The first successful replantation of an amputated human extremity was performed in 1962. Experience with such procedures has rapidly increased. Techniques have improved, allowing successful replantation even at the digital level. Its newness and the importance of proper patient selection justify considering limb replantation as an entity.

HISTORICAL ASPECTS

Man's long-standing interest in restoration or replacement of severed human parts is amply demonstrated in legend, illustrations, and reports of crude surgical maneuvers. Modern surgical investigation directly related to replantation began in 1887 when Halsted divided and repaired all structures of the hind limb of dogs except the femoral artery and vein. These experiments were stimulated by Dr. Halsted's interest in postmastectomy edema and were not reported until 1922. In 1903, Hopfner described experiments in which dogs' limbs were amputated and replanted using a nonsuture method of vascular anastomosis, with maintenance of viability up to 11 days in one animal. Shortly thereafter, Carrel and Guthrie were also able to replant an extremity in a dog with short-term survival. In 1908, Carrel described a dog leg homograft that survived for 22 days. Very few experimental attempts at replantation were recorded between 1908 and the report of Lachinsky in 1960. Subsequently, several investigators have described experimental replantation and have added a substantial amount of information regarding the technique and physiologic effects of extremity replantation.

In 1944, a protocol for replantation of amputated human extremities was formulated and published. In 1962, a 12-year-old boy presented at the Massachusetts General Hospital shortly after sustaining a traumatic amputation of the right arm below the shoulder. Dr. Ronald Malt, then a resident in surgery, made the decision to attempt replantation, summoned a number of surgical colleagues, and promptly performed the first successful limb replantation. The efforts of a number of laboratory workers and particularly the careful, objective report of successful limb replantation in two patients by Malt and McKhann stimulated worldwide interest in replantation.

The first successful replantation at a digital level was performed by Komatsu and Tamai on July 7, 1965. The laboratory development of techniques and instrumentation for microvascular surgery has stimulated increasing interest and experience in digital replantation.

CLINICAL EXPERIENCE WITH REPLANTATION

Replantation experience, including all levels of amputation, numbers several hundred patients. Operations have been carried out in many geographic areas and it is of interest that the largest single institutional series are from China and Australia. It is likely that the total number of replantation procedures performed is considerably greater than that reported. Variations in the completeness and timing of scientific reporting allow only general conclusions to be drawn from the recorded clinical experience.

Age

Replantation has been reported in patients from 20 months to nearly 60 years of age. It is quite clear that the best functional results have been obtained in younger patients. The long period of rehabilitation and the decreasing likelihood of good functional recovery with increasing age suggest that replantation should be attempted only in the most ideal situation in patients over 45 years of age.

Level of Amputation

Replantation of the upper extremity has been performed at virtually every level. Perhaps because of the size of the blood vessels involved, initial success has been somewhat more likely in the higher amputations. The ultimate functional recovery is considerably better with more distal wounds, probably because nerve regeneration is more complete after distal injuries.
Etiology of Amputation

Attempts at replantation have followed traumatic amputation due to a wide variety of wounding agents, including automobile accidents, industrial machines, clothes dryers, and assorted sharp instruments (machetes, meat cleavers). Experience indicates clearly that sharp, incised wounds are more favorable for both initial and long-range successful replantation. In general, avulsion wounds have resulted in less complete neural regeneration, and replantation after such wounds should be attempted only under special circumstances. Wounds that would be considered too dirty for primary closure or in which the time interval dictates against primary closure should certainly not be considered acceptable for attempted replantation.

Results

The success rate in achieving extremity viability is approximately 75 per cent for major upper extremity replantations and just over 50 per cent for digital replantations. Because it seems likely that the most successful cases have been reported, these may be optimistic figures. Early failure has usually been described as due to circulatory inadequacy or infection. Late failure has virtually always been due to faulty innervation.

With current techniques, the end result after extremity replantation is never perfect. For practical purposes, the end result is dependent upon the extent of nerve regeneration. Experience with extremity replantation confirms the long accepted observation that peripheral nerve regeneration is more complete (1) in young persons, (2) in sharply incised wounds, and (3) in more distal wounds. The collected replant material does not permit correlation of either technique or timing of nerve repair with the ultimate degree of regeneration. Many surgeons now feel that primary repair of nerve trunks by epineural or interfascicular suture is highly desirable when possible. Early secondary repair has been successfully performed in many instances. It is also not possible to define accurately functional success in extremity replantation. In general, the procedure is considered successful if the patient and the evaluating physician feel that the extremity function is preferable to that of currently available prostheses (Fig. 1). Using this criterion, the outcome of replantation operations has been termed successful in a high percentage of patients reported.

Incomplete Traumatic Amputation

It is obvious that the incompletely severed extremity offers virtually the same surgical challenge as complete amputation. Reviews of replantation have customarily not included cases of incomplete amputation because the presence of a viable tissue pedicle introduces so many variables into the assessment of results that even general conclusions become impossible. It is recognized, however, that one of the principal benefits of the recent interest in extremity replantation is a trend to more careful assessment of the badly injured extremity and the consequent salvage of extremities that might formerly have been amputated.

Bilateral Replantation

A single instance of bilateral upper extremity replantation is known. The patient was a 12-year-old boy who sustained bilateral complete amputation of the upper extremities above the midhumeral level. Replantation was completed, but circulatory failure necessitated amputation of one arm and infection necessitated amputation of the other below the elbow, improving the outlook for prosthetic function. This experience suggests that bilateral replantation is technically feasible and is of interest in that no cardiovascular systemic effects were observed.

Summary

Experience with upper extremity replantation is encouraging. Better understanding of the basic processes

Figure 1. Photograph of a patient 14 months after replantation of a severed right arm. (From Williams, G. R.: Monogr. Surg. Sci., 3:53, 1966.)
involved and particularly of peripheral nerve regeneration should lead to improved results.

**BASIC CONSIDERATIONS IN REPLANTATION**
Extremity replantation involves many basic considerations. Most obvious is the necessity for detailed anatomic knowledge. Even more than with many other operations, surgical restoration of an amputated extremity requires knowledge of wound healing, the factors that influence healing, and the time required for the healing process. Currently, inadequate understanding of the healing process of peripheral nerves is the greatest single cause of imperfect results after replantation. The observation that infection is a major cause of early failure after limb replantation emphasizes the need for knowledge of surgical microbiology and for understanding the methods of minimizing, detecting, and treating bacterial infection. A basic problem shared with other vascular procedures but uniquely severe in replantation is the phenomenon of ischemia and restoration of blood flow. Several important questions regarding ischemia and restoration of flow may be posed. What is the maximal period of ischemia that will allow restoration of function by re-establishing circulation? What factors modify the period of permissible ischemia and, particularly, how can this period be prolonged? What problems are associated with restoration of blood flow and how can these be minimized or prevented?

**Ischemia**
When blood flow to an extremity is completely interrupted (as in traumatic amputation), the available oxygen is quickly exhausted and anaerobic metabolism begins. Ultimately, an irreversible state is reached when restoration of blood flow will no longer result in recovery. The length of time between the onset of ischemia and the state of irreversibility varies widely from one tissue to another. Skeletal muscle is the tissue in an extremity that is most sensitive to ischemia, followed by skin, fat, nerves, and bone. In experimental preparations, the ability of skeletal muscle to contract after electrical stimulation diminishes after 2 hours of ischemia and is totally lost after 4 hours. Few gross or microscopic changes can be detected in ischemic muscle until 4 to 6 hours after ischemia is produced, although depletion of glycogen and ATP has been described. Most studies of the maximal period of tolerance for ischemia have involved re-establishing flow after varying periods of ischemia in a variety of experimental preparations and studying the morphologic, physiologic, or biochemical changes that occur. When flow is restored in experimental preparations, necrosis of some skeletal muscle cells follows an ischemic period of about 2 hours duration, and necrosis is very extensive after an ischemic period of 8 hours. There is some species variation in the resistance of muscle to ischemia and presumably this is true of other tissues. In the rat, the permissible period of skin ischemia is about 8 hours. It is generally stated that fat, nerve, and bone are more resistant to ischemia, but precise experimental definition is lacking.

Basic studies of the effect of ischemia on skeletal muscle and skin, briefly cited in the preceding paragraph, suggest that an extremity replanted with adequate restoration of circulation after 6 to 8 hours should survive with good recovery of skeletal muscle contractility. This has been confirmed by limb replantation experiments in dogs.

For obvious reasons, extension of the tolerable period of limb ischemia is desirable in clinical replantation. The oldest and perhaps most widely used agent to accomplish this is hypothermia. Presumably, hypothermia slows the metabolic processes that lead to an irreversible state. The optimal degree of hypothermia and the exact period of protection that might be offered by hypothermia are not precisely defined. Lapinsky has reported survival of a replanted, cooled dog leg after 25 hours. It seems significant that cooling during the period of ischemia has been shown to minimize some of the events, particularly edema, that follow restoration of circulation.

Clearing the vasculature of the amputated extremity by perfusion should theoretically prevent the intravascular coagulation of blood and might remove some of the metabolic products of anaerobic metabolism. Such clearing has been shown to be useful in prolonging the life of experimental animals after replantation. The efficacy of several perfusates in clearing the microcirculation has been studied and the most effective was found to be saline with heparin. Prolonged perfusion using nonoxygenated solutions has no rationale.

**Restoration of Circulation**
When blood flow is re-established to an ischemic limb, femoral arterial flow rapidly rises to a level exceeding the preamputation flow in the experimental animal. In addition, there is a marked increase in bleeding from the distal muscle ends and a visible reddening of the skin, which has been described as reactive hyperemia. An increase in limb weight occurs rapidly for approximately 2 hours and then increases very slowly for about a week, at which time the edema begins to subside.

Studies of the microcirculation of both skin and muscle show that after ischemia of more than a few minutes' duration the restoration of flow in major vessels is not followed by uniform flow in the microcirculation. Rather, the return of flow is patchy, with some areas filling well and others not at all. The role of lymphatic interruption in the formation of edema is not clear, but there is some evidence that lymph channel reconstruction in the experimental animal reduces the extent of edema.

The principal recognized systemic effect of restoration of blood flow to a replanted extremity is the frequent development of shock. The appearance of shock after replantation is not consistent, but it has been described both clinically and experimentally. This shock has been extensively investigated and at least three explanations for its appearance have been suggested. Most evidence suggests that the shock is due to blood and fluid loss into the replanted extrem-
FLUID loss into a traumatized extremity was carefully studied by Blalock in classic studies that showed that traumatic shock was not due to a tissue-elaborated toxin. The same conclusion with regard to tourniquet shock and replantation shock was reached after experiments by others. Since shock is not universally encountered after experimental re plantation, it seems probable that the original condition of the animal, the blood loss during the amputation, the amount of fluid administration during the procedure, types of anesthesia, and perhaps other factors have served to confuse the experimental results. The concept that a vasodilator toxic substance is elaborated in ischemic tissue and causes shock on restoration of circulation has had proponents since the work of Cannon. The question is not whether such a substance might be elaborated after prolonged ischemia but whether the effect is clinically significant under the conditions in which replantation might be attempted. Recent experiments again indicate that it is unlikely that a tissue toxin of significance is elaborated during periods of ischemia of up to 8 hours. Mehl has suggested that shock in the postreplant period is due to fall in pH, and improved survival using an amine buffer in his experiments was impressive. Certainly this work demonstrates the importance of control of pH, whether it is the primary cause of shock or secondary to it.

TECHNICAL CONSIDERATIONS

The Decision to Attempt Replantation

Replantation should be considered in every instance of upper extremity traumatic amputation. Since the functional result of replantation is imperfect at best and since the procedure entails definite risk to the patient, a number of factors should be carefully considered before a decision is made to proceed with the replant operation. The operation is more strongly indicated in young than old persons, both because of the significance of extremity loss and because the reported results of functional recovery in younger patients have been more favorable. The wound should be one that is acceptable for primary repair. Wounds that are badly contaminated and grossly avulsed should probably be excluded from consideration. The presence of significant associated injury should be carefully ascertained and probably constitutes a contraindication to replantation. The time interval between wounding and anticipated restoration of circulation should be less than 10 hours, although this is not an absolute figure. If the extremity has been promptly cooled and the circulation can be cleared during the first 8 hours, the time interval may be up to 20 hours. Finally, the impact of replantation, the expectation of multiple operations, and the necessity for at least 2 years of rehabilitative therapy should be considered in each patient.

Lower extremity replantation is indicated only in exceptional circumstances, such as loss or threatened loss of the other leg. The principal reason for this is that the function of the lower leg is relatively well accomplished by available prostheses. Also of importance is the fact that a shortened, anesthetic lower extremity is a constant and significant handicap during the period between replantation and very unpredictable nerve regeneration. It is obvious that improved methods of managing peripheral nerve injury will alter the indications for attempting to replant lower extremities.

The Replantation “Team”

All aspects of replantation are integral to other more common surgical procedures, yet experience indicates that preliminary review of the subject by all personnel to be involved will avoid recurring problems and improve the likelihood of success. Laboratory experience with the procedure is strongly recommended.

General, vascular, and orthopedic surgical skills are necessary for major replantation, and microsurgical skills are required for digital replantations. At least two, and as many as four or five, surgeons should compose the replantation team.

The anesthesiologist should be sensitive to the likelihood of hypovolemia. He should anticipate rapid, sizable blood loss when the extremity circulation is re-established. The problem of replantation shock and acidosis should be recognized and prevented or promptly treated by administration of blood, fluid, and bicarbonate.

Specialized facilities are required in the postoperative period, and the availability of physiotherapy and a spectrum of rehabilitative services is highly desirable.

Steps in Replantation

Control of bleeding from the amputation wound and careful assessment of the general condition of the patient and of the extremity are preliminary to making a decision to attempt replantation. Preoperative x-ray examination of the extremity and the wound is usually indicated. In avulsion injuries, x-ray examination of the cervical spine is indicated to rule out evidence of nerve root avulsion. If such evidence is present, myelography should be performed prior to attempting what might be a hopeless replantation. The extremity should be cooled by immersion in a sterile solution. When operating room conditions are available, the vasculature of the extremity should be cleared with balanced salt solution to which heparin and an antibiotic have been added. An intravenous infusion set is adequate, and the perfusion is discontinued when venous drainage becomes clear. Occasionally, extraction of thrombus material by means of a balloon catheter may be necessary. Both the extremity and the amputation wound are carefully prepared for replantation. In addition to mechanically cleaning the skin surrounding the wounds, extensive irrigation of the wounds with large volumes of sterile saline is important. Bone stabilization and fixation are initial steps in replantation (Fig. 2). It is essential to shorten the bone at all levels of amputation to allow approximation of other structures. The type of bone fixation depends upon the degree of comminution of the fracture and the anatomic level. A variety of intramedullary devices and plates have been used successfully, and evidence does not strongly favor one method over another. When bone fixation is complete, reconstruc-
tion of the veins is begun. This is perhaps the most critical technical step in the replantation procedure. As many large veins as possible should be identified and careful anastomoses performed. Gentle dilation of the vein ends and placement of traction stay sutures allow construction of accurate, maximal-size, end-to-end anastomoses. Very fine synthetic suture is placed with continuous or interrupted technique. Following completion of at least two, and preferably several, venous anastomoses, the arterial anastomosis is performed. In amputations distal to the bifurcation of the brachial artery, both the radial and ulnar arteries should be repaired. Vein grafts from the saphenous system can be used to bridge gaps in either arteries or veins. On release of vascular clamps, hemorrhage from the distal muscle ends should be anticipated. This is apt to be massive, and transfusions will usually be necessary at this time. Establishing hemostasis will involve time, pressure, and patient ligation of multiple bleeding points. At this point, débridement of the amputation wound should be completed, as non-vascularized tissue can be accurately identified for the first time. Thorough débridement is important in preventing infection, and its value cannot be overemphasized.

Management of the divided peripheral nerves is controversial. Early opinions were generally that secondary definitive nerve suture should be performed. Experience with exceedingly difficult secondary operations in dense scar and the hazard of vascular damage have convinced many surgeons that primary nerve suture should be performed when possible. Very careful interfascicular suture using magnification gives the best chance for a useful regeneration. Repair of the muscles is then performed by means of interrupted sutures in the muscle fascia. Subcutaneous tissue and skin closure is routine. Drainage of the wound is indicated in many instances. If adequate skin coverage is unavailable, grafting may be necessary, and tendon, bone, nerve, and vessels must be covered by flap tissue. Following the completion of the procedure, the arm should be elevated and protected by padded splinting in a position of function.

Postoperative Management

Postoperative care of the replanted extremity involves efforts to maintain circulation, protect the extremity against injury, and preserve functional capacity until nerve regeneration occurs. Anticoagulant therapy, fasciotomy, and methods of minimizing edema
should be considered in the early postoperative period. The failure of heparin to improve results in experimental replantation and the complications often associated with effective levels of heparin have led to the recommendation that it not be used routinely after replantation proximal to the hand. Heparin and/or dextran are generally used after digital replantation. Fasciotomy may be critical in maintaining adequate circulation and should be performed freely but probably not routinely. Edema is controlled principally by elevation, gently and carefully applied elastic compression, and careful attention to serum protein level. The formation of edema is rapid in the first few hours after replantation, and care to avoid constricting dressings in this period is important.

The anesthetic arm is protected by padding, frequent position changes, and skin care. Physiotherapy should be employed very early in the postoperative period to preserve range of motion and joint function in the extremity. Muscle stimulation is added when healing of the wounds is well established. The cooperation, advice, and assistance of a physiotherapy unit is invaluable in the management of these patients and probably essential in obtaining a satisfactory functional result.

The risk of infection is minimized by appropriate selection of patients, careful and complete débridement, good surgical technique, and early, adequate antibiotic therapy. Antibiotic administration is begun prior to the replantation operation, and high intravenous doses of broad-spectrum antibiotics are continued for several days. Prophylaxis against tetanus should not be forgotten. Life-threatening infection is an indication for amputation.

Hypovolemia and its attendant cardiovascular and renal problems is the principal threat to the patient in the early postoperative period. Blood replacement prior to and during the replantation procedure should be as complete as possible, and further blood and fluid administration may be required as fluid is sequestered in the extremity in the postoperative period. Careful attention to blood pH, serum electrolytes, and urine output should allow prompt correction of abnormalities before major damage occurs.

The postoperative replantation patient requires far more than the usual psychological support from the managing team. The attempt to save an extremity will involve a long rehabilitation period, several subsequent operations, and a lengthy period of doubt about the extent of functional recovery. The managing physician and the many ancillary personnel involved in such procedures must realize the importance of establishing good rapport and maintaining support during this long period of treatment.

Most patients will require one or more secondary procedures for nerve repair or grafting, and many will require subsequent orthopedic reconstructive procedures. These are not unique to replantation. Wound infection is not so destructive to nerve repair as it is to the healing of bone or tendon.

During the long period of convalescence following extremity replantation, frequent review of the course, problems, and outlook by all participating personnel is important. The best interests of the patient are served by appropriate timing of subsequent procedures, recognition of problems, and prompt recognition of failure if it should occur. The difficult decision to amputate a replanted extremity is often made more easily and promptly by a multidiscipline review of the patient's progress.

**REPLANTATION OF DIGITS**

The replacement of any amputated part distal to the distal wrist crease, whether it be single or multiple digits or amputation through the metacarpal bones, is considered to be digital replantation. The development of microsurgical techniques for repair of vascular and neural injuries and clinical success in digital replantation, first achieved by Komatsu and Tamai in July, 1966, created a surge of interest in digital replantation that is still increasing in momentum. Currently, success rates of 40 to 70 per cent are being reported in series of digital replantation procedures.

**Indications for Replantation**

The selection of patients for digital replantation takes into account the same factors mentioned for more proximal replantation. Specifically, replantation is indicated with multiple injuries or single amputation of a thumb or index finger. A single, complete, or incomplete amputation in any of the three ulnar digits should be replanted only if there are extenuating circumstances.

**Operative Techniques**

The steps in digital replantation are similar to those in major extremity amputation. Skeletal fixation is achieved initially, followed by repair of the extensor mechanism and dorsal veins, with an attempt made to repair at least two dorsal veins and the dorsal skin. Following repair of the above structures, the volar surface of the finger or thumb is approached, with digital arterial repair being accomplished initially. Finally, the neural anastomoses are followed by the flexor profundus tendon suture and volar skin closure. The neural and vascular anastomoses are carried out using an operating room microscope and employing well-documented microsurgical instruments and technique. All digits to be replanted should be shortened in bony length in order to allow vascular anastomoses without tension. Failure of digital replantation has most often been associated with inordinate tension on the venous anastomosis with subsequent thrombosis.

**Postoperative Management**

Of extreme importance following this precise technical accomplishment is diligent postoperative care. Observations should be made at half-hourly intervals of the color and capillary return of the replanted digit. With any suspicion of a venous or arterial thrombosis, the individual is returned to the operating room for operative evaluation of the anastomotic site and reanastomosis. The digit will exemplify a reactive hypervemia in like manner to the extremity of a major replant. In digital replantation, in contrast to major
extremity replantation, anticoagulants are used in the form of heparin for a period of approximately one week to ten days in conjunction with aspirin and dipyridamole. Immobilization of the extremity is continued for a period of four weeks, at which time active and passive motion exercises are undertaken as one would in general digital rehabilitation following traumatic injury to the osteotendinous structures.

Discussion

The primary aim in replantation surgery is to obtain extremity survival. Of equal importance, satisfactory function must be achieved. The major limiting factor to satisfactory function seems to be tendon motion. Subsequent reconstructive procedures will restore satisfactory tendon motion in a significant percentage of replanted digits. Satisfactory survival and function after digital replantation is dependent on the availability of microsurgery. The general principles of hand reconstructive surgery must be followed.

SELECTED REFERENCES


This is the original description of the first successful human replantation experience, which, more than any other factor, stimulated interest in the possibility of extremity salvage by replantation.


This is an extensive review of the pertinent literature concerning the experimental basis for limb replantation, including the authors' investigative experience.


An excellent review of the subject of both major and digital replantation by an authority.

REFERENCES


