

Hand Transplantation: Current Status

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I. Position of the American Society for Surgery of the Hand

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Hand transplantation has been performed since September of 1998. Preliminary clinical experience based on 14 patients has underscored the importance of patient motivation and compliance, intensive hand therapy, and close post-transplantation surveillance. Acceptable functional and cosmetic outcomes, particularly for bilateral amputees, have been achieved and are similar to hand replantation at equivalent levels. However, major return of two-point discrimination or intrinsic muscle function is not to be expected.

At present, ongoing heavy immunosuppression is required for allograft survival with unknown long-term risks. Although there have been no life-threatening adverse events, complications include allograft rejection and loss, tissue necrosis, and osteomyelitis. Furthermore, the effects of chronic rejection on the allograft function and survival have not yet been determined. Because there are many significant contraindications to both the surgical procedure and the immunosuppressive protocol, careful pre-operative, medical and psychological screening is mandatory.

In summary, hand transplantation is still an experimental procedure that may enhance the function and/or appearance of carefully selected patients. Further research and progress in transplant immunology are needed before it can be considered a consistently safe and efficacious practice.

II. Background

September 2001
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Outcomes for 10 Hand Transplant Patients

At the recent conference of the International Federation of Societies for Surgery of the Hand (IFSSH) in June 2001, information related to ten patients with upper limb composite tissue transfer (hand transplantation) was reported. The first patient, a 48-year-old New Zealand businessman, had surgery in Lyon, France, in September of 1998 with an international multi-discipline team. (2) (3) However, he failed to maintain the needed immune suppression medication post-operatively and when chronic rejection was present, had his transplanted hand amputated on February 2, 2001, in London by Dr. Nadley Hakim, one of the original team members. (4) Other patients with hand transplantations were reported from United States (N=2), China (N=3), Italy (N=1), France (N=1), Malaysia (N=1), and Austria (N=1) (including one bilateral hand-forearm transplant). They have had either too short follow-up or inadequate data to evaluate the preliminary outcomes. (5) (6) (7) Two hand transplantations (included in those listed above) have been performed in the United States at Louisville, Kentucky, at the Jewish Hospital, one reported with a year

follow-up. This first patient, a 38-year-old emergency medical technician, has had continued “transplant success” as reported in November 2000. (8) A viable limb with reported improving function and sensation at a protective level appears to be present. Continuation of intermittent problems related to immune suppression has been noted. The second limb transplant has also been successful from a viability perspective, but continues to be faced with ongoing evidence of chronic rejection, currently controlled with immunologic suppressive medication.

Expected Outcomes and Risks

As hand surgeons and members of the American Society for Surgery of the Hand, we must ask, “What do we currently know of the expected outcome and risks associated with hand transplantation?” “Is this an operative procedure that we should recommend to an inquiring patient?”

In addressing these questions, we recognize several factors:

1. Hand surgeons clearly possess the needed technical skills to perform a successful hand or upper limb transplantation as evidenced by the experience in limb replantation.
2. Upper limb transplantation is now occurring in several areas throughout the world.
3. Advances in organ transplant (in particular, donor-related kidney and liver with careful tissue HLA matching) have demonstrated improved organ and patient survival in many life-threatening conditions. Success in transplantation of solid organs has steadily improved both technically and with improved immune suppression.
4. Public perception and expectations are high, yet they are without a clear understanding of the inherent risks of these procedures, both acute risks and chronic immune suppression risks.
5. We know that the hand is a complex organ of nerves, muscle, tendon, and vessels covered by an immune intolerant skin. Both humoral and cell mediated immune suppression is required. (9) While hand transplants have been contrasted to kidney transplants, a transplanted hand is not equivalent to any parenchymal tissue such as the kidney or liver. (10) (11) (12) And while a comparison of a hand transplant to a kidney transplant as equal with respect to the “improved quality of life”, statistics and analysis clearly demonstrate that kidney transplants save lives when one appreciates that with sustained renal dialysis, there is a mortality rate of 21%.

Measuring Success

How do we judge the success of hand transplants? At this point in time, the metrics of success are not clear. (1) (10) (11) Most agree that hand transplant success should be measured at several levels. The first level of success is sustained revascularization without rejection, now approaching two and half years with controlled untoward events. The second level of success is a limb with sensibility, proprioception, and central acceptance. The third level is the sum of the associated risks of infection, tumor, and other complications associated with immune suppression, counterbalanced against the potential gain of a functioning hand. Finally, function of that vital organ of sensation and communication must be restored sufficiently so that the patient has the perception that his or her new hand is a natural part of the recipient’s body. While the digits of the transplanted hand will move and provide pinch and grasp because of the connections to the extrinsic forearm muscles, movement resulting from independent action of the transplanted intrinsic muscles has not been observed. Furthermore, it is not clear that sensibility, so essential to hand expression and advanced manual skills, will be present. The hand is considered by many to be a representative mirror of the mind. (11) It must provide coordinated bimanual skills. It must reflect central perceptions of coordinated, integrated meaning. From most observations of the results of composite tissue transplantation to date, the measurement of function of the human hand transplantation at this level has not been convincingly demonstrated.

Results of Animal Studies

Animal models have been extensively studied, and the results are not encouraging. Lee and Mathes have presented many of the current concerns. (13) Jensen and Mackinnon have reviewed over 250 publications on the subject of results of limb allograft transplantation in experimental models. (14) Failure rates are beyond acceptable limits. (15) (16) A successful transplant in animal experimental models remains a challenge simply because of the large amounts of immune suppression required for survival of the transplant. The complications of such medications, at least in animal models, are currently overwhelming. (17) (18) (19) (20) It appears at the present time nearly impossible to provide a viable limb in the experimental models without significant risks from the immune suppressive medications. Post transplant risks in animals including acute rejection, medication toxicity (both nephrotoxicity and neurotoxicity), and infection from opportunistic organisms remain significant challenges. Despite disappointing results in the pig and primate, hopeful research continues. (21)

Most authorities believe that these same risks are also present in the human model. Renal transplants have an average of 1.5 septic episodes per year, and 80% have at least one serious infectious episode within the first year post transplant. (22) (23) Malignant tumors related to immune suppression are reported between 8-20%, with carcinomas of the skin and lips at 30%. (24) (25) Finally, historical data on renal and liver transplants indicate that the overall survival at fifteen years ranges between 30 - 60% depending upon the age of donor, HLA matching, age and disease status of the donor, and time from transplant. (26) (27) Recognizing these facts related to single organ transplantation, there must also be concern that a hand transplant might develop chronic rejection and therefore need to have the transplantation procedure repeated eight to ten years from the index procedure to continue to provide the intended purpose. The potential need for a second transplant, combined with the risk of long-term immune suppression, is important historical information that must be presented to a potential hand transplant recipient.

Ethical Concerns

Ethical concerns must also be considered in the delicate balance of risk and reward when evaluating a patient for limb transplant. (28) What is the patient's ability to understand the risks and make appropriate judgments? Are the patient's expectations realistic? Is the patient's psyche prepared for rejection events, repeated control of infectious episodes, the daily required immune suppression medications, the concern of the unknown related to ultimate function and potential chronic rejection? How good is this "quality of life" with a new limb when daily medications are required to maintain its viability? Can a limb be easily removed (amputated) if both surgeon and patient recognized that chronic rejection is occurring with so much personal time and effort invested by both the surgeon and patient? Mr. Hallam and his surgeons struggled over this issue for many months before the limb was finally amputated in England. (4)

The transplanted hand, like the transplanted pancreas or a vocal cord, may provide improved quality of life, but the impact of a transplanted hand has not been objectively measured. Hand transplant may improve the patient's psyche, family interactions, and even give a sense of fullness. However, before hand transplants can move forward to the potential that they represent (and that potential is acknowledged to be very great), these procedures should achieve a greater measure of success 1) in sustained animal models; 2) with compatible HLA matching of potential donor to the recipient; 3) with improved bench to bedside immune suppression without requirements of long-term immune treatment; and 4) with recipient tissue tolerance alone or with low risk immune suppression.

Caution

We applaud the studious approach of the current pioneering investigators of hand transplantation but strongly encourage them to proceed slowly, cautiously, and with measured concern of the risk and benefits to man. For those that wish to go forward with any type of composite tissue transfer, it is important that transplant teams be developed that are experienced in large organ transplants, aware of advances in immune suppression medications, and include hand surgeons within such teams who not only bring

microsurgical skills but also the ability to provide a clear understanding to the potential recipient a knowledge of hand function by which success may be measured. At this time, the ASSH continues to urge great caution and a measured approach to the patient requesting a limb transplant. We encourage all surgeons to await the outcomes of the current human experimental studies before additional combined trials are considered. The public, especially those with traumatic loss of limb, must be carefully counseled and advised regarding the substantial risks to limb and life associated with these procedures to date.