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The History of Arm Transplantation

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Earl Owen, world-renowned pioneer of microsurgery and a good friend of mine, first voiced the idea of a hand transplant more than 30 years ago in a speech at Edinburgh University, but it was not until the mid-1990s that he decided it was both technically and immunologically possible. The only reported previous hand transplant attempt had taken place in Ecuador in 1964 and had failed due to initial absence of any anti-rejection drug use, allowing immediate severe rejection. Earl trained and practised in London for many years (and was awarded a Hunterian Professorship in 1968) and hoped to perform the world's first hand transplant here.

With this in mind, and with encouraging results of successful skin, nerve and joint human transplants, he approached me in 1998 and I contacted the Royal College of Surgeons and the UK's Transplant Service Authority to ask for permission for such an operation to go ahead. However, British authorities were unconvinced and had doubts about the ethics of the procedure for a single limb. They believed that putting a healthy patient on potentially dangerous immunosuppressants could not be justified at this stage, despite the long term successes with experimental animal composite tissue transplants with a cocktail of recently proven powerful drugs.

Earl was keen to form a team of experts in preparation for the procedure, so I suggested we contact Max Dubernard in Lyon, Head of Transplantation

and urology at the city's Edouard Herriot Hospital, where Earl had been a visiting professor for 20 years. Max had carried out France's first pancreas transplant in 1976 and was not only one of France's top surgeons, but also a prominent local politician who ran his own department. He was excited by Earl's suggestion and agreed that the proposed forearm transplant could go ahead in his department in Lyons. Earl quietly began assembling a skilled international team composed of transplant, orthopaedic and hand microsurgeons, anaesthetists, a psychiatrist and a psychologist specialising in body image disturbances.

The hand surgeons knew they could attach a hand and the transplant surgeons knew about controlling the rejection of donated internal organs. However, what we could not predict was how the body would react to receiving a hand — an organ made up of many tissue types: nerve, artery, tendon, muscle, bone and the tissue that rejects most violently, of course, the skin.

The results of experiments on primates using earlier immunosuppressives had been abysmal. Most died secondary to complications from the immunosuppressant drugs. Primates may be the closest animal model to man, but following transplantation of any organ, they require more immunosuppression than man. These experiments were conducted in the mid-1980s, with just the one drug, but since then, we have been using combination therapy, where much lower doses of several drugs are used, with improved results.

There was still the ethical objection to putting someone on potentially life-threatening immunosuppressants for a "quality-of-life" operation.[1] However, one may argue that such operations are already routine — kidney and pancreas transplants are done so that people do not have to endure a lifetime of dialysis or insulin injections and are not in themselves life-saving operations. Other members of the "international team" preferred our first case to be a double amputee, where the benefits would potentially be wider for the patient, but Earl conservatively argued that the area of skin on two forearms and hands may be too much for the immunosuppressive cocktail to protect. If this were to be the case and the transplant failed because of it, it would set back limb transplantation many years. We agreed to go ahead with a single hand transplant knowing that skin is the most difficult body tissue to immunosuppress.

When internal organs are given for transplantation, patients are of course very grateful for the gift. However, when the donor has provided his hands, a patient would need to be able to cope psychologically with the constant reminder that "their" hands have come from a dead person and been used to carry out the day-to-day activities of that other person's life. The recipient would need to be carefully chosen and have certain characteristics to sustain his enthusiasm through the early post-operative months. Whereas organ transplants need to work as soon as transplanted, yet cannot be seen, a hand transplant cannot function for some considerable time (as nerve regeneration slowly recovers) yet it is immediately and permanently seen.

A gentleman called Clint Hallam was well known to Earl and was one of three people short-listed for a hand transplant. Hallam, determined for many years to have the operation, had contacted Earl and confirmed his willingness to travel for surgery anywhere and at any time. Now he underwent another series of psychological and physical checks and was commenced on a course of forearm strengthening exercises. Hallam was considered a suitable patient by the consultant psychiatrist, with a "strong constitution and solid resolve". Augmented consent forms and legal contracts were drawn up in conjunction with Australian and French lawyers. These contracts cleared the surgeons of responsibility for any risks and complications involved in the operation. Mr. Hallam agreed to adhere to a regular schedule of post-operative physiotherapy and a strict regimen of immunosuppressive medication. He agreed to attend regular follow-up appointments, blood drug level tests and biopsies, and to undergo tests to monitor nerve regeneration and hand function.

The surgical team was drawn from around the world and therefore its members needed to agree on a time to convene and then wait for a donor to become available. The date was set for the beginning of September 1998. However, after a week, there was still no suitable donor whose hand would match Hallam's for size, shape colour, and hair distribution and he became restless and agitated. With the proposal to reconvene again in November, the team began to disperse. The Australians were about to board a plane to Sydney, Max Dubernard was on a train to Paris and Marco Lanzetta was driving back to Milan when news came through that a suitable donor had been found by the excellent Etablissement Français des Greffes organisation, which had placed their resources on the alert for such a donor.

A 41-year-old Frenchman had been in a motorbike accident, suffered a fractured skull and died from a blood clot on the brain. His next-of-kin was traced and permission for his organs to be removed was given, the family feeling that at least some good might come of the unhappy incident.

Hallam was told to prepare for surgery the following morning. The Australians were stopped from boarding their flight, and Max went from Paris to harvest the forearm. In London, I got a call at midnight and, after performing two early morning kidney transplants, I flew to France later that day, joining Marco, who had reached Milan and turned back to drive again over the Alps to Lyon to join the others.

The actual operation went very smoothly, a tribute to the whole team, which had rehearsed the procedure many times. This team included the very experienced theatre staffs from both the transplant and the orthopaedic surgery and the anaesthetic departments, whose heads of divisions, as well as their most experienced staff members, all volunteered readily to be available for the procedure "at any time while the team was in waiting".

The operation commenced mid-morning and ended before midnight on September 23, 1998. The preparation of the donor and recipient ends was both intriguing and obsessive, taking more time than was expected from the previous practice sessions in the Lyon University's anatomy school. The orthopaedic team joined the forearm bones 10 cm from the wrist with a plate and six screws for each bone. Several muscles and tendons were joined before the Zeiss motorised operating microscope was focused and the ulnar and radial arteries were joined with microsutures. A large vein was then joined and the time came for the release of the tourniquet! This was the most anxious part of the procedure and Earl describes the moment he gave the order as defining for him a new concept of the word "stress". The white limb gradually became pink and the team relaxed as the anaesthetists checked all parameters as the team took a break.

The operation proceeded after that at a more leisurely pace as the median and ulnar nerves were joined, some 21 came from the wrist under the microscope as accurately as possible. This was interesting as the donor nerves were thinner and coloured a pale yellow, greatly contrasting with the recipient's fatter thicker white fascicles. After this, the tendons, some muscles and finally the skin were repaired. Skin grafts were taken from the right thigh to both allow for post-operative swelling and to provide

observable islands of recipient skin within the donor skin surrounds. A loose dressing support was applied and the patient was shifted to the recovery ward. A brachial block had been administered before he awoke so that the patient could not immediately test out our joints by using his forearm muscles, which could jeopardise the joints. The block was continued for the first week.

The surgery was technically successful, and so was the adherence to the immunosuppressive regime which had started preoperatively with intravenous anti-lymphocyte serum and first doses of the immunosuppressive cocktail of drugs.[2,3]

"My hand's back", said Hallam on emerging from the anaesthetic. "It's almost like I'd lost an old friend years ago, and suddenly it's back".

Congratulations arrived from Jacques Chirac, the French President. Dan Rather, CBS News presenter, stated: "It's the kind of quantum leap in modern medicine that, when it happens, is stunning. Transplant surgery that is simply staggering because it holds so much promise". In the first three months following the operation, Clint Hallam was under close supervision and adhered to his schedules of observations, exercises and drugs. The team was surprised by the evidence of the rapid return of nerve regeneration, and the fast rate of nail growth in the donor hand. Clint Hallam left the hospital area on January 1, 1999 assuring us that he would be continuing the very satisfactory progress of his transplant and was expected to return to Australia for continuation of the protocol.

It was now the team's task to perform the first successful double arm transplant — another world first! In the last few months of 1998, we awaited a suitable donor for the potential double hand transplant patient — a man who had lost his arms in an explosion. Each time a suitable donor was found, permission was not granted by the next-of-kin. Technically, the transplant surgeons did not need permission, because in France, one is presumed to have consented to organ donation on one's death unless otherwise stated, but we felt it was necessary to make an exception and have the relatives' cooperation for these unusual cases.

The eminent hand and transplant surgeons flew into Lyon from around the world three times since June 1999, but finally, 12 days into 2000, the call came to say a donor had been found. The team members were alerted immediately. I had to abandon a lecture tour in California, Earl flew out of

Sydney, and four Italian specialists drove from Milan to join Max Dubernard and our augmented French colleagues.

The father of the donor involved in the world's first double hand transplant was paralysed down one side of his body. He understood what it was like to not have the use of a limb, and he agreed to the operation when many other parents had refused. His 19-year-old son had fallen from a bridge. He was on a life-support machine for several days and his family hoped for a recovery, but sadly this did not occur.

The recipient of the new hands, Denis Chatelier, was a 33-year-old house painter and father of two, whose hands were blown off when a home-made rocket he was showing to his nephews exploded prematurely. He longed to live a normal life with his family again. When he saw the television report of the first single hand transplant in 1998, Chatelier had contacted Max Dubernard.

Chatelier described himself as a *battant*, a fighter, and a *croyant*, a believer. He was fit and in good shape for the seventeen-hour operation and up to two years of physiotherapy. Max agreed to go ahead: "He is strong-willed and tenacious", he told colleagues.

In the early hours of Thursday, January 13, along with his kidneys, liver and heart, the young donor's hands and forearms were removed. Prosthetic hands supplied by our team, were fitted to provide a normal appearance for his funeral. The donor limbs were perfused with preservation fluid, placed in dry plastic bags and carried in a cool box.

Earl had led the first transplant. This time Max was to be in charge. We began at 6 am. Fifty surgeons, specialists and nurses worked on Chatelier, who lay with arms outstretched on the hand surgery operating mini-tables as if crucified; a separate team of four surgeons for each donor hand and each host arm. He had been sedated and then anaesthetised. The procedures followed the protocol of the Hallam operation. Some of the details are now described.

Tourniquets were applied to his arms and incisions were made on each to expose the deeper structures. The nerves, arteries, veins and muscles were dissected and tagged and the forearm bones transversely cut with an electric saw so that the grafted limbs would be the same length. At the same time, in an adjoining theatre, the donor hands were similarly dissected and tagged. About 10 cm of the donor arm would also be used. First, the two forearm

bones, the radius and ulna, were joined, using small titanium plates with holes for 4.5 mm stainless steel screws to go through; then the arteries and cephalic veins were connected and the first arterial clamps were removed. The tourniquets were loosened and the hands' cool white turned pink. The surgeons left them undisturbed for 20 minutes covered with warm, wet sponges. Next were the muscles, then the tendons, interwoven with the muscles where possible, and finally, the skin. It took until 11 pm.

Although confident of attaching the hands, we had been wary of any unforeseen complications. Patients can lose a lot of blood when two wound sites are opened, and if either of our first two transplant patients had died, it would have meant calling a halt to any further such transplants. However, at midnight in each case, we could relax and watch as the patient's arms were bandaged following the successful operation.

In the days that followed, Chatelier's progress was good. A cocktail of four immunosuppressants and steroids was given. The same mix used in the first transplant 15 months before, and one that had proved very effective. The patient was told not to try to move his fingers. That would come later, after extensive passive physiotherapy and then supported at first with thin rubber bands attached to provide gentle resistance and then to be followed by intensive more active physiotherapy over the next three months.

At the time of writing, a total of 25 new arms have been transplanted in seven countries, and 24 are reported to be doing well. I am still trying to organise Britain's first single transplant. In Austria and Italy, other operations are being planned. The international experience has included the following centres: Lyon (France), Louisville (USA), Guangzhou (China), Insbruck (Austria), Monza (Italy), Guangzi (China), Harbin (China), Brussels (Belgium) and Malaysia. An International Registry on Hand and Composite Tissue Transplantation has been initiated.

Unfortunately, the final chapter in the story of the world's first successful hand transplant patient, Mr. Hallam, has ended less than satisfactorily. Over the months following his operation, it became clear that Mr. Hallam had been less than honest with the transplant team. He had originally told the team that his hand had been lost in an industrial accident; however it later emerged that it had been severed during an accident in prison in New Zealand, where Mr. Hallam was serving a sentence following convictions for fraud. The psychiatrist later admitted that Mr. Hallam had actually not

been a good choice for the transplant. Mr. Hallam proved to be unreliable. He irregularly disappeared and travelled around the world and could not be contacted for weeks on end. He did not turn up for check-ups and he did not comply with his anti-rejection drug therapy, taking the medication as and when he felt like it, therefore causing illness and gradual rejection.

At the transplant's peak function, Mr. Hallam could use the hand to grab objects, use a knife and fork, write with a pen and even play basketball with his children. Following his non-compliance with treatment, however, he began to lose some of the function and the hand became inflamed from chronic rejection. In November 2000, Mr. Hallam asked for the hand to be amputated, but then changed his mind and pledged that he would try once again and would take the necessary medication. He was given a supply of drugs, but when these ran out he did not obtain more. On January 31, 2001, more than two years after the transplant surgery, Mr. Hallam contacted me once more. One look at his hand convinced me that there was no alternative, but to amputate, as the chronic rejection was severe but, surprisingly, there were no symptoms of a systemic rejection reaction. The hand was painful, suggesting, I believe, successful nerve regeneration.

It was with sadness that I removed the hand. We had given Mr. Hallam the chance of having the new hand he had repeatedly requested, and the surgery was successful. He destroyed his chances by failing to take his medication. I was just relieved that there had been no serious complications and that Mr. Hallam was still in good health. He admits that he is fully responsible for the rejection. Pathologists have studied the amputated hand to determine the rates of rejection of the various types of tissue.

However, Mr. Chatelier is doing well and is adhering to the anti-rejection therapy. The hands have no signs of rejection, are functioning particularly well with good feeling and he is in good health. His town in France's west coast has given him full support and he is already making woodwork model seagulls for sale!

In the last few years, we have taken significant steps in the transplantation of hands and much has been learned. Although the necessary expertise and the immunosuppressant drugs have been available for some time, hand transplantation has not been attempted until recently. The hand is still a special symbol, representing personal identity in the way that other tissues do not. The hand represents a sort of halfway house in terms of personal

identity, between internal organs and brain tissue. Opponents of brain tissue transplants reject the argument that they are not simply about restoring normal function to the recipient: they may also alter the recipient's identity in a profoundly problematic way — so that the person who gave consent to receiving the tissue is no longer the same person after the transplant. Similarly, we need to consider the wider function of the hand in relation to identity, as an instrument of physical intimacy, of contact with others, of consummate skills in artists and musicians, of agency itself (for example, the use of "hand" to represent agency in such phrases as "the hand of Fate", "by his own hand", "the hand of God"). It is given in marriage, washed to escape blame, expresses our feelings, and carries out our commands. The intimacy function of the hand might even, more speculatively, be thought in some to give rise to rights to those with whom the donor and recipient of the transplanted hand have been intimate.

To the hand, man owes his survival and achievements. I have written this chapter on behalf of the original international transplant team of which I was part, and which included:

Professor Earl Owen (Sydney)
Professor Jean Michel Dubernard (Lyon)
Professor G. Herzbert (Lyon)
Professor Xavier Martin (Lyon)
Drs. Hari Kapila (Sydney), Marco Lanzetta (Milan and Sydney) and
Dr. M. Dawahra (Lyon)

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