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A Historical, Clinical, and Ethical Overview of the Emerging Science of Facial Transplantation

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In the past 5 years, a total of 16 facial transplantation surgeries have been performed in France, China, Spain, and the United States. Facial transplantation has become a surgical option in clinical situations in which soft tissue and bone loss is accompanied by severe cosmetic, sensory, and functional deficiencies due to disease, trauma, or congenital malformations. With the introduction of facial tissue transplantation surgery came complex clinical, technological, and ethical patient care issues. These complex issues included determining patient selection criteria, refining donor tissue procurement techniques, predicting expected functional outcomes, appreciating the limitations of obtaining a fully informed consent for an innovative procedure, and deliberating the immunological response and postoperative immunosuppressant requirements of the recipient. In addition, psychological implications for the patient, societal consequences, and ethical concerns have been discussed. The short-term results have been positive. Results to date indicate that the clinical, technical, and immunological patient care issues in this emerging science appear to mirror those of other reconstructive and organ transplantation procedures. The long-term physical, emotional, and psychological effects on the recipient patient, as well as long-term consequences to the donor's family, are yet to be validated.

In the past 5 years, a total of 16 facial transplantation surgeries have been performed in France, China, Spain, and the United States. Facial transplantation has become a surgical option in clinical situations in which soft tissue and bone loss is accompanied by severe cosmetic, sensory, and functional deficiencies due to disease (Hui-Chou, Nam, & Rodriguez, 2010), trauma (Devauchelle et al., 2006; Pomahac et al., 2011; Ravindra, Wu, McKinney, Xu, & Ildstad, 2009; Siemionow et al., 2010), or congenital malformations (Barker et al., 2007). The procedure is considered an option only when all conventional reconstructive methods have failed (Barker et al., 2007; Morris et al., 2007).

With the introduction of facial tissue transplantation surgery came complex clinical, technological, and ethical patient care issues (Barker et al., 2007; Chenggang et al., 2008; Devauchelle et al., 2006; Morris et al., 2004, 2007). These complex issues included determining patient selection criteria (Butler, Clarke, & Hettiaratchy, 2005; Pushpakumar et al., 2010), refining donor tissue procurement techniques (Meninguad, Paraskevas, Ingallina, Bouhana, & Lantieri, 2008; Pushpakumar et al., 2010), predicting expected functional outcomes (Landin, Cavadas, Gonzalez, Rodriguez, & Caballero, 2008; Pushpakumar et al., 2010), appreciating the limitations of obtaining a fully informed consent for an innovative procedure (Hurlburt, 2007; King, 2002; Reitsma & Moreno, 2006; Renshaw, Clarke, Diver, Ashcroft, & Butler, 2006), and deliberating the immunological response and postoperative immunosuppressant requirements of the recipient (Petit, Paraskevas, Minnus, Lee, & Lantieri, 2004; Pomahac, Aflaki, Chandraker, & Pribaz, 2008; Swearingen et al., 2008; Wu, Xu, Ravindra, & Ildstad, 2009). In addition, psychological implications for the patient (Clarke & Butler, 2009; Morris et al., 2007; Swindell, 2006), societal consequences (Furr et al., 2006; Kalliainen, 2010), and ethical concerns (Hurlburt, 2007; O'Neill & Godden, 2009; Renshaw et al., 2006) have been described.

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The U.S. Department of Defense has acknowledged the emerging field of facial tissue transplantation as a research priority (Kowalczyk, 2009). U.S. military troops are equipped with better body armor today than during prior times of war (Johns Hopkins University Applied Physics Laboratory, 2009) and field triage and transportation mechanisms have been dramatically improved (Jenkins, 2011). Consequently, military men and woman are returning home with devastating, life-altering injuries that would have killed them in previous war times (Johns Hopkins University Applied Physics Laboratory, 2009). Among them are soldiers who have suffered partial or full facial deformities (Brigham and Women's Hospital, 2011). The Department of Defense has awarded $3.4 million to Brigham and Women's Hospital in Boston, MA, to advance face transplantation technology and patient care (Brigham and Women's Hospital, 2011). Brigham and Women's staff performed the nation's second face transplant in April, 2009, and have performed three additional facial transplantation procedures since that time.

HISTORICAL SUMMARY OF TRANSPLANTATION

Solid Organ Transplant

Legendary accounts of organ transplantation date back to 348 AD when brothers Cosmos and Damian are said to have transplanted the leg of a recently deceased black Ethiopian man to a White man whose cancerous leg they had amputated (Barker et al., 2007; Gander et al., 2006). In modern times, it was not until the mid-1950s that the first reported successful kidney transplant was performed (Tilney, 2003). The field of transplant medicine advanced dramatically during the subsequent 50 years prevailing over clinical and technical challenges for caregivers, as well as moral and ethical issues for donors, recipients, and society as a whole (Tilney, 2003). Advances in knowledge about immune function and surgical techniques gave way to successful transplantation of other organs including livers, hearts, lungs, pancreases, abdominal organs, cornea, skin, and bone (Tilney, 2003; Vasilic et al. 2008). These organ and tissue transplants are now generally considered routine, life-sustaining surgical procedures (Vasilic et al., 2008). However, a persistent challenge to the expansion of transplantation efforts is the shortage of available organs for transplantation (U.S. Department of Health and Human Services, 2010). The gap between those needing organs and the availability of willing donors continues to widen (Roberts, 2003).

Composite Tissue Allotransplantation

The term "organ transplant" generally presumes the implantation of a kidney, heart, and other solid internal organ. Composite transplantation consists of the implantation of a combination tissue graft that may include bone, skin, muscle, tendon, and nerve (The University of Texas MD Anderson Cancer Center, 2011; Wu et al., 2009). Such transplant procedures have been undertaken to replace body parts lost to disease (Hui-Chou et al., 2010), trauma (Devauchelle et al., 2006; Pomahac et al., 2011; Ravindra et al., 2009; Siemionow et al., 2010), or congenital malformations (Barker et al., 2007). Composite tissue transplantation procedures to date have included hand, abdominal wall, tongue, larynx, face (Morris et al., 2004; Swearingen et al., 2008; Wu et al., 2009), esophagus, and a vascularized knee (Wu et al., 2009). Composite tissue allotransplantation is an option when multiple reconstructive surgical attempts have failed to resolve severe functional and aesthetic deficits (Barker et al., 2007; Morris et al., 2007). An estimated 7 million people per year in the United States could benefit from composite tissue allotransplantation (Barker et al., 2007; Gander et al., 2006; Wu et al., 2009).

Notably, the legendary account of the earliest organ transplant was the transplantation of a limb (Barker et al., 2007; Gander et al., 2006). Other reports of early composite tissue transplantation efforts are the transplantation of a nose by Gaspare Tagliacozzi in the late 16th century, and in the early 20th century, the successful transplant of a hind leg of a dog by Alexis Carrel and the heterotopic allotransplantation of the heads of dogs by Guthrie (Barker et al., 2007). However, the immunological barriers to successful organ transplantation were as yet unconquered (Barker et al., 2007).

A total of approximately 62 hand transplantation procedures in 46 patients have been performed throughout the world (Jewish Hospital & St. Mary's Healthcare, Kleinert Institute, Kleinert Kutz Hand Care Center, & University of Louisville School Of Medicine, 2011). In many respects, the success of hand transplantation surgery supported the advent of facial transplantation efforts as many technical, clinical, and ethical challenges are shared (Barker et al., 2007).

EMERGING SCIENCE OF FACIAL TRANSPLANTATION

The complexity of the human face's functional and aesthetic properties, and the prospect of reassigning such complexities from one human being to another, has "captured the interest and imagination of the media, scientists, physicians, and the lay public" (Barker et al., 2007, p. 233). The role of the

face in the expression of emotion, and as the gateway to an individual's social interactions (Barker et al., 2007), gives the prospect of this type of transplant a very different gestalt than the solid organ transplantation of a heart, lung, or kidney (Prior & Klein, 2011).

Early deliberations regarding the appropriateness and feasibility of facial transplantation surgery generated significant discussion (Barker et al., 2007; Morris et al., 2004; Powell, 2006). A multiplicity of factors regarding facial transplantation surgery and its subsequent treatment were illuminated by these discussions (Alexander, Alam, Gullane, Lengelé, & Adamson, 2010; Morris et al., 2004; O'Neill & Godden, 2009; Powell, 2006; Wiggins et al., 2004). Factors included those inherent to innovative surgical procedures: the surgeon's autonomy and capacity for therapeutic decision making, the lack of capacity to obtain a fully informed consent, and the uncertain nature of a risk-benefit ratio analysis (Kalliainen, 2010; King, 2002; Paradis et al., 2010; Reitsma & Moreno, 2006). In addition, factors common to the broader science of transplantation were included: the development of donation protocols and the prioritization for organ distribution (Blogowski, 2009; Kalliainen, 2010) and subjecting recipients to lifelong immunosuppressive therapies posttransplant (Bermudez, 2006; Blogowski, 2009; Kalliainen, 2010; Petit et al., 2004). Importantly, factors unique to facial transplantation surgery were also discussed: the potential for significant psychological consequences for the recipient (Clarke & Butler, 2009; Morris et al., 2007; Swindell, 2006) including questions regarding personal identity and subjectivity (Clarke & Butler, 2009; Fitchett, 2008; Morris et al., 2007; Swindell, 2006), societal consequences (Furr et al., 2006; Kalliainen, 2010), and ethical concerns (Hurlburt, 2007; O'Neill & Godden, 2009; Renshaw et al., 2006).

To follow is a synthesis of the literature as background for the emerging science of facial transplantation. The review is divided into three sections: clinical considerations, psychosocial consequences, and ethical issues.

Clinical Considerations

Of the 16 face transplant procedures performed, two of the patients have died. The patient who underwent the second-ever face transplant procedure in China in April 2006 died 27 months after transplant (Hui-Chou et al., 2010). The patient who received the first simultaneous face-bilateral hand transplant in France in April 2009 died 2 months after transplant of septic shock (Siemionow, Zor, & Gordon, 2010). Despite these deaths, the procedure has been lauded as a practical and feasible option for those with devastating disfigurements (Devauchelle et al., 2006; Pomahac et al., 2011; Siemionow et al., 2010). Several of the other transplant patients have regained function, as well as sensory and motor capabilities, while reportedly adjusting well psychologically to their new "organ" (Devauchelle et al., 2006; Pomahac et al., 2011; Siemionow et al., 2010).

Immunology

Immunological response is inevitable after the transplantation of tissue (Tilney, 2003). In 1954, Dr. Joseph Murray led a team of surgeons in the first successful solid organ transplant, a kidney (Barker et al., 2007; Morris et al., 2007; Tilney, 2003). The donor and recipient patients were identical twins mitigating the risk of a devastating immunological response (Barker et al., 2007; Morris et al., 2007). This hallmark surgical procedure is regarded as one of the greatest breakthroughs of modern medicine (Barker et al., 2007). However, the advancement of organ transplantation science has been realized only because of advances in immunosuppressive therapy and tissue typing processes (Barker et al., 2007; Gander et al., 2006; Morris et al., 2007; Pomahac et al., 2008). Kidney, liver, heart, pancreas, intestine, lung, and heart–lung organ transplantation procedures are now considered routine (U.S. Department of Health and Human Services, 2010).

The tragedies of wartime have often coincided with revolutions in medical science and the field of immunology is no exception (Gander et al., 2006). Following the Battle of Britain during World War II, significant progress was made understanding the immune response when severely disfigured fighter pilots received skin grafts (Gander et al., 2006). Discoveries made during this period provide the framework for the field of transplant immunology (Gander et al., 2006). Skin is recognized for its immunogenic properties, and because it is a major component in facial transplantation, many early discussions reported trepidation about anticipated issues of acute and chronic rejection (Barker et al., 2007; Morris et al., 2007; Swearingen et al., 2008; Wu et al., 2009).

The patient receiving a facial transplantation will require a lifelong immunosuppressive medication regimen (Morris et al., 2004, 2007; Swearingen et al., 2008; Wu et al., 2009). Side effects and the propensity to create conditions that may shorten the life span are well-established consequences of this class of medications (Morris et al., 2004, 2007; O'Neill & Godden, 2009; Powell, 2006; Swearingen et al., 2008; Wu et al., 2009). In life-saving situations, the risk-benefit ratio is considered acceptable; however, subjecting patients to these risks following reconstructive surgical procedures has been controversial (Morris et al., 2004). In addition, patient selection criteria must include a comprehensive evaluation of the

potential for the patient to remain adherent to the required lifelong therapies (Chenggang et al., 2008; Pomahac et al., 2008; Pushpakumar et al., 2010). Postoperatively, facial transplant recipients have experienced varying levels of rejection (Devauchelle et al., 2006; Morris et al., 2007; Pomahac et al., 2011; Siemionow et al., 2010). However, all are reported to have successfully responded to increased or altered immunosuppressive therapies (Devauchelle et al., 2006; Morris et al., 2007; Pomahac et al., 2011; Siemionow et al., 2010). No episode of rejection had resulted in graft loss, though the cause of death of the second face transplant patient has been reported to follow an episode of acute rejection after the patient ceased immunosuppressive therapy and initiated herbal therapy at the suggestion of witch doctors in his remote village (Chenggang et al., 2008). The speculation that controlling rejection following facial transplantation would require high-intensity immunosuppressive therapy has been unsubstantiated, and recipients have been maintained on dosages similar to patients postrenal transplant (Gander et al., 2006; Swearingen et al., 2008). Extensive work continues in the area of immunology and specifically, the potential for inducing donor-specific tolerance (Swearingen et al., 2008).

Technical Processes

The technical procedures and sophisticated microvascular techniques used during facial transplantation procedures are similar to those used in other complex reconstructive surgical procedures (Pushpakumar et al., 2010). Facial transplantation procedures have been undertaken after conventional methods of reconstruction have been attempted and failed (Barker et al., 2007; Gander et al., 2006; Morris et al., 2007; Swearingen et al., 2008). All currently transplanted patients had previously undergone multiple surgical procedures and revisions prior to face transplant, which was considered an extreme and unusual intervention (Devauchelle et al., 2006; Pomahac et al., 2011; Siemionow et al., 2010). Some case reports describe surgical results, including both aesthetic and functional outcomes, which are superior to conventional reconstructive treatments (Pomahac et al., 2011).

Psychosocial Consequences

The psychosocial consequences of facial transplantation surgery are multifactorial (Barker et al., 2008; Clarke & Butler, 2009; Fitchett, 2008; Furr et al., 2006; Hui-Chou et al., 2010; Kalliainen, 2010; Morris et al., 2007; Swindell, 2006). Among these factors are understanding the "role of face" in social interactions (Morris et al., 2007), interpreting how facial expression affects an individual's personal identity and societal roles (Fitchett, 2008; Furr et al., 2006), quantifying the impact of an individual's facial disfigurement on his/her self-esteem (Morris et al., 2007), evaluating a patient's expectations regarding the outcome of facial transplant surgery (Barker et al., 2007), and assessing the availability of appropriate social supports for the transplant recipient postoperatively (Hui-Chou et al., 2010; Morris et al., 2007). The potential for facial transplantation surgery to alleviate long-term psychosocial difficulties for disfigured individuals remains unknown due to the novel nature of the procedure (Furr et al., 2006). Case reports of early transplants have reported positive results regarding renewed social interaction without psychological disturbance (Pomahac et al., 2011).

Clark and Butler (2009) describe the following criteria for consideration to ensure appropriate patient selection for the procedure: "...issues of altered appearance and identity, adjustment to change, the management of suboptimal adherence to immunosuppression, ... and how we present and understand risk, particularly related to immunosuppression and rejection" (p. 1087).

The donor family must also be considered as the psychosocial ramifications of donating a loved one's face may be complex (Fitchett, 2008). Issues of identity and the thought that a loved one "lives on" may foster complications for the grieving family during, and subsequent to, the decision to participate in facial tissue donation (Fitchett, 2008). The results of the transplant, however, do not represent a physical replication of the donor as the transplanted tissue takes on the facial structural support of the recipient. Nor does the recipient again look like his/her original self (Fitchett, 2008).

Ethical Impact of Facial Transplantation

The novel and innovative nature of facial transplantation surgery has captured the attention and imagination of health care providers, patients, and society as a whole (Belanger, Harris, Nikolis, & Danino, 2009). The ethical questions regarding the procedure and subsequent treatment were widely discussed and central to early debates on the feasibility of this innovative surgery (Barker et al., 2007). Ethical arguments as to the appropriateness of the procedure were abundant, both in favor (Alexander et al., 2010; Kalliainen, 2010; Morris et al., 2007) and against (Kalliainen, 2010; Morris et al., 2004; Strong, 2010).

The most frequently discussed ethical question was that of subjecting individuals to required lifelong immunosuppressive therapy following transplantation (O'Neil & Godden, 2009; Powell, 2006;

Renshaw et al., 2006; Wu et al., 2009). An increased risk of developing diabetes, infection, cancers, and renal toxicity exist with this therapy (O'Neil & Godden, 2009; Powell, 2006; Renshaw et al., 2006). Critics argue that facial transplant surgery is not "life-saving" in the same manner as heart, lung, or kidney transplants, and therefore the risks of immunosuppressive therapy may outweigh the benefits of the procedure (Morris et al., 2004; Strong, 2010). Proponents argue that restoring functional capabilities is life-restoring and dramatically improves the patient's quality of life (Alexander et al., 2010; Clarke & Butler, 2009; Pomahac et al., 2011). Should the patient develop a resistant infection or becomes nonadherent to immunosuppressive therapy which results in graft rejection, graft loss may result (Strong, 2010; Wu et al., 2009). Few options remain for the patient should this occur (Strong, 2010).

In addition, the ability to obtain a fully informed consent assuring patient autonomy is difficult with innovative procedures (Reitsma & Moreno, 2006). However, institutional review board's approval has been obtained before undertaking the procedure (Siemionow & Gordon, 2010). As this procedure is still considered experimental, the financial burden for such procedures has been absorbed by the health care system (Kalliainen, 2010). If the patient fails to comply with necessary treatment to preserve their transplant, the health care system must support them through subsequent surgical interventions and treatment, presumably at great financial cost (Kalliainen, 2010).

Publications speculate on future trends and ask what implications the facial transplantation has for future cosmetic procedures (Belanger et al., 2009; O'Neill & Godden, 2009; Powell, 2006). Although it seems unlikely that the procedure would ever become routine as a means of changing one's identity, media representations and film productions have suggested that this may be the case. The argument about the level of disfigurement that may be acceptable in the future as indication for the surgery is also prevalent (Chenggang et al., 2008; O'Neill & Godden, 2009).

The decision to subject a patient to lifelong immunosuppressive therapy as well as to a variety of other medical complications that this type of surgical procedure may generate may potentially create ethical questions for the health care team members (Clarke et al., 2007). Studies addressing the attitudes and opinions of health care team members toward facial transplant surgery and these ethical questions have been conducted (Clarke et al., 2007; Mathes, Kumar, & Ploplys, 2009; Prior & Klein, 2011; Vasilic et al., 2008). However, all were done during the conceptual phase of facial transplantation surgery.

CONCLUSION

The complex clinical, technical, and immunological patient care issues in this emerging science appear to mirror those of other reconstructive and organ transplantation procedures (Devauchelle et al., 2006; Siemionow et al., 2010). The short-term results have been positive; however, the long-term physical, emotional, and psychological effects on the recipient patient, as well as long-term consequences to the donor's family are yet to be validated (Siemionow & Gordon, 2010). Ethical arguments as to the appropriateness of the procedure were abundant during the conceptual phase of the procedure.

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