INVITED COMMENT ON HAND TRANSPLANTATION

MY REFLECTIONS AND OPINIONS ON HAND TRANSPLANTATION

A) Donor

Pre-conditions:

Compatibility of tissue without specific antibodies, compatibility of blood groups (cross-match negative).

Donor should be operated in the same Hospital as the recipient – better organization of synchronous operation and, above all, feasibility of achieving a short ischemia time of the extremity to be transplanted

- Age should correspond to the age of the recipient, not much younger or older
- Same sex
- No tumours, nor infectious diseases
- Same colour of skin
- Size and shape of hands or forearms should be appropriate (x-ray)
- No history of hand injuries

B) Recipient:

Pre-conditions:

1. Anatomical pre-conditions:
   Amputation of both hands – this is because:
   a) for patients with an unilateral amputation, the co-ordination between brain and the intact hand will be so good that training the transplanted hand will be extremely difficult and troublesome. Consequently would only be possible by actively suppressing the function of the intact hand.
   b) transplantation of both hands requires only slightly more time, work and effort, whilst the postoperative training programme and the immune therapy will be the same as for patients who have only had one hand transplanted.

Level of amputation – the ideal level is the distal third of the forearm (ideally both at the same, or nearly the same, level).

Additionally: *eye injury or defective vision* (*reduced eyesight*) is not a contraindication because blind people, or those with defective vision, have an increased sense of touch, and enhanced sensitivity of their hands (braille).

Amputation of both upper arms: both at the same length – the final result here will be problematic due to poor nerve regeneration, as after brachial plexus lesions.

2. Psychic and mental profile of the patient:

- prepared to take risks and accept the challenge
- ability to take stress and endure strain
- unflinching desire to have functioning and feeling hands
- great consistency and steadfastness in taking medicines
- positive attitude and strength of mind
- very disciplined, ambitious
- intelligent
- ready to co-operate
- performance-oriented
- determined to make sacrifices
- prepared to communicate with the team
- total acceptance of his situation (no self-pity)
- ready to live with new hands (disregarding the fact they belonged to a dead man).

3. Social environment:
   Extremely good, well-balanced relationship with partner and family. Acceptance by the therapy team.
4. Time between amputation and transplantation:
   The accident may have happened more than 2 years ago: in our case the accident had occurred more than 6 years previously.

C) Doctors' Team

Good teamwork between doctors and therapists of all disciplines (immunologists, hand surgeons, hand therapists).

Doctors in the team should speak the same language as the patient and should ideally come from one hospital (if this is not the case there will have to be one person to whom the patient relates most closely: this person should speak his native language and be ready to communicate on his behalf).

In numerous pre-operative talks the patient must be informed about all stages of the therapy, and of all possible complications and disadvantages which can occur if the operation is not successful. He must also be aware of all the side effects of his medicines. The patient will also have to demonstrate great zest for learning regarding his body, and the correlation of brain and hands.

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INVITED COMMENT ON HAND TRANSPLANTATION

HAND TRANSPLANTATION – RISKS OF IMMUNOSUPPRESSION

Upper limb transplantation has yet to establish its place in clinical practice. Now that a small number of upper limb transplants have been performed, it is timely to consider the risks and benefits of such as undertaking. It seems logical that the benefits would be maximized by selection of recipients who have suffered bilateral rather than unilateral limb loss as their preoperative disability and by inference their motivation and compliance would be greater.

The limited experience to date has shown no cases of graft loss from acute rejection. One graft has suffered chronic rejection and has been removed in a recent high profile case. It is of note that the immunosuppression was stopped about 60 days earlier, suggesting that the tempo of rejection was rather slower than for organs such as the heart or kidney. Skin is a highly immunogenic organ and this observation suggests that some other component of the graft might have contributed to creating a degree of tolerance; one candidate for this might be the cells of the bone marrow, inducing tolerance by microchimerism (the symbiotic survival of circulating host and donor lymphoid cells). There is little doubt however that there will be a need for long-term immunosuppression, most likely based on Tacrolimus, steroids, and mycophenolate mofetil or azathioprine.

The immediate risks of the implantation procedure can be predicted by comparison to reimplantation surgery (autotransplants). Where the allograft differs is in the need for long-term immunosuppression which creates four potential problems:

Firstly there will be an increased risk of opportunist infections such as cytomegalovirus, pneumocystis and aspergillus which can be reduced but not eliminated by the use of prophylaxis with antiviral and antifungal agents.

Secondly the risk of certain types of tumour will be increased, particularly skin tumours (there is a greater than 100-fold increased risk of skin cancer in light exposed skin in renal graft recipients), and B-cell lymphoma driven by Epstein–Barr virus which affects 1–2% of renal and liver graft recipients each year, and up to 15% of intestinal transplant patients where the requirement for immunosuppression is greater. Mortality is of the order of 50%.

The third problem is toxicity of the immunosuppressive agents, particularly neurotoxicity, nephrotoxicity and diabetes with tacrolimus, diabetes, cataract and osteoporosis with steroids and bone marrow suppression and gastro-intestinal toxicity with mycophenolate mofetil.

The fourth problem is the risk of non-compliance with medications, which is more likely with a graft which is not life-sustaining (based on comparisons of heart and kidney recipients). The drugs require close monitoring and there is a need for compliance with dose taking and clinic attendance. Non-compliance is predicted to occur regularly in 10–20% of renal transplant recipients and is likely to lead to graft failure.

A further risk to consider is the potential impact of limb transplantation on rates of organ donation nationally, because of concerns of the physical disfigurement of the body following removal of the limbs, which does not occur with donation of the internal organs. In Italy this problem has been addressed by securing prosthetic limbs to the cadaveric donor, but concern has been raised by the ethics committee of The British Transplantation Society that the establishment of a limb transplant programme could have a negative impact on organ donation generally.

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