Further information

• BMJ careers advice zone : www.bmjcareers.com/ advicezone

• A summary of *Informing Choices* is available as a pdf on bmj.com

• You can also order a free copy of it in booklet form by emailing kmcpartlin@bmjgroup.com

• Please email rmacdonald@bmj.com if you are

interested in coming to an event that *BMJ Careers* is hosting later in the year to help take the suggestions in the report forward. We would also be interested to hear of any career initiatives that you have in your area

cult for doctors who are not from the United Kingdom to get access to specialist registrar programmes. This belief is held by only 59% of UK doctors in training.

These results may be because this group of doctors has limited access to the first four sources of careers advice and guidance rated by the respondents as being the most useful: firstly, more experienced peers; secondly, senior doctors; thirdly, family and friends who are doctors; and fourthly, peer group.

Career Focus was rated the fifth most useful source, and we hope that a new web based service, the *BMJ careers advice zone*, which we are launching today, will further meet the needs of doctors and medical students in their quest for accessible, impartial careers advice. It should go some of the way to help fill the void in providing useful and high quality careers advice and guidance. It also recognises the valuable contribution of both advisers and peers, formal and informal.

Here's how it works: we will publish, on the web, a selection of career queries together with responses from other readers and our panel of more than 200 experienced advisers, who are mostly Career Focus authors. There are around 80 topics covering a whole range of issues, so whether it's choosing a career, what training to do, or how to deal with work related health problems or discrimination, the advice zone should be able to help. It can be used to submit a career query to our panel, search the database of existing questions and advice, and to share career experiences with other users. (Please go to www.bmjcareers.com/advicezone for more details on how it works in practice.)

The advice zone can't offer a confidential counselling service, but we hope that all the questions and answers that we publish from both readers and advisers will grow into a high quality, valued, and accessible database of careers advice. Judging by the findings from *Informing Choices*, such a service comes not a moment too soon.

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Extending the boundaries of transplantation

Recent hand transplants may herald a new era

C olid organ transplantation has been one of the most striking medical success stories of the past 50 years. Today even the most complex cardiac transplants are viewed as routine, although it is only 35 years since the first successful heart transplant was performed. One of the main reasons for this success is the introduction of new more specific immunosuppressants that have improved our ability to control the transplant patient's immune response. This has reduced the incidence of acute graft loss and the side effects of immunosuppressive regimens. These factors have led some transplant teams to suggest that transplantation should no longer be reserved for life threatening conditions but be used for any problem that can be solved with allogenic tissue. Citing this rationale, surgeons have begun using cadaveric tissue to reconstruct structural, non-life threatening defects of the human body. Over the past five years 20 hand transplants and a laryngeal transplant have been successfully carried out.12 Others have transplanted knees, nerves, and even the flexor tendon apparatus of the hand.³⁻⁵ However, reconstructive transplantation is very different from other forms of transplantation. Whether it is appropriate at the present time is the subject of debate.

Reconstructive transplantation differs from other forms of transplantation in numerous ways. It is performed in healthy patients who have a normal life expectancy; they do not have a chronic disease that can be improved by a transplant. The allograft they receive increases the quality of their life and not its duration. At the same time these procedures require a level of immunosuppression equivalent to other transplants. This exposes the patient to the same risks as other allograft recipients. Not surprisingly, reconstructive transplants have generated a sizeable amount of controversy.⁶ Many critics argue that the risk to the recipient is not acceptable.⁷

Essentially, three criteria must be met to justify these operations. Firstly, is there a genuine clinical need for reconstructive transplants? Secondly, can a good outcome be assured? Finally, does the benefit of the transplant outweigh the risk to the patient from the required immunosuppressive regimen?

Is there a clinical need?

The first of these questions is probably the easiest to answer. Most of the defects being considered for transplantation lead to high physical and psychological morbidity. For example, loss of the hand is a devastating

BMA cohort study of 1995 medical graduates. Seventh report. London: BMA, June 2002.

event, particularly if it is bilateral. Most such patients are young, and many are unable to live independently. Despite advances in surgery, it is impossible to reconstruct the hand with autologous tissues. The only therapeutic alternative to reconstruction is a prosthesis. Prostheses have limited function and cannot reproduce either the intricate actions of a hand or its appearance. The only way of providing these patients with a replacement limb that looks normal and can function well is to use allogenic tissue. With other situations, such as loss of the larynx, the need for allogenic tissue is even clearer. The larynx, unlike the hand, cannot be replaced by a prosthesis; the only potential solution to its loss is transplantation. In these specific clinical scenarios, a potent argument can be made for the use of cadaveric tissue for reconstruction.

Is good outcome assured?

The second criterion, that good outcomes from these transplants be assured, may be harder to achieve. The functional demands on reconstructive transplants are greater than solid organ transplants. A hand has to perform a myriad of complex tasks to fulfil its role whereas a heart only has to pump blood to be useful. Despite this, the initial results of both hand transplants and the sole laryngeal transplant have been encouraging. Most of the hand transplants have reasonable function, working better than prostheses but not as well as replanted limbs.¹ The recipient of the laryngeal transplant is able to talk with good force and tone.²

These initial favourable results may, however, deteriorate with time. All transplants are at risk of chronic rejection, a poorly understood phenomenon that leads to the loss of 50% of renal allografts 10 years after transplant.⁸ It is likely that chronic rejection will also affect the current cohort of reconstructive transplants. This means that a transplanted hand that is working well today may be functionally useless in 10 years' time. In solid organ transplantation, this incidence of long term graft loss is acceptable for several reasons. Firstly, in a life threatening situation, any organ, even one that only lasts five years, is better than no organ. Secondly, given that many solid organ recipients have a chronic disease, an allograft that survives 10 years may outlive the patient. This is not the situation for reconstructive transplantation. These procedures are being performed in young patients who have a normal life expectancy. They require an allograft that works well not just for 10 years but for 40-50 years. Preventing chronic rejection is important if other reconstructive transplants, such as face transplant, were to be considered as loss of limb could be dealt with by amputation but loss of a transplanted face would be devastating.9 If chronic rejection cannot be prevented then the transplant will only have been of temporary benefit, making it harder to justify the risk of the procedure. Only time will tell if chronic rejection will preclude the successful long term outcome of the current reconstructive transplants.

Does benefit outweigh risk?

If adequate function cannot be assured in the long term then the final goal, that the benefit to the patient of the transplant outweighs the risk, may not be obtainable. It is hard to make objective judgments about the risk-benefit ratio of reconstructive transplants because the benefit, improvement in quality of life, is difficult to measure objectively. It is clear that if good long term function can be guaranteed and the risk from any required treatment regimen minimised, the balance would swing in favour of these procedures. This could lead to the wider and more successful application of reconstructive transplantation.

Excitingly, there is a potential way of achieving this double goal of increasing benefit while decreasing risk. Much experimental and clinical research in transplantation is focused on developing a state known as immunological tolerance.¹⁰ In this situation, a recipient does not mount an immune response to donor tissue but remains responsive to all other stimuli. This lack of immune reactivity to the donor obviates the need for immunosuppression and may simultaneously prevent chronic rejection. Clinical tolerance has been achieved to renal allografts.11 Tolerogenic regimens have reduced the need for immunosuppression for other recipients of organ transplants.¹² An increasing amount of experimental research is looking at ways of applying tolerance protocols to reconstructive allografts.¹³ ¹⁴ If successful, this could be the prerequisite for the widespread clinical use of transplantation in reconstructive surgery. In the meantime, we will have to wait and see if the current immunosuppression based procedures herald a new era for transplantation or just another false dawn.

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1 www.handregistry.com (accessed 30 May 2003).

- www.nahuregisu.ycom/accessed 50 May 2005).
 Strome M, Stein J, Esclamado R, Hicks D, Lorenz RR, Braun W, et al. Laryngeal transplantation and 40-month follow-up. N Engl J Med 2001;344:1676-9.
- 3 Hofmann GO, Kirschner MH, Wagner FD et al. Allogenic vascularized transplantation of human femoral diaphyses and total knee joints—first clinical experiences. *Transplant Proc* 1998;30:2754-61.
- 4 Mackinnon SE, Doolabh VB, Novak CB, Trulock EP. Clinical outcome following nerve allograft transplantation. *Plast Reconstr Surg* 2001;107:1419-29.
- Guimberteau JC, Baudet J, Panconi B, Boileau R, Potaux L. Human allotransplant of a digital flexion system vascularized on the ulnar pedicle: a preliminary report and 1-year follow-up of two cases. *Plast Reconstr Surg* 1992;89;1135-47.
 Lee WPA. The debate over hand transplantation. *J Hand Surg*
- Lee WPA. The debate over hand transplantation. J Hand Surg 2002;27A:757-75.
 Strickland JW. Hand transplant—technology over good sense. Indiana
- Hand Center Newsletter 1999;3:2-4.
 Kouwenhoven EA. Jizermans INM. de Bruin RWE Etiology and
- 8 Kouwenhoven EA, Ijzermans JNM, de Bruin RWF. Etiology and pathophysiology of chronic transplant dysfunction. *Transplant Int* 2000;13:385-401.
- 9 Hettiaratchy S, Butler PE. Face transplantation—fantasy or the future? Lancet 2002;360:5-6.
- 10 Waldmann H. Therapeutic approaches for transplantation. *Curr Opin* Immunol 2001;13:606-10.
- 11 Buhler LH, Spitzer TR, Sykes M, Sachs DH, Delmonico FL, Tolkoff-Rubin N, et al. Induction of kidney allograft tolerance after transient lymphohematopoietic chimerism in patients with multiple myeloma and end-stage renal disease. *Transplantation* 2002;74:1405-9.
- 12 Starzl TF, Murase N, Abu-Elmagd K, Gray EA, Shapiro R, Eghtesad B, et al. Tolerogenic immunosuppression for organ transplantation. *Lancet* 2003;361:1502-10.
- 2005,011,0210.
 13 Foster RD, Fan L, Neipp M, Kaufman C, McCalmont T, Ascher N, et al. Donor-specific tolerance induction in composite tissue allografts. *Am J Surg* 1998;176:418-21.
- 14 Lee WP, Rubin JP, Bourget JL. Tolerance to limb allografts between swine matched for major histocompatibility complex antigens. *Plas Reconstr* Surg 2001;107:1482-90.