

# Virtual Mentor

American Medical Association Journal of Ethics  
May 2010, Volume 12, Number 5: 378-382.

## JOURNAL DISCUSSION

### Ethical Issues in Face Transplantation

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**Barker JH, Brown CS, Cunningham M, et al. Ethical considerations in human facial tissue allotransplantation. *Ann Plast Surg.* 2008;60(1):103-109.**

The miraculous transplantation of a leg by the third-century saints Cosmas and Damian [1] became a medical reality in 1998 with the first successful hand transplant in France. In 2005, the same French team performed the first successful face transplant. Since then, 10 facial allotransplantations have been performed in France, China, the United States, and Spain. Two recipients are now dead as a result, one from tissue rejection and one from infection. Critics question whether the benefit is worth the risk. Plastic surgeons weigh Sir Harold Gillies' reconstructive principle of replacing like with like against the Hippocratic dictum *primum non nocere*, or "first do no harm." The risks of lifelong immunosuppression, including infection, malignancy, and end-organ toxicity, seem *prima facie* prohibitive in the context of a nonlifesaving intervention. But severe facial disfigurement to the degree that confers eligibility consideration is not a trivial thing. These are not merely "cosmetic defects," but conditions that render the patient unable to properly eat, breathe, or speak. Furthermore, the face is essential for communication and relating to others, which is the foundation for how we understand ourselves as human [2]. Restoring the face with composite tissue allotransplantation can provide results that are unattainable with current reconstructive techniques.

The operation is still considered experimental and is only performed under research protocols. Hence, the main ethical issue at stake is the use of humans as subjects in clinical research. Does a therapeutic equipoise exist; that is, are experts truly divided on whether intervening is better than not intervening when the risks and benefits of both courses are considered? If the answer to that question is "yes, clinical equipoise exists," then a host of ethical concerns come to the fore. In this paper, John Barker and others from the University of Louisville summarize key ethical concerns addressed in a series of articles from the 2004 summer issue of the *American Journal of Bioethics* [3, 4]. Their goal was to distill for plastic surgeons the questions that ethicists considered most salient. These papers were all written before the first facial allotransplantation had been performed and the general sentiment was one of caution. The University of Louisville pioneered hand transplantation in the United States, and Barker uses the Louisville team's ethical guidelines and experience to address these concerns.

Seven of the most commonly cited concerns were: (1) rejection and drug toxicity rates, (2) implications for donor population, (3) patient selection and compliance, (4) existence of other reconstructive options, (5) functional recovery, (6) psychological implications for the patient, and (7) informed consent.

The first six concerns regard the fundamental risk-benefit analysis, which, in the Louisville team's thinking, favors the proposed benefits. (At this point we have some data to support or refute these concerns [5].) The issue of informed consent must be attended to continually in the realms of surgery and human experimentation.

### **Addressing These Concerns**

*Rejection rates and drug toxicity.* It was the relative success of composite tissue allotransplantation for the hand that made consideration of facial tissue allotransplantation a viable option [6]. The immunosuppression regimens are basically the same. Currently, four of the 10 facial transplants performed have published data on the outcomes. All report one or more episodes of acute rejection that resolved with changes in the immunosuppression regimen. The current thought is that if the episodes of acute rejection are recognized and treated early, they are manageable, and no living recipients have developed chronic rejection, although there are no long-term data [7].

Face transplant currently has a 20 percent mortality rate. One patient in China died after stopping his medications and refusing further medical intervention. The 30-year-old burn patient who received a total face transplant and bilateral hand transplant in France died of a myocardial infarction during an operation for an overwhelming infection of the transplanted facial tissue.

*Implications for society of facial tissue donation.* Organ donation in the United States relies on the generosity of a pool of donors that is far smaller than the list of potential recipients. The question is whether or not the practice of facial tissue transplantation will decrease the overall availability of organs. This depends on the public's perception of the appropriateness of the use of donated organs, which is closely tied to patient selection. For example, when Mickey Mantle (who developed liver failure from alcoholism) received a liver after being listed for a very short period of time, there was a public outcry regarding the criteria for the allocation of livers [8]. Although liver donations did not decrease after the Mickey Mantle case, the concern is that highly visible failures in facial transplantation may decrease the overall donor pool, affecting all those waiting on transplant lists. Currently there is no indication that face transplants have had an influence on organ donation overall.

*Patient selection, exit strategies, and psychological implications.* The patient is the main variable in all considerations of the ethical appropriateness of facial transplantation. Concerns regarding rejection and drug toxicity must be understood in relation to the individual with the devastating facial defect. Choosing a patient who is relatively young and healthy, who is psychologically stable, and who has multiple reconstructive options left if the transplant fails (i.e., a "lifeboat" or "exit

strategy”) minimizes the possible risks, leaving possible benefits in the clear majority. An example is Pascal Coler, the 29-year-old French man who was horribly disfigured with a massive plexiform neurofibroma. He is young, healthy, and if his graft is rejected he still has many reconstructive options. The Chinese patient, who was unable to cope with continuing the necessary medications and who lived in a village more than two days’ travel from his surgeon, was not so fortunate.

Multiple algorithms and safeguards have been proposed to try to ensure proper patient selection for face transplantation. Obviously the defects addressed should involve areas that cannot be adequately reconstructed with traditional techniques (e.g., eyelids, nose, mouth, and maxilla). Patients must be screened for psychological or psychiatric issues that might impede their complying with medication or coping with a changed appearance and the rigorous follow-up and constant monitoring required. However, the character of the surgeons and the institutions involved in these operations cannot be downplayed. An algorithm for selecting a potential transplant candidate is only as good as those applying it. Francis Moore stressed this in 1988 when he wrote that innovations in transplantation should not be performed for purposes of institutional prestige or professional recognition [9].

*Informed consent.* Informed consent has become the foundation for the interaction between the surgeon and his or her patient and a legal and ethical requirement for invasive interventions. Beauchamp and Childress describe seven key elements of informed consent: (1) competence to understand and decide, (2) voluntariness in choice, (3) physician’s or researcher’s disclosure of material information, (4) recommendation of a plan, (5) understanding, (6) patient decision in favor of a plan, and (7) authorization of a chosen plan [10]. It is not difficult to see the challenges to satisfying these elements in the case of facial tissue allotransplantation. Anthony Renshaw and others recently published a thoughtful analysis of informed consent in face transplantation and conclude that the ambiguities surrounding outcomes in this procedure did not preclude proper informed consent [11].

## **Discussion**

Facial transplantation allows reconstructive surgeons to follow one of their first principles: replace like with like. When successful, replacing like with like results in a superior aesthetic and functional outcome for the patient. Achieving this outcome is important for restoration of the severely disfigured individual, inasmuch as the face constitutes an essential part of what makes us human. Facial tissue allotransplantation has the potential to restore a functional face with significantly fewer operations than traditional reconstructive techniques and makes it possible to reconstruct parts of the face that cannot be restored by traditional means.

Much of the discussion of the risks associated with facial transplantation is utilitarian. It includes, for example, the arguments that functional recovery may not be as good as hoped, or that the donation of facial tissue may cause significant distress within the donor’s family, or that having a face that is not his or her own may be an insurmountable psychological hurdle for the patient. These are all

outcome-based concerns, not normative proscriptions against performing a transplant. They define what is to be weighed on the “risks” side of the equation. Hence proper patient selection becomes key.

The team at Johns Hopkins and the University of Maryland recently reviewed the published outcomes data on the first four facial allotransplantations [5]. They reiterate the importance of patient selection and suggest that good candidates include burn patients; patients with midface, perioral, and periorbital defects; children born with severe facial anomalies; and patients with aggressive benign tumors. They also suggest that, because harvest times are relatively long, only brain-dead donors, whose organs are still being perfused by their cardiopulmonary systems, should be used. (Theoretically, harvesting facial tissues after cardiac death would lead to long periods of ischemia that would jeopardize the viability of the transplant.) To minimize possible infectious complications, the viral serology of both donor and recipient should be checked.

It has been 12 years since the first successful composite tissue allotransplantation. Hand transplantation—the paradigm of composite tissue allotransplantation—remains an infrequently performed operation and is still extremely expensive. It is currently only being performed in a few elite research centers around the world. A recent article calculated a cost-benefit analysis in terms of quality-adjusted life years and determined that hand transplantation was essentially a cost-prohibitive option [12]. Unless there are significant advances in immunosuppressive regimens, it is likely that facial transplantation, like hand, will remain the bailiwick of a few specialized research institutions for some time. Continued work on the basic science of tolerance in composite tissue allografts, refinement of surgical techniques, and complete transparency in reporting the successes and failures of all transplants are all necessary components of advancing this field. Going forward, proper patient selection will be the essential element in determining success and hence the ethical permissibility of the endeavor.

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