused proximal to the anastomosis by the same route that 35 per cent diodrast was injected for the arteriograms described previously, *i.e.,* through a subcutaneous polyethylene side tube from the skin of the costovertebral area to the lumen of the long saphenous artery (Fig. 6). Sodium heparin, Lederle, (0.25 mg. per Kg. of body weight in 10 cc. of saline) was given shortly after operation into the left femoral artery and repeated every two hours, in some animals every three hours, day and night. The right side tube was used only for postoperative arteriograms. Unlike human beings with arterial injuries, dogs continually move about following operation, and unless the side tube has a relatively thick wall, it will kink and leak after a few days of heparin administration. The side tubes in this preliminary study of intra-arterial heparinization were too thin, and in most instances subcutaneous leakage of heparin necessitated cessation of therapy about the fifth day. A thicker side tube is now being used (0.4 mm. i.d. and 1.0 mm. o.d.) which is attached to the main tube in a manner that eliminates the necessity of intubating a branch of the femoral artery, thereby simplifying the operative technic and sparing another artery for collateral circulation.

Postoperative observations. The follow-up observations were made with oscillometry and periodic arteriograms in the manner described previously. The anastomosis of the uninjected artery reflected the systemic effect of the intra-arterial heparin administration and the irrigated intubation showed the combined local and systemic effect of the heparin. By contrasting the results in the two femoral intubations, the local effect of heparin could be evaluated in a series of animals.

Since dogs as well as human beings vary in their responses to a given dose of heparin, coagulation times were done preoperatively and at intervals postoperatively to evaluate the daily heparin effects in these animals. Investigators in this field have been impressed with the inadequacies of coagulation times in evaluating the effect of heparin. Control clotting times vary widely even in the same animal from time to time. One of the factors responsible is the varying amount of trauma incident on transferring blood from the animal's vein to the tube. Another factor is the ambiguous nature of most endpoints. In addition, the actual fluidity and coagulability of the blood probably varies normally from time to time according to the relative concentrations of heparin and thromboplastin (and other clotting substances) in the circulating blood.[18-20] The concentration of heparin cofactor in the plasma may also vary and thus alter the response to a given dosage of heparin.[21, 22]

An attempt was made to control the first factor by letting the blood flow freely through a No. 20 B-D needle with exclusion of air into the clean syringe lined with liquid petrolatum after uniformly direct venepunctures. The sample was then transferred carefully to a glass tube of 5 mm. i.d., bent in the form of a semicircle of 6 cm. radius.[23] This tube was moved uniformly at definite intervals until complete clotting occurred. In an attempt to make the end-points more precise the times of the earliest definite fibrin precipitation and the complete immobility of the blood in the tube were measured by stop watch

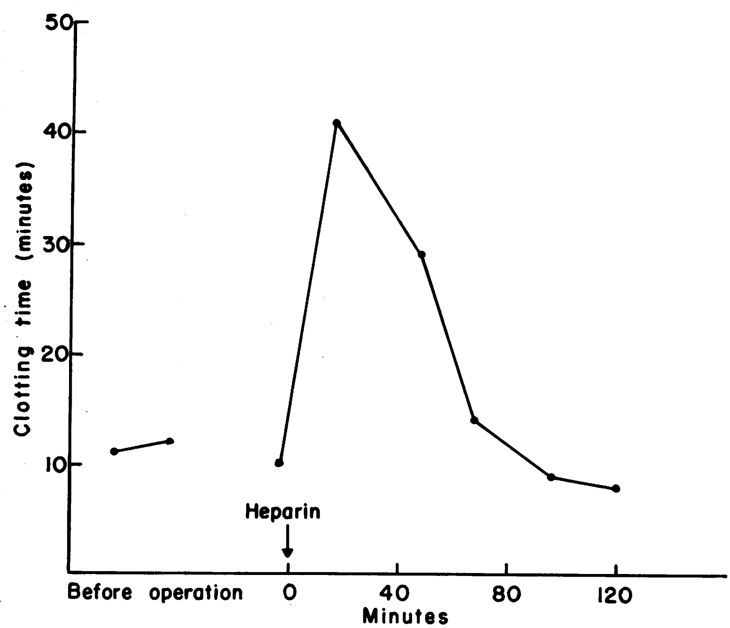


FIG. 12.—The response of the venous clotting time to the intra-arterial injection of 4 mg. of sodium heparin in 10 cc. of saline in a 16 Kg. dog.

and these two durations averaged to determine the clotting time for each sample. Since it has been repeatedly emphasized that both phases of coagulation are proportional in length, the average of the duration of the first phase (prothrombin conversion to thrombin) and the duration of the first plus the second phase (fibrinogen conversion to fibrin) should give a more reproducible value for the coagulability of each sample.[23]

RESULTS

The above procedures have been done on eight dogs. Only two will be reported here because technical difficulties made the results in the other animals hard to interpret, although the general pattern of reactions was similar.

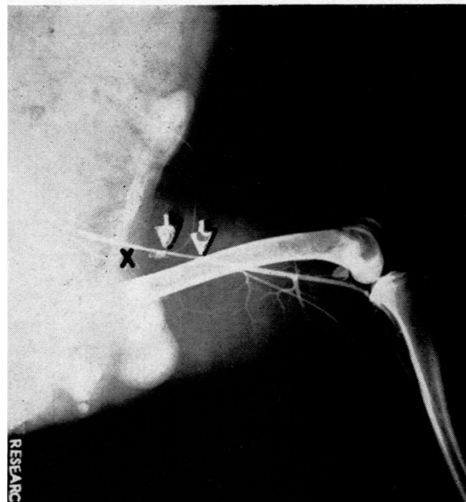
Dog 1 (16 Kg.). Four mg. of sodium heparin was given in 10 cc. of saline into the left artery every two hours for 120 hours, until subcutaneous leakage necessitated cessation of therapy. Four of the 60 doses scheduled were omitted, leaving a total of 216 mg. of sodium heparin in 540 cc. of saline given during this period. Figure 12 shows the marked prolongation of coagulation time caused by 0.25 mg. heparin/Kg. of body weight on the first day. This response became less marked during the next four days.

The left or heparinized artery was patent on the fourth postoperative day (Fig. 13). The right or control artery was open by arteriography on the third day but thrombosed on the fourth postoperative day. The right or control artery exceeded the average duration of patency in polyethylene intubations of the femoral artery by about 24 hours. The left or heparinized artery exceeded the average duration of patency by at least 48 hours.

Dog 2 (24 Kg.). Six mg. of sodium heparin was given in 10 cc. of saline into the left artery every three hours for 114 hours until leakage from the side tube prevented further therapy. These 38 injections totaled 228 mg. of heparin in 380 cc. of saline. The clotting time response to this 0.25 mg. of heparin per Kg. of body weight was slight (not more than double the control level) throughout the period of heparinization.

The left or heparinized artery was patent on the fourth postoperative day (Fig. 14). Oscillations remained about 2 plus until the seventh postoperative day. The right or control anastomosis was patent by roentgen ray on the second day and thrombosed on the third postoperative day. The right or control artery had the same duration of patency as the average of polyethylene intubations in unheparinized animals. The left or heparinized anastomosis exceeded this average duration of patency by at least 48 hours and possibly by 96 hours.

FIG. 13



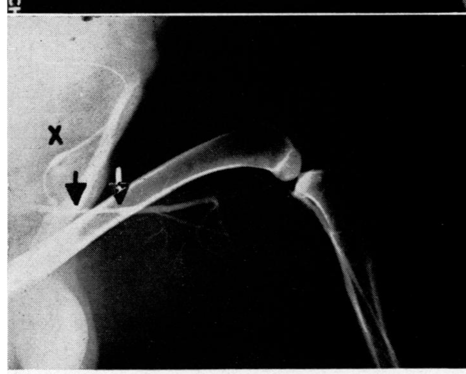


FIG. 14

FIG. 13.—The roentgen-ray of the heparinized artery of the animal in Figure 12 on the fourth postoperative day. Arrows indicate the ends of the polyethylene tube and X, a leak in the side tube which prevented further intra-arterial heparin administration on the fifth postoperative day.

FIG. 14.—An arteriogram of the heparinized femoral artery on the fourth postoperative day. Arrows indicate the ends of the polyethylene tube and X, a leak in the side tube which prevented further intra-arterial heparinization on the fifth postoperative day.

DISCUSSION

Intravenous anticoagulants are often contraindicated in war wounds, since the latter are frequently multiple and complicated by latent visceral bleeding. Furthermore, the administration and control of anticoagulants are often impractical under battle conditions. It occurred to the author that heparin might be given intra-arterially proximal to the anastomosis with constant or intermittent infusions in concentrations which would prove effective locally and yet not raise the general clotting time to a dangerous level. Heparin was chosen for intra-arterial use, because it is a potent, physiologic anticoagulant which acts instantly in a physicochemical manner.[20] It is also rapidly inactivated by nontoxic protamine sulfate given intravenously.

Although these investigations are still in progress, using a different method of intra-arterial heparin administration, two cases have been presented since they represent the general pattern of the results to date.

Although the clotting time responses to intra-arterial heparin injections in dog No. 1 became less marked with each succeeding postoperative day, the control artery seems to have obtained some systemic heparin effect, since it exceeded the average duration of patency by about 24 hours. The left or heparinized side remained patent even longer and appears to have had an added local effect.

A lack of systemic heparin effect is indicated by the clotting time studies in dog No. 2, which received the same 0.25 mg. of heparin per Kg. of body weight every three hours instead of every two hours as in dog No. 1. This lack of general effect is further evinced by the thrombosis of the uninjected artery in the usual length of time. A significant local effect is suggested by the greatly prolonged patency of the left or heparinized anastomosis.

These two examples suggest a definite local action of the intra-arterial heparin in doses not generally effective or dangerous. Although these are typical of other results, the statistical proof of this idea awaits further investigation. Furthermore, the mechanical effect of local irrigation must be ruled out by injecting similar amounts of saline without heparin in the control arteries.

Bleeding into the incision was the only complication of this technic, and its rare occurrence was due to copious leakage of heparin subcutaneously. If this route of heparin administration proves effective, it may be equally advantageous to give vasodilators in this manner, thereby delivering the various agents to the important arterioles of the muscles and deeper structures, and inducing a local hyperemia by dint of the borrowing-lending mechanism of blood distribution.[24-26] Antibiotics may likewise prove more effective by this route.

SUMMARY

1. In a preliminary study the reaction to pure polyethylene in the subcutaneous tissues of rats was similar to that caused by the relatively well tolerated lucite. The capacity of the polyethylene surface for delaying the *in vitro* coagulation of blood was also found to be similar to lucite, being about twice that of glass and nearly as great as paraffin and collodion. Surface tension studies in glass and polyethylene tubing showed that polyethylene, like lucite, follows Lampert's rule that the capacity of a surface for delaying coagulation is inversely proportional to its "wettability."

2. Polyethylene tubes were used to bridge gaps in the thoracic aorta of dogs after the method of Hufnagel.

In an initial group of 14 anastomoses, two polyethylene tubes remained patent for periods of 9 and 12 months when the dogs were killed. Half of the deaths in this group were due to aortic rupture with fatal hemothorax. In a second series of nine intubations, five animals were apparently healthy at the end of three months. Two of these five later developed fatal mesenteric embolism following aortograms with large doses of intravenous thorotrast. Two remained well for periods of six and eight months when they were killed.

Of the four permanent intubations one was completely patent 12 months postoperatively, two were partially thrombosed, and one was completely thrombosed. Marked enlargement of collateral pathways sustained normal function in the dog with complete thrombosis.

3. Anastomoses of the femoral artery with lucite and polyethylene tubes were performed with a new instrument for facilitating the insertion of artificial tubes. They were followed by frequent oscillometric examinations and daily arteriograms. The anastomoses with plastic tubes were compared with arterial ligations, suture anastomosis, and an anastomosis with venous-lined polyethylene tubes.

The average duration of patency of the polyethylene tubes was two days, while the slightly larger lucite tubes remained patent for three days. This average period of patency in polyethylene intubations was not prolonged by lining the tubes with silicone or soaking them in heparin preoperatively. During and after thrombosis of these tubes abundant collateral circulation developed and the limb was never acutely ischemic. Conversely, the animals with arterial ligations developed markedly ischemic limbs for the 24-hour period following ligation. The intima coaptation technics were much superior to the plastic tube anastomoses in respect to the avoidance of thrombosis. Since these more physiologic technics are usually impractical under battle conditions, further study of the simple anastomoses with plastic tubes was undertaken using supplementary anticoagulant therapy.

4. Because intravenous anticoagulants are contraindicated in most war wounds, study was initiated on a method for giving intra-arterial heparin proximal to the anastomoses of the femoral artery. The heparin was infused through the left side tube used for postoperative arteriograms and the right or uninjected artery acted as a control. Venous clotting times were also done to evaluate the systemic effect of the intra-arterial heparin. Typical cases were presented to indicate the kind of results which have occurred to date. They suggest that an adequate local effect may be achieved without prolonging the general clotting time significantly.

CONCLUSIONS

1. Pure polyethylene, like lucite, is relatively well tolerated in the tissues surrounding the femoral artery of dogs and in the subcutaneous tissues of

dogs and rats. The mediastinal tissues of dogs also showed slight to moderate reaction to pure polyethylene.

2. Polyethylene has a capacity for delaying the *in vitro* coagulation of blood which is similar to that of lucite, being about twice that of glass and nearly as great as paraffin and collodion.

3. Polyethylene repels water relatively well and, like lucite, follows Lampert's rule that the capacity of a surface for delaying coagulation is inversely proportional to its "wettability."

4. Polyethylene tubes will permanently bridge gaps in the thoracic aorta of dogs. Many of these anastomoses, however, are complicated by thrombosis, embolism, and aortic rupture.

5. Anastomoses of the femoral arteries of dogs with polyethylene and lucite tubes have average durations of patency of two and three days, respectively. Lining the polyethylene tubes with silicone or saturating them with heparin preoperatively did not increase the average duration of patency.

6. A new instrument for retracting the walls of arteries facilitates the insertion of these artificial tubes.

7. Although the plastic tube anastomoses are inferior to intima coaptation technics in respect to the avoidance of thrombosis, their gradual occlusion over a period of days stimulates collateral circulation and prevents the marked ischemia which follows arterial ligation.

8. In battle injuries to arteries repaired with plastic tubes, assurance of patency of the anastomoses beyond the period of post-traumatic edema would probably require supplementary anticoagulant therapy. Although intravenous anticoagulants are usually impractical in war wounds, a new method for the intra-arterial administration of heparin has shown promise and merits further study.

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