Replantation of Amputated Extremities

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INTRODUCTION

A review of the current status of replantation of limbs seems particularly timely for several reasons. Extremity replantation has now been accomplished in widely varying geographic regions, and the experience gained with these procedures is sufficiently uniform to permit formulation of an outline for management of patients following traumatic amputation. Furthermore, enough time has elapsed since replantation in a small number of cases to allow the drawing of tentative conclusions regarding long-range results. The interest of the lay public in replantation has been considerable, and this has at least two effects. First, there is widespread awareness that replantation can be achieved, which should result in prompt referral of patients to centers where an informed opinion regarding replantation can be obtained. A second, and less desirable, result of lay publicity is the suggestion that replantation is in the realm of science fiction. This may have the effect of deterring the inherently conservative physician from becoming knowledgeable regarding the possibilities of replantation. The present discussion of replantation will consist of a review of the experimental and clinical experience directly pertaining to limb replantation, and a consideration of the problems encountered either in the laboratory or in the hospital. Finally, an outline will be presented for management of the patient requiring a replantation procedure.

EXPERIMENTAL REPLANTATION

In 1903, Hopfen reported three experiments in which dogs' legs were completely amputated and replanted. Death occurred at 1, 6, and 11 days but a viable replanted extremity was achieved in two animals for several days. Replantation of a limb after complete amputation was next reported by Carrel and Guthrie, in 1906.13 The replanted hind limb of a single dog survived for 50 hr, when gangrene necessitated sacrifice of the animal. It seems clear that the gangrene was secondary to swelling within a plaster dressing. This report is distinguished by the following comment: "Absolutely no blood escaped from the vessels at the lines of anastomosis." These investigators clearly anticipated both replantation and transplantation

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of extremities in the human. In a second publication, in 1908, Carrell mentions a successful leg homograft of at least 22 days' duration. These experiments were logical extensions of the work of several investigators, notably Halsted and associates, whose experiments, beginning in 1887, were performed on animals in which the femoral artery and vein were left intact. These studies, and those of Reichert, demonstrate the pattern of vascular regeneration across the amputation wound and are of interest even today. In 1943, Blakemore and associates briefly mentioned two animals in which the leg was amputated and replanted successfully, using nonsuture techniques for vascular anastomosis. Since 1960, several papers concerned with the technical aspects of experimental replantation have been published. Lapchinsky reports 67 experiments involving limb replantation, with 16 successful procedures. MacDonald and associates mention an 80 per cent success rate for experimental replantation in dogs using suture technique for vascular anastomosis, but do not give the number of animals involved. Snyder and associates report a series of experiments in which the pump oxygenator was used to perfuse the amputated extremity prior to replantation. Survival up to 44 days with a viable replanted extremity is reported. Eiken et al. report 27

Fig. 1 (upper left). Amputated dog limb. Ligatures on major vessels and tagging sutures on nerve are visible.

Fig. 2 (upper right). Technical performance of arterial anastomosis demonstrating use of standard vascular instruments and suture material.

Fig. 3 (lower left). Completed vascular anastomoses. Repair of oblique osteotomy is visible.

Fig. 4 (lower right). Completed replantation. Filling of superficial veins is apparent.
experiments in which the amputated hind limbs of animals were replanted after 1 to 3 hr of ischemia at room temperature. Microsurgical techniques were utilized for vascular anastomosis, and the extremities were perfused using low molecular weight dextran prior to replantation. Of the 27 experiments, 16 were initially successful, but 11 of the 16 animals died or were sacrificed because of complications within 15 days of replantation.

In previously reported experiments from our laboratory, the left hind limbs of unselected mongrel dogs under pentobarbital anesthesia were carefully amputated under sterile conditions, using fine hemostats, meticulous hemostasis, and fine ligature material. The femoral artery and vein were divided between ligatures. The major nerves were simply severed, and the femur was divided by an oblique osteotomy (Fig. 1). The amputated extremity was put aside in the laboratory at room temperature, and, after varying periods of time, replantation was

Fig. 5. Arteriogram of an animal with a gangrenous extremity following replantation. Patency of arterial trunk to a point just above the amputation wound is demonstrated.
performed. The extremity was not perfused, and no anticoagulants were used at any time. The re plantation was begun by shortening the femur approximately 2 cm. Bone fixation was accomplished with an intramedullary rod and stainless steel plate across the osteotomy. Standard atraumatic vascular clamps were placed on the veins, and the vein ends were cut across just proximal to the previously placed ligatures. Venous anastomosis was then carried out with either 5-0 or 6-0 arterial sutures of silk, placed as a continuous suture with standard vascular instruments (Fig. 2). No magnifying devices of any kind were utilized. When the venous anastomosis had been completed, the clamps were removed and placed on the arterial ends, which were then trimmed and anastomosed in exactly the same fashion (Fig. 3). The major lymphatic channel was not repaired. The nerves were repaired with epineural sutures of arterial silk. The muscles were carefully approximated by sutures in the muscle sheaths, and the skin was closed with subcuticular sutures (Fig. 4). In all, 16 experiments were performed, and 12 animals survived the procedure. The 4 animals that did not survive were anesthetized for longer than 10 hr, and these animals died, without regaining consciousness, within 2 hr of the completion of re plantation. In the 12 animals surviving the operative procedure, the replanted extremity remained viable in 9. In experiments 2, 4, and 10, discoloration of the amputated extremity was noted in the early postoperative course and rapidly progressed to frank necrosis. In one of these animals thrombus was noted in the vein at the time the ligated end was trimmed away. Although this was removed, early thrombosis apparently recurred (Fig. 5). Of the 9 animals with viable extremities, 3 died, from 2 weeks to several months after re plantation. One animal died during anesthesia for arteriography at 2 weeks after re plantation. The extremity was viable at the time of the animal’s death. A second animal severely chewed the obviously anesthetic extremity, and was sacrificed for this reason. A third animal died at the animal farm of unknown causes, but the extremity was viable at the time of the animal’s death. The remaining 6 animals were followed for periods up to 16 months after re plantation.

The results of several series of animal experiments are recorded in Table 1.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Number of experiments</th>
<th>Early success(^a)</th>
<th>Late success(^a)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hopfner(^{24})</td>
<td>1903</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>Magnesium coupling device for anastomoses</td>
</tr>
<tr>
<td>Carrel and Guthrie(^{13})</td>
<td>1906</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>Vitallium device for anastomoses</td>
</tr>
<tr>
<td>Blakemore (et al.)^1</td>
<td>1942</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>Successful transplant after 28 hr</td>
</tr>
<tr>
<td>Lapchinsky(^{42})</td>
<td>1960</td>
<td>67</td>
<td></td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Snyder (et al.)^15</td>
<td>1960</td>
<td></td>
<td></td>
<td>44 days</td>
<td>Used pump oxygenator</td>
</tr>
<tr>
<td>MacDonald (et al.)^45</td>
<td>1962</td>
<td></td>
<td></td>
<td>80%</td>
<td>Suture technique</td>
</tr>
<tr>
<td>Eiken (et al.)^18,40</td>
<td>1964</td>
<td>27</td>
<td>16</td>
<td>5</td>
<td>Suture anastomoses</td>
</tr>
<tr>
<td>Williams (et al.)^30</td>
<td>1966</td>
<td>16</td>
<td>9</td>
<td>6</td>
<td></td>
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\(^a\) Early success is before 2 weeks; late success is from 2 weeks on.
Although comparison of these series is meaningless, it seems clear that dogs' limbs can be amputated and replanted with a relatively high degree of initial success. Neither perfusion of the limb prior to replantation nor use of microsurgical techniques for vessel anastomosis is critical to success under the conditions of these experiments.

**Clinical Experience**

Replantation of amputated extremities was accomplished in the laboratory more than 50 years prior to the initial report of clinical success. The early experiments were clearly designed to furnish proof that replantation could be achieved in the human, and this possibility has been reiterated at intervals since that time. Successful restoration of partially amputated extremities has been reported several times. Undoubtedly these experiences are important in demonstrating the surgical principles of replantation. However, the difficulties in comparing cases and in determining the significance of the remaining tissue bridge for both immediate and long-range success have led to the conclusion that these injuries should be considered separately from complete amputation. It is certainly clear that all the surgical techniques involved in replanting amputated extremities have been known for several years, and it is difficult to understand why successful replantation was not accomplished prior to 1962. Among the possible explanations is the fact that traumatic amputation is not commonly encountered in a patient whose general condition permits an early and lengthy operative procedure for a non-life-endangering situation. There is little question but that there has been an emotional barrier to attempting replantation, and traditional teaching with regard to the fate of peripheral nerve injuries may have contributed to this pessimism.

Comments in the preceding paragraph should emphasize the credit due Malt and his associates for performing the first reported successful replantation of an extremity following complete amputation in a human. The operation was performed May 23, 1962, on a 12-year-old boy who sustained amputation of the right arm below the shoulder. The patient was admitted to the hospital within 30 min of the injury, and had no associated injuries. His general condition was good. The extremity was packed in ice, and replantation was begun promptly. Circulation was restored by venous and then by arterial anastomoses in approximately 4 hr, following which the bone, nerve, and muscles were repaired. No anticoagulants were used, and the postoperative course was uneventful. Physiotherapy was begun early, and suture of the median and ulnar nerves and grafting of the musculocutaneous and radial nerves were carried out approximately 4 months after the replantation. At 2 years there was a protective level of sensation in the hand, with some return of intrinsic muscle function in the hand and good return of forearm and finger flexors.

Malt and McChanner report a second patient with complete amputation of the right arm in the region of the midhumerus incurred in a train accident, in September 1963. This patient was seen shortly after injury, and the replantation procedure was carried out immediately. Circulation was restored in 5 hr. Extensive skin loss necessitated flap coverage, which was accomplished from the abdomen.
Eight months after replantation, the patient was working as a machinist supervisor. At that time shoulder and elbow motion were limited, but there was fair strength in the finger and thumb flexors. The patient died of an unrelated illness 18 months after replantation.47

Shorey and associates34 have reported the case of a 42-year-old man whose right arm was amputated by a book trimmer, 7 cm above the wrist. The vascular system was perfused with a saline solution containing heparin, and replantation was begun 1 1/2 hr after injury. Circulation was restored after approximately 3 1/2 hr by arterial, followed by venous, anastomosis, using suture technique. Four veins and the radial artery were repaired; the ulnar artery was ligated. Heparin was administered systemically. The postoperative course was complicated by marked edema, necessitating relaxing incisions on the dorsum of the hand. Skin damage necessitated amputation of the fifth finger approximately 1 month after injury. Secondary nerve repair was carried out at 5 months, and a procedure to restore extensor function of the fingers was performed later. Approximately 14 months after the injury, function in the hand was limited by fibrosis, but finger flexion and extension were present and satisfactory return of sensation had occurred.

Repair of a very similar injury was reported by Ch'en et al.31 and by Horn and Lund.36 A 27-year-old man sustained an amputation just above the right wrist, apparently in an industrial accident. Both arteries and two veins were repaired, using non-suture technique. Circulation was restored in 4 hr. Primary nerve repair was accomplished at the initial procedure. The patient was given systemic heparin for 3 days. Marked swelling necessitated longitudinal incisions in the skin in the early postoperative period. A second operation was required to permit union of the radius. Seven months after replantation, there was reasonable return of finger motion and some evidence of return of intrinsic muscles of the hand. A protective level of sensation was apparently present.

Amputation of the right arm at midhumerus in a train accident was reported by Shaftan et al.78 The patient, a 28-year-old man, was seen immediately after injury, and replantation was performed. The duration of ischemia was not given. Dextran was administered. A wound hematoma necessitated early reoperation. Eighteen months after repair the nerve-reconstructive procedures had not been completed.

A single patient has been reported from the University of Oklahoma Medical Center.90 The patient was a 22-year-old college student, whose right arm was amputated when he reached into a high-speed commercial water extractor. The impact of the amputation was such that the patient was not knocked from his feet during injury. Initial bleeding was quite minor, and the patient's roommate, who is now a medical student, promptly retrieved the extremity, placed it in a cold towel, and took both the patient and the extremity to the college medical facility. The patient was transported 70 miles to the University of Oklahoma Medical Center, arriving less than 2 hr after injury. On arrival the patient was in excellent general condition, with no evidence of excessive blood loss. The extremity was transported in a tub of ice (Fig. 6), and was in excellent condition. After X-rays of the humerus were taken, the patient was removed to the operating room, where both the extremity and the proximal wound were minimally debrided (Figs. 7,
REPLANTATION OF AMPUTATED EXTREMITIES

Fig. 6. Container with arm on arrival at the University of Oklahoma Medical Center

Fig. 7. X-ray of right upper extremity demonstrating fracture line at extreme corner with no evidence of proximal skeletal injury.
Fig. 8 (upper). Amputated arm before debridement and perfusion. The avulsion injury of the nerves is evident. The sterile extension tube used for arterial perfusion is visible on the table.

Fig. 9 (lower). Amputated extremity is held in position just prior to beginning replantation.
Fig. 10. X-ray of replanted extremity at 8 months, demonstrating good healing at fracture site.
Fig. 11 (upper). Patient 1 year after replantation. Deformity of the hand and atrophy of the forearm are evident.

Fig. 12 (lower). Patient 14 months after replantation, demonstrating range of shoulder and elbow motion.
8, and 9). The extremity was perfused by gravity, using a standard intravenous bottle with a sterile extension tube. This tube was an excellent cannula for the distal end of the brachial artery. The perfusion mixture consisted of 500 cc of normal saline containing 10,000,000 units of penicillin and 50 mg of aqueous heparin. The return of perfusate through the vein ends was prompt, and no sizeable thrombi were observed. The first step in replantation was repair of the badly comminuted fracture of the humerus, using multiple screws and plates. The humerus was shortened approximately 1 1/2 in. The single brachial vein, the cephalic vein, and the brachial artery were repaired in that order, using interrupted 5-0 arterial silk sutures. When circulation was restored, almost exactly 5 hr after the injury, bleeding from the distal musculature was impressive, and required rapid transfusion of 1500 cc of whole blood. The badly attenuated nerves were managed by tacking the proximal and distal ends of the ulnar and median nerves together, doing a formal anastomosis on the musculocutaneous nerve, and tacking the proximal radial to the median nerve, as the distal radial nerve was not identified. The muscles were approximated with interrupted sutures and the skin with the same material. A drain was inserted. Circulation remained adequate in the postoperative period, which was quite uneventful. No systemic anticoagulants were used. The arm was elevated, but moderate swelling occurred, reaching a maximum at 1 week and subsiding slowly. Physiotherapy was started on the second day and was continued. Excision of neuromas of the median and ulnar nerves was carried out 12 weeks after injury. The median nerve ends could be anastomosed under some tension, and a free graft of median antibrachial cutaneous nerve was used to bridge the gap in the ulnar nerve. Twelve weeks after this procedure, the radial nerve was repaired by resecting a long neuroma in the proximal radial nerve, locating the distal radial nerve in the lateral side of the arm, and bridging the

![Fig. 13. Hand at 14 months after replantation, demonstrating active finger flexion. Atrophy of thenar and hypothenar spaces is obvious.](image-url)
Table 2. Summary of clinical replantation procedures

<table>
<thead>
<tr>
<th>Author</th>
<th>Age of patient</th>
<th>Date of operation</th>
<th>Amputation site</th>
<th>Duration of total ischemia</th>
<th>Early results</th>
<th>Duration of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malt et al.</td>
<td>12 yr</td>
<td>May 1962</td>
<td>Right arm at shoulder</td>
<td>3 1/2 hr</td>
<td>Good</td>
<td>2 yr</td>
</tr>
<tr>
<td>Malt et al.</td>
<td>44 yr</td>
<td>Sept. 1963</td>
<td>Lower half of right humerus</td>
<td>5</td>
<td>Good</td>
<td>18 mo</td>
</tr>
<tr>
<td>Shorey et al.</td>
<td>42 yr</td>
<td>Aug. 1962</td>
<td>Right arm 7 cm proximal to wrist</td>
<td>3 1/2 hr</td>
<td>Marked edema, relaxing incision</td>
<td>14 mo</td>
</tr>
<tr>
<td>Ch’en et al.</td>
<td>27 yr</td>
<td>Jan. 1963</td>
<td>Right arm just above wrist</td>
<td>4</td>
<td>Marked edema</td>
<td>7 mo</td>
</tr>
<tr>
<td>Shaften et al.</td>
<td>28 yr</td>
<td>July 1964</td>
<td>Right upper arm</td>
<td></td>
<td>Bleeding necessitated reoperation</td>
<td>18 mo</td>
</tr>
<tr>
<td>Williams et al.</td>
<td>20 yr</td>
<td>Mar. 1964</td>
<td>Right arm at midhumerus</td>
<td>5</td>
<td>Good</td>
<td>18 mo</td>
</tr>
<tr>
<td>Thompson</td>
<td>19 yr</td>
<td>Sept. 1965</td>
<td>Right arm at midhumerus</td>
<td>6</td>
<td>Good</td>
<td>7 mo</td>
</tr>
</tbody>
</table>

* All patients were male.

A gap between the two with a free graft of the sural nerve. Eighteen months after replantation and approximately 1 year after the second nerve graft, the patient has reasonably good sensation over much of the forearm and can detect pain and pressure in the palm of the hand. There is slight sensation in the fingers, but this could not be considered protective. There is reasonably good return of forearm and finger flexors, and there is early evidence of forearm and finger extensor return. No intrinsic muscle return can be appreciated. The patient has good shoulder and elbow motion, and the joints of the wrist and hand are in good condition (Figs. 10 to 13).

The cases reported in preceding paragraphs, and included in Table 2, undoubtedly do not describe the total experience with replanting amputated extremities. Malt mentions several cases not yet reported. Almost certainly, other procedures have been performed but not yet reported, for a variety of reasons, including insufficient length of follow-up. It is also probable that a number of unsuccessful replantation procedures have been performed.

Reluctance to report such experience is understandable, but knowledge of the circumstances under which failure occurred and an evaluation of the problems encountered could very well provide important information for future procedures.

Problems in Replantation

Experimental and clinical observations recorded to date, as well as experience with physiologically similar situations, have served to point out a number of problems involved in the management of patients before, during, and after replantation procedures. Though these problems are obviously closely interrelated, it may be helpful to consider them separately.
Shock and the Crush Syndrome

In experimental replantation the principal observed systemic effect is depression of the cardiovascular system, which may proceed to shock and death. A similar phenomenon has been reported in the human following replantation. It is of considerable interest that explanations of this phenomenon appear to be going through almost exactly the same cycle as that encountered in understanding the nature of traumatic shock in the first third of this century. Traumatic shock, which had been previously blamed on release of toxic substances by injured tissue, was shown by Blalock and Roome to be due to demonstrable loss of blood and fluid into the injured area. The experiments of Wilson and Roome on tourniquet shock established essentially the same explanation, that is, loss of a significant amount of fluid into the injured area accounting for the cardiovascular phenomena observed.

During World War II, the crush syndrome was recognized, and there was initial interest in the possibility that the renal lesions and renal failure associated with this syndrome might be caused by release of myoglobin from injured muscle. Despite an enormous amount of interest, the cause of the renal lesions is not entirely clear to this date, but probably they are due to circulatory phenomena. It is of interest that Selby and associates have demonstrated the presence of a vaso-depressor substance in ischemic tissue which had been long suspected, but the significance of this substance in the profound shock which may follow restoration of flow to ischemic areas has not been proven. The similarities among tourniquet shock, the crush syndrome, and shock following replantation are obvious.

In explaining the shock observed after replanting an amputated extremity Lapchinsky has again raised the question of toxemia, and this has been mentioned clinically as well. The nature of the fluid loss into the replanted limb has been carefully studied by Eiken and associates, who have demonstrated a plasma loss into the extremity which is quite compatible with the extent of loss shown by Johnson and Blalock to result in death of a high percentage of dogs. Mcll and associates have reported that the pH of blood returning from an extremity following replantation is 6.5. The arterial pH of animals following replantation has been studied over a period of several hours, and a fall in pH, associated with falling cardiac output and ultimate shock and death, has been demonstrated. These investigators feel that pH changes resulting from return to the circulation of metabolic products explain in large part the observed cardiovascular phenomenon after replantation.

Edema in the Replanted Extremity

Edema has consistently been observed in the experimentally replanted extremity, and was accurately described by Halsted et al. Most observers have agreed that the edema appears promptly in the postoperative period, reaches a maximum in a matter of several days to 1 week, and subsides slowly during the second week after replantation (Fig. 14). Formation of edema in the replanted extremity has been studied by Eiken and associates in acute experiments utilizing a continuously weighed amputated extremity perfused through tubing from the original donor. These studies demonstrate consistent, rapid formation of edema during the first 2 hr of perfusion, which continues to increase slowly up to 28 hr.
Fig. 14. Appearance of a replanted leg 24 hr after operation. Edema is relatively mild

The extent of the edema appeared to increase with the duration of ischemia prior to re-establishment of circulation, and in extremities cooled to 4°C during the period of ischemia there was significantly less formation of edema during prolonged perfusion. When recirculation was carried out in limbs ischemic for 6 hr at normal temperatures, the plasma loss after 6 hr of recirculation was approximately 50% of the estimated plasma volume at the beginning of the experiment.

It is assumed that the edema is accumulation of fluid primarily in the extracellular space and that this is caused by ischemic injury to the vascular system. The extent to which there is intracellular shift of fluid, and the significance of this shift, are unknown. The importance of lymphatic interruption in the formation of edema following replantation has not been clearly determined, but MacDonald states that there appeared to be less edema in replanted extremities in animals when the major lymphatic vessel was restored surgically at the time of replantation.

In addition to the effect of edema in depleting circulating fluid volume, the accumulation of fluid in the replanted extremity is itself a significant problem. The effects of edema on circulation have been demonstrated experimentally by Hinshaw. In situations in which the restored circulation is marginal, marked edema may result in inadequate circulation and subsequent necrosis. Of perhaps greater importance, the edema may, by interference with microcirculation or by direct cellular effect, influence ultimate cellular recovery and, therefore, long-range return of function.
Methods for control of edema after replantation have not been studied experimentally, although the importance of cooling the ischemic extremity to limit the extent of edema has been suggested. Clinically, most observers have felt that elevation of the extremity is indicated. The value of mild compression dressings is debatable, but the use of constricting dressings is catastrophic. The observation of the rapid occurrence of edema during the first 2 hr after injury, at least in the experimental preparation, is clinically significant. Obviously, measures to prevent edema should be undertaken prior to or during this period, and, furthermore, effective concentrations of antibiotic in the wound must be achieved during this period of time.

*Restoration and Maintenance of Adequate Circulation*

The factors governing intravascular thrombosis in the amputated extremity during the period in which there is no circulation are incompletely understood. The occurrence of thrombus in the venous system has been observed experimentally in 1 of 16 animals in the author's experience. Clinically, thrombus material has been expressed from the venous systems during perfusion of the extremity prior to replantation, and Thompson has reported a venous thrombus which could not be completely removed by perfusion but which was removed by insertion of a balloon-tipped catheter. It seems reasonable to conclude that time is a factor in the development of intravascular thrombosis.

Perfusion of the extremity prior to re-establishing circulation appears to offer advantages, although the author's experiments indicate that this is not essential. Perfusion by gravity using a standard intravenous setup with a sterile extension tube is convenient, and should avoid damaging pressures generated by a syringe. Mehl et al. have suggested that a saline solution containing heparin is a better perfusate than dextrose solutions, dextran, plasma, or fibrinolysin for clearing the smaller vessels. Standard lactated Ringer's solution containing heparin may be even more suitable. Additional theoretical advantages of dextran have been mentioned by Enerson. Recognition of the low pH of blood returning from the ischemic extremity has led to the suggestion that systemic amine buffer be given when circulation is re-established. Addition of large doses of nonirritating antibiotic to the perfusate seems reasonable, but the value of this maneuver has not been proven.

In re-establishing circulation, it is generally agreed that the venous anastomoses should be performed first in order to prevent excessive loss of blood or the necessity for temporarily cross-clamping a completed arterial anastomosis. Herbsman and associates disagree with this, apparently because it prolongs the period of total ischemia. Repair of the veins is technically difficult, and adequate repair is critical to successful replantation. The technique described by Shaw is helpful. The fact that empty veins collapse to an even greater degree than do empty arteries increases the necessity for use of carefully placed interrupted sutures in this anastomosis. The availability of large veins will vary, both with individuals and with the level of amputation, but as many venous anastomoses as are technically possible should be attempted. The arterial anastomosis is performed utilizing standard techniques. It is clear that both arteries and veins of a size encountered
in upper extremity amputations, at least down to the level of the wrist, can be satisfactorily repaired using suture techniques. Numerous methods of nonsuture anastomosis have been advocated, though at present the major advantage of such methods is that they may be faster and more applicable to a mass-casualty situation. The use of automatic anastomotic devices has been mentioned by Lapchinsky. There has been increasing interest in the use of microsurgical techniques in vascular anastomosis. As surgeons become increasingly familiar with microsurgical techniques, it is likely that the use of such techniques will become more widespread. It is to be emphasized that replantation of extremities is not dependent upon the availability of such techniques. It is the author's opinion that microsurgery will play a more important role in the suture of nerves than in the suture of blood vessels in extremity replantations.

Restoration of circulation results in increased bleeding from the distal muscle ends. The fact that no vessels were ligated at the time of amputation, combined with the ischemic vasodilation present in the distal vascular system, results in impressive hemorrhage. It seems worthwhile to emphasize that transfusion will almost certainly be necessary, even though little blood loss may have been encountered up to this point.

Both experimental and clinical evidence accumulated to date indicate that if adequate circulation is restored initially, the chances of secondary failure of circulation are relatively slight. This observation, together with the knowledge that heparin does not prevent platelet thrombi and the observed increase in bleeding complications, particularly wound hematomas, associated with the use of heparin, have led most workers to omit the use of anticoagulants in the treatment of patients following replantation. It is clear, however, that the rapidly increasing edema in the first few hours after injury poses a threat, both theoretical and real, to circulation in the replanted extremity. In addition, the plasma loss into the extremity and resulting hemoconcentration may result in significantly increased viscosity of the blood with obvious disadvantages. It has been demonstrated repeatedly that when the hematocrit exceeds 40 per cent the blood viscosity rapidly increases. This is probably even more significant in a cooled extremity.

Therapeutic measures of primary importance in maintaining circulation include control of edema, a consideration of anticoagulants, avoidance of hemoconcentration, and a consideration of the use of low molecular weight dextran. The use of anticoagulants has been mentioned in the preceding paragraphs and is currently discouraged. The methods employed in minimizing edema have also been discussed. It is clear that these methods are incomplete, but it is equally clear that, provided adequate circulation is initially restored, edema will not compromise circulation to the point of tissue necrosis. The use of low molecular weight dextran to maintain circulation, particularly at the level of microcirculation, has firm experimental support. Although the value of low molecular weight dextran in this particular situation has not been objectively established, there is theoretical indication for its administration early in the postreplantation period.

Wound Infection

The greatest single cause of failure following both experimental and clinical replantation is said to be infection. From the previous discussion it is
obvious that many factors favoring the development of clinical infection in an inevitably contaminated wound are present following replantation. The length of time between amputation and replantation is obviously important, and the increased probability of infection adds to the necessity for prompt operation. Inadequate debridement of the replantation wound is, of course, an invitation to serious infection, but in an ischemic limb identification of permanently devitalized tissue is difficult. Finally, the development of edema, changes in blood viscosity, and possible disturbances in the microcirculation favor the development of infection in the replantation wound.

The dangers of infection are minimized by early operation, by thorough débride ment after circulation is re-established, and by adherence to long-established surgical principles of hemostasis, avoidance of dead space, and meticulous suture techniques. That antibiotics in the usual dosage schedules fail to prevent wound infection has been demonstrated many times. On the other hand, the presence of antibiotic levels during wounding is effective in preventing wound infection, and for this reason the use of antibiotics, in the solution used to perfuse the isolated extremity, and in intravenous doses early in the pre- and intraoperative management of the patient, seems clearly indicated.

Permissible Time Lapse Prior to Replantation

Numerous factors may delay patients with traumatic amputations from reaching medical facilities where replantation can be attempted. It is critical to establish time limits beyond which successful replantation cannot be achieved, or beyond which the risk to the patient becomes excessive. It can be stated at the outset that these limits have not been clearly established, but a reasonable amount of data related to permissible periods of ischemia is available.

In the author's experimental series, the amputated extremities remained at room temperature during the period between amputation and replantation. Of 12 completed operations, the animals have been divided into three groups based upon the period of total ischemia (Table 3). This time period began when the last structure in the leg was divided, and ended on release of the vascular clamps restoring circulation in the major vessels. In five animals this period of ischemia was between 1 and 4 hr. Three of the five procedures resulted in a viable extremity. In a second group of six animals, the period of total ischemia as defined was 4 to 6 hr. In all six experiments, the extremities remained viable for prolonged periods of time. In a single animal, extremity survival was achieved after 7 hr and 45 min of ischemia. Four early postoperative deaths were encountered in attempting to enlarge this group. This information suggests strongly that replantation can be

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<th>Time interval (hr)</th>
<th>Survivors</th>
<th>Viable extremity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>4-6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Over 6</td>
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</table>
successful if circulation is established within 6 hr, even when nothing has been
done to preserve the limb.

Tolerance of tissue to ischemia has been of interest for years. In an ischemic
extremity, skeletal muscle is the first tissue to be irreversibly injured. In animal
experiments by Harman and associates,\textsuperscript{28, 29} and by Scully and associates,\textsuperscript{30} histol-
ogical evidence of irreversible damage to skeletal muscle was observed at be-
tween 4 and 6 hr of ischemia. The biochemical changes in ischemic tissues have
been studied by LePage.\textsuperscript{44}

There is a great deal of evidence that cooling of the amputated extremity prior
to replantation prolongs the permissible period of ischemia prior to development
of irreversible tissue changes.\textsuperscript{37} Lapchinsky\textsuperscript{43} achieved successful replantation of
extremities cooled to 2 to 4 C up to 28 hr after injury. The marked increase in
tissue tolerance to ischemia afforded by hypothermia was studied experimentally
by Brooks and Duncan,\textsuperscript{7} and by Allen,\textsuperscript{4} 25 years ago. Eiken and associates\textsuperscript{32} have
demonstrated both the increase in length of ischemia tolerable in the cooled ex-
tremity and the beneficial effects of hypothermia in minimizing edema and
plasma loss.

Use of the pump oxygenator to prolong the period between amputation and
replantation has been suggested by Snyder \textit{et al}.\textsuperscript{75} and the use of hyperbaric oxy-
genation\textsuperscript{4} to preserve viability of an extremity has been discussed by Malt.\textsuperscript{47}
Possibly either or both of these may find useful application in the future. At the
present time, it seems reasonable to conclude that a promptly cooled and cleanly
amputated extremity might be replanted with a chance of success up to 24 hr.
The chances of successful replantation diminish with the duration of time prior
to undertaking the operation, and experience may demonstrate that the actual
period in which replantation can be successful is less than the theoretical 24 hr.
Certainly this time interval is long enough to allow transport of most patients
to centers where facilities for replantation are available. When cooling of the am-
putated member has not been accomplished promptly after injury or when there is
gross contamination and extensive damage to tissue, the decision to attempt re-
plantation after 6 to 8 hr should be made with extreme caution.

\textit{Restoration of Function}

Final judgment of the value of replantation will depend upon the extent to which
useful function of the extremity is regained. Laboratory experience with replanting
extremities furnishes limited information regarding functional return, not only
because the observations of return are crude but also because the return of function
to a dog's leg can hardly be equated with reasonable return of function to the hu-
man hand. A final reservation regarding experimental evidence concerns the
fact that therapy and training to aid in restoration of function cannot be precisely
evaluated.

In dog replantation the best long-range results have been reported by Lap-
chinsky,\textsuperscript{43} who reports virtually complete return of function, as evaluated by clinical
observation and by electromyography. Eiken \textit{et al}.\textsuperscript{18} have reported long-range
results in 18 dogs. In all animals there was evidence of residual neurological
damage. The animals were observed for periods of from 3 to 29 months, and de-
ficits ranged from a toedrop (in all animals), to permanent contractions of the
Fig. 15. Appearance of an animal 1 year after replantation of the left rear extremity. Normal gross appearance and stance.

Fig. 16. Approximately 1 year after replantation, animal demonstrates footdrop and weightbearing on dorsum of foot.
knee and lack of weightbearing. There was residual weakness in the extremity in all animals, but some evidence of return of sensation was present in 17 of 18. The authors have followed six animals after replantation for 12 to 16 months. 20 Of these animals, four resumed weightbearing, usually in about 1 month. (Fig. 15). In all these animals footdrop was present, and the animals were frequently observed to bear weight on the dorsum of the foot (Fig. 16). In two animals there was persistent edema, and in one animal this was marked. This animal had chronic osteomyelitis at the site of bone division with thrombosis of both the femoral artery and the femoral vein, apparently secondary to the adjacent abscess. In the remaining animals, at autopsy the musculature of the extremity was grossly normal and the major vessels were patent (Figs. 17, 18, and 19).

From the preceding discussion, it is clear that only a few cases of human replantation have been followed for sufficient periods of time to judge the final result. A considerable degree of functional return is possible, but the frequency with which such results can be obtained is unknown. Certainly the major recognized problems in return of function are related to peripheral nerve regeneration.

The management of peripheral nerve injury involves two important considerations. The first consideration is furnishing the optimum conditions for nerve re-
Fig. 18. Reproduction of an arteriogram performed 1 month after replantation. Method of bone fixation and presence of patent major arterial trunks are demonstrated.

generation, and the second is a program designed to protect and maintain the de-
nervated structures during the interval between injury and reinnervation.

There are few subjects more controversial than the management of peripheral nerve injuries. A massive literature has accumulated on the subject, and extensive review of this literature is beyond the scope of this monograph. A great deal of basic information is available regarding the biochemical and morphological aspects of injury to peripheral nerves, and the regenerative processes which follow such injury.2, 32, 33, 36, 67, 88 The controversy lies in the selection of therapeutic measures incorporating the best utilization of basic information to allow the most complete degree of return of function in a severed peripheral nerve. Much of the available information has been obtained in connection with military experience, and
both clinical and experimental research in the management of peripheral nerve injuries appear to slacken in peacetime.\textsuperscript{18, 67, 69, 80, 85, 90}

In furnishing optimum conditions for nerve regeneration, the first problem is the timing of nerve repair. Although there is little doubt that primary repair has many advantages, the bulk of opinion appears to be that primary repair should be attempted only in exceptional instances.\textsuperscript{2, 83, 92} Such instances include injuries in which the mechanism of injury is a clean laceration and where associated injuries permit careful and unhurried primary anastomosis. Obviously, these conditions will not often be encountered in traumatic amputation, but, when they exist, primary repair of major nerves should be carefully considered.

The majority of traumatic amputations will involve some force other than a clean-cutting injury. The major argument against primary nerve anastomosis in these injuries is inability to distinguish the extent of the nerve injury grossly. This is particularly true in avulsion-type injuries. Related to this argument is the reasoning that primary repair under less than optimum conditions may lead to prolonged waiting for return of nerve function, thereby compromising the chance of ultimate success. A third reason for avoiding primary nerve anastomosis is reluctance on the part of the surgeon to dissect extensively in the already damaged distal tissue in order to locate accurately, and particularly in order to free distal nerve trunks sufficiently to allow resection of the damaged areas and anastomosis.
Finally, the technical replantation is usually a lengthy procedure, and adding the time-consuming preparation and performance of nerve anastomosis may be unwise.47

Technical methods of nerve anastomosis are the subject of much past and present controversy. There is general agreement that meticulous preparation and accurate anatomical alignment of the nerve ends are important in allowing maximal effective regeneration.5,14,23 A clean cut at right angles to the nerve through normal nerve tissue should give the most advantageous wound for complete regeneration. Several methods have been described by which this can be achieved. The ordinary method has been to sever the nerve against a relatively firm object, such as a tongue blade, using the sharpest blade available, preferably a razor blade. The transection should, of course, be through normal nerve tissue, either in the acute situation or at reoperation. Frozen sections may well be helpful in determining the extent of neuroma formation in secondary operation. The nerve ends should be carefully aligned, using whatever landmarks are available, and anastomosis performed utilizing epineural sutures of very fine suture material. Numerous nonsuture techniques for nerve anastomosis have been advocated in the past and have enjoyed periods of popularity.77,82,88 The current feeling appears to be that suture anastomosis is preferable. The slang stitch, previously widely advocated, appears to have been abandoned. In an attempt to prevent fixation of anastomoses and perhaps ingrowth of fibrous tissue from surrounding structures, wrapping of nerve anastomoses with various substances has been investigated for decades. A history of such attempts and a discussion of the rationale are furnished by Spurling and Weiss.77,88 Recent interest in the technique of peripheral nerve anastomoses includes the work on Millipore wrapping by Campbell and Bassett,9 and the use of adsorbable wrapping, such as collagen, as described by Kline and Hayes.41 Improved technical methods of suture anastomosis using the operating room microscope may result in better return of neural function, although this has not been demonstrated conclusively.18,78 Bridging of gaps in peripheral nerves, necessitated by loss of neural tissue or by extensive resections of neuromas, has been a discouraging problem.9,88 At present free nerve grafts appear to offer the best chance of success.5,25

The expected degree of return of function in peripheral nerves is known to vary with the level of nerve section, with the extent of damage to the nerve, and with the character of neural repair. These factors are difficult to evaluate in the individual patient. In addition to division of peripheral nerve trunks in traumatic amputation, there is the added factor of ischemia for whatever period of time circulation is interrupted. In animals this has been demonstrated to reduce the expected degree of regeneration.69 Most of the large series of reported peripheral nerve injuries are wartime series, and it hardly seems fair to accept these figures as representative of what might be achieved under ideal civilian hospital conditions.17 It is possible that the functional regenerative capacity when all major nerves are divided, as in traumatic amputation, may differ from that observed in single or even double nerve injuries. The experimentally demonstrated species difference in nerve regeneration makes extrapolation from animals to humans of data regarding expected regeneration quite difficult.42,63,67,80,88 It is most interesting
that troublesome pain syndromes have not been mentioned in clinical reports of replanted extremities.

The second major aspect of management of the extensive peripheral nerve injuries involved in replantation is protection of the distal extremity during the period of denervation. Extreme care with regard to pressure and trophic changes in the extremity must begin immediately following replantation. Physiotherapy, particularly passive motion of all joints distal to the line of amputation to prevent stiffening, should begin quite early in the postoperative period. Galvanic stimulation of denervated muscles is thought by most to be valuable in maintaining these muscles through long periods of denervation. Electromyography is valuable in determining the progress of regeneration in conjunction with the more traditional observation of Tinel's sign and careful observation of returning muscle function. It should be emphasized that a brilliant initial result may be converted to failure by inadequate or improper physiotherapy.

**Current Outline of Clinical Management**

*Indications for Replantation*

The demonstration that amputated extremities can be replanted successfully and even that reasonably good long-range functional return can be expected does not constitute an indication for replantation in every instance following traumatic amputation. The first consideration, as has been strongly and properly emphasized by Malt, is the condition of the patient. Failure to detect life-threatening injuries in the enthusiasm for early replantation is tragic, and prevention of the occurrence requires repeated warnings.

In addition to the problem of associated injuries, the age and preaccident condition of the patient are obviously important. Of equal importance, but somewhat more difficult to evaluate, is the individual requirement of the patient for the amputated extremity. Is the extremity sufficiently important to this individual to warrant prolonged convalescence with multiple operations? Will the resultant time loss jeopardize the patient's family and job? Are facilities available which will permit the prolonged, specialized, and expensive care necessary after such a procedure?

There is a serious question regarding indications for attempting replantation of a lower extremity. The arm is basically a lever which places the hand in proper position. The hand, at the present time, is mechanically irreplaceable, and there is no substitute even remotely comparable. In addition to this, a patient with an immobilized arm can carry out a great many activities and may relatively rapidly re-enter a modified active existence. On the other hand, the function of the lower extremity is largely that of weightbearing, and mechanical substitutes, while not perfect, are reasonably satisfactory. In addition, the patient with a disabled lower extremity is likely to be relatively immobile during the period of illness. A final consideration is that shortening of an upper extremity is functionally acceptable, but shortening of the lower extremity can be a relatively difficult problem.

*Initial Management after Traumatic Amputation*

The immediate concern after traumatic amputation is the life of the patient. Massive bleeding must be controlled. Associated injuries, particularly those which
are life-threatening, must be managed. The initial management of the amputated extremity should consist of immersion in ice water. Although normal saline may be satisfactory, the addition of large amounts of salt to the water is unwarranted. Immediate perfusion of the vasculature of such extremities under less than optimum conditions should be discouraged.

Facilities Necessary for Replantation Procedures

Most broadly trained general surgeons are capable of performing a replantation procedure. Experienced advice and assistance regarding the most suitable method of handling the skeletal and neural injuries are helpful. In the author's experience, the operating team consisted of two senior general surgeons with interest in vascular surgery, a senior orthopedic surgeon, and a resident in surgery, all with laboratory experience in replantation. The Division of Neurosurgery was of great assistance in the subsequent peripheral nerve procedures. The amount of assistance, the nature of the technical complications, and the facilities involved in postoperative management are considerable, and argue for transport of patients to well-equipped centers for definitive treatment.

Technique of Replantation

Although speed in transporting the patient and the extremity to a center where definitive operation can be carried out is essential to success, there is no excuse for beginning the actual procedure until the patient's condition will permit a lengthy procedure and the responsible physicians are confident that no life-endangering injury has been overlooked. It seems important that one person be in charge of the replantation procedure. The hazards of compartmented, poorly coordinated fields of treatment hardly require emphasis. If sufficient trained surgeons are available, time may be saved by having one surgical team debride the patent, or central, end of the amputation wound and prepare the vessels and nerves for anastomosis, while a second team removes the amputated extremity from its cold environment and begins preparing it for replantation. Initially, the major artery in the extremity is located and perfusion by gravity flow is instituted. Currently, the perfusate of choice appears to be lactated Ringer's solution containing small amounts of heparin and large doses of nonirritating antibiotic. Theoretical considerations governing the choice of perfusate have been discussed elsewhere in this paper. Perfusion should be continued until clear perfusate can be identified from the major vein ends. If this is not achieved, the balloon catheter may be helpful. Under most conditions the initial step in replantation should be stabilization of the bone. This stabilization is exceedingly helpful in technical performance of the vascular anastomoses and, perhaps more important, prevents disruption of the vascular anastomoses during the necessary bone fixation. The method of bone fixation does not appear to be critical, but will depend upon the site of transection, the state of the fragments, and the training and inclinations of the surgeons involved. It must be emphasized that the bone should be shortened. This is helpful with both vascular and nerve anastomoses, and is absolutely essential in repairing the severed muscles. The necessity for shortening the bone can also be used to improve stability at the fracture site, particularly with regard to rotation. The vein anastomoses are performed and have been discussed. The importance of the
venous anastomosis cannot be overemphasized. As many veins as can be located of sufficient size to permit anastomosis should be joined. In more distal amputations, the importance of doing the venous anastomosis first decreases. The arterial anastomosis (or anastomoses, depending upon the level of amputation) is no less critical to success, but technically is a good deal easier to achieve. The injured ends of the artery can be safely trimmed away to permit accurate anastomosis. Gaps in either artery or vein can be repaired, using autogenous saphenous vein. When circulation is established, impressive bleeding from the distal structures is to be expected. This is in part due to reactive hyperemia, and it may be necessary to use firm pressure over the distal wound for a few minutes prior to beginning more formal methods of hemostasis. This hemorrhage is most impressive when the amputation is at levels involving muscle. Transfusion will usually be necessary at this point, if it has not been necessary previously during the procedure. A decision should then be made regarding nerve repair. This has been discussed in preceding pages. In the usual instance, the appropriate nerve ends will simply be tacked together with fine stitches to permit subsequent identification. At this point, bone continuity, circulation, and nerve repair of one sort or the other have been achieved in the wound, which is relatively dry. A decision can now be made about excising devitalized tissue, and this should be done carefully but thoroughly. The importance of complete debridement in prevention of postoperative wound complications, and particularly infection, should not require emphasis. The repair of the muscles or tendons should be anatomically accurate, and should involve as little additional surgical trauma as possible. The expectation of swelling in the extremity and possible collections of fluid in the wound has led most authors to suggest simple drainage. Where large tissue planes are involved, suction catheters should be considered. Closure of subcutaneous tissue and skin should be carefully performed. It is essential that the vessel and nerve anastomoses be covered with soft tissue. Where this is not possible, flap coverage should be considered, and can usually be accomplished with a thoracoabdominal flap. Where such anastomoses are covered with good muscle, skin defects may be left open for subsequent grafting.

The prevention of shock subsequent to re-establishment of circulation is begun, either before or during the replantation procedure, by the use of intravenous infusions of balanced salt solutions. In patients who are well hydrated, some evidence favors the use of mannitol during the operative procedure. Particularly when large masses of tissue are restored by replantation, or when the period of ischemia has been prolonged, thought should be given to prevention of acidosis after establishment of circulation. This may be accomplished by the use of bicarbonate or by the use of amine buffers. Measurement at frequent intervals in the postoperative period, of peripheral blood pressure, central venous pressure, and urinary output should allow detection and correction of the previously discussed metabolic influences of replantation.

Edema in the replanted extremity may be minimized by mild elevation of the extremity. The extremity should be placed in a carefully padded splint which maintains a position of function. Mild elastic compression of the extremity may be advisable, but must be very carefully applied and frequently observed.

For a number of reasons, it is the author's feeling that, other than administra-
tion of heparin in the perfusate used to clear the extremity circulation, anticoagulants should not be utilized in the postoperative period. This is based primarily on evidence of the questionable efficacy of heparin in preventing small vessel thrombosis, on the low incidence of observed later thrombosis of vessels, and, finally, on the high incidence of wound hematomas clearly associated with the use of effective levels of heparin. The systemic use of low molecular weight dextran in the immediate postoperative course has a good deal of experimental support, and if this compound becomes widely available it should be considered.

Physiotherapy, designed to prevent joint stiffness, should be begun within the first few days of injury. Galvanic stimulation of muscles appears to offer benefits in preventing irreversible deterioration prior to reinnervation.

Secondary repair of nerves should be performed as soon after 3 weeks as possible. The hazard of infection, particularly associated with nerve anastomosis, has perhaps been overemphasized. 17

The surgeon must carefully follow these patients through the prolonged period of convalescence and rehabilitation. The novelty and pleasure of having an amputated extremity replanted may well become tarnished after months of daily physiotherapy and two or three subsequent procedures. Careful evaluation of progress, and support and encouragement of the patient during this time, are obviously important.

A final point in the outline of management is the necessity for accurate observation and reporting of results, particularly late results, which should permit continuous modification of recommended methods of managing a replantation.

Conclusions

1. In carefully selected patients replantation after traumatic amputation can be attempted with reasonable expectation of success.
2. Sufficient experimental and clinical experience has accumulated to permit an outline of technical methods which have been satisfactorily employed in re-planting amputated extremities and identification of problems encountered.
3. The technique required and problems encountered in replanting amputated extremities differ qualitatively, at least, from those encountered in other surgical endeavors, and justify special interest and emphasis.
4. The facilities and talent necessary for replantation are widely available, and the procedure should become a part of the standard surgical armamentarium.

References


