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President's Message

Bessam K. Farjo, MD *Manchester, England*

There has been much debate lately among leading figures in our field on the issue of government regulation of hair restoration surgery. The debate was sparked when we learned that health officials in the Canadian government had contacted hair physicians in what appeared to be a consultation phase in preparation of government regulation on who is qualified to perform cosmetic procedures including hair transplants.

For a long time we have known that in Singapore, for instance, only plastic surgeons are allowed to perform hair transplants. In the UK, new regulations were introduced in 2002 with the intent of preventing "non-specialists" from performing procedures as well as setting minimum standards and regular inspections of premises. More recently, in Turkey and France similar regulations were enforced. Last week, I was contacted by a colleague in the Kurdish part of Iraq asking for ISHRS assistance. The health authorities over there, despite more pressing local issues, were trying to enforce unreasonable demands and regulations in relation to the nature of hair transplantation.

The question is what role can or should the ISHRS play here and is it possible for our Society to have a voice that has influence with the various regulators? You may argue that hair surgery is too small a field for governments to bother with, but we can easily be swept under as part of a wider regulation of private cosmetic surgery. To study all this and make recommendations, I have appointed an ad hoc committee to compile a report for the Board of Governors. I am delighted that Dr. Paul Rose has agreed to chair this committee.

In the last few weeks, two more ISHRS-sponsored workshops took place and both were successful and very well attended. Much appreciation goes to Tommy Hwang and his faculty for the workshop in Korea, and also to Bob Leonard, Ciro De Sio, and Piero Schiavazzi and faculty and staff for the Rome workshop. Since then we have received many applications from members across the world to host regional workshops demonstrating the popularity of this format. I can see a time when the ISHRS has annual regional workshops in each of South East Asia, Middle East, Europe, and South America.

In today's age of such educational opportunities, camaraderie, and friendship, I am surprised I still come across some dubious claims and sales tactics. A couple of months ago, I operated on a patient without any issues. He obviously enquired from a number of other people at the time but about 3 weeks ago he received an email from a well-known European company who preaches exclusive FUE. The email warned him about the "perils" of strip surgery with a string of graphic photos of donor harvesting and widened scars. On the internet forums, it is not uncommon to find statements by doctors' paid personnel saying the only decent transplants are done in the USA or Canada. One company in England even told a patient recently that he'll be wasting his time coming to us because their doctor trained me in the first place!

We as medical practitioners have to take direct responsibility for what our staff or employers say or claim to the public and our patients. We are the ones who took the Hippocratic Oath and agreed to bide by the code of ethics of the various bodies we belong to—including the ISHRS.

When I first started in practice at a young age, I didn't personally know any of my competition. They were the enemy and not as good as me as far as I was concerned. This may have showed in front of patients. I started to meet one or two of them at ISHRS meetings and a few years later we got together to form the British Association of Hair Restoration Surgeons. Suddenly we all discovered that we are not that different and maybe have similar goals and concerns. A good deal of respect and camaraderie resulted from this. Our next Annual Scientific

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Co-editors' Messages

Paco Jimenez, MD *Las Palmas, Spain*

Words are important. Some have a clear and concise meaning that require little or no explanation. Others have nuances or shades of meaning that make the reader look twice. And then there are some words that always seem to leave a positive impression. They are like "magical words" that, on their mere utterance, evoke a sense of attraction. We can see this effect from the following perspective. We are the experts, and know what really works and what is purely marketing ("smoke"). As a dermatologist, I have observed over the years that "laser" is one of those magical words. I observe how my patients receive a very positive impression when I tell them that they are going to receive laser treatment; however, when I tell them that a laser is not indicated for their particular lesion, I feel as if I am letting them down. This magical "laser" word entered the field of hair restoration surgery around 14 years ago, when CO_2 laser devices were first used to make the recipient sites by drilling holes. It soon became an object of interest, and some surgeons clearly took advantage of this laser from a marketing standpoint. However, the course of time put things in order, and since the laser did not offer any real advantage to the patient and to the surgical technique (the same holes could be drilled with a much cheaper 1mm punch, blade, or needle), it was soon forgotten. Over the past 2–3 years, the laser has made a comeback, now for the stimulation of hair growth. Again, it is a great marketing tool and is perceived positively by patients, but until scientific studies show clear evidence of its efficacy it will be difficult for it to win over those as skeptical as myself.

Besides laser, in hair restoration surgery we also have other "magical" words: cloning, micrograft, follicular unit, microscopic dissection, follicular unit extraction…. All these words are positively received by the lay public and have something in common: They imply microscopic detail, meticulous tasking, minimal invasiveness, innovation, technology. We should be grateful to those who coined these wonderful sounding terms. However, we have not been that fortunate with other terms like, for example, "strip harvesting." This term is not a magical word at all. If by curiosity you enter one of those Internet forums, you will soon read comments that associate strip harvesting with "rake-like marks" and bad, painful scars. And certainly, in strip harvesting we are removing a long piece of scalp skin creating a wound that will be sutured leaving a linear scar, but we could do a better job and improve the communication and perception for the public simply by changing to a better term. As an analogy, I hope you would agree that follicular unit extraction is a much better sounding term and better perceived by the public than 1mm punch grafting, and yet they describe the same procedure: the removal of hundreds or thousands of follicular units using small cylindrical steel punches, leaving hundreds or thousands of holes that will end up in pinpoint scars in the donor scalp.

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Bernard Nusbaum, MD *Coral Gables, Florida*

While the incidence of infection in hair transplant procedures has been, and still remains, quite low, times are changing with the emergence of resistant strains of bacteria with increasing rates of colonization in the general population. As might be predicted, these new bacterial strains are resistant to our current first-line antibiotics, including those usually given for pre-operative prophylaxis. Interestingly, the "pendulum swings" and traditional antibiotics such as sulfas and tetracyclines have come to the rescue as effective drugs against these new strains. In our lead article, Robert True addresses the timely issue of Hair Transplantation in the Age of MRSA (methicillin-resistant staph aureus) and, in a review from the Facial Plastics literature, Shelly Kabaker describes the impact of this problem in facelift procedures. Some of you have already seen patients with MRSA in your practice. Even if you have not, the information presented is invaluable as we need to be well educated and prepared for encountering such a possibility. Standardization of protocols to minimize the risk of infection to our patients and to ourselves and staff members is extensively reviewed by Nilofer Farjo in her article, "Infection Control and Policy Development in Hair Restoration."

We certainly appreciate the excellent article written by our Editor Emeritus, Bill Parsley, which outlines the multiplicity of factors that affect the most central issue of our surgical results: graft survival. As Dr. Parsley relates in his article, much remains to be learned in this field. To address everyday, practical issues, excellent "pearls" are provided by Marcelo Pitchon through his International Column with an article written by Maria and José Muricy describing a technique for achieving maximum number of follicular units while avoiding a tension closure. In addition, Jae Pak, William Rassman, et al., present a novel suture material, the "Quill," for achieving a deep closure of the donor area with efficiency, while, at the same time, they share valuable pearls for dealing with the ever-dreaded tension closure. Dr. Kamran Jazayeri presents an interesting case report utilizing a novel donor source for eyelash transplantation.

We are honored to be able to present the very exciting basic science research of MoonKyu Kim and one of our former Platinum Follicle Award winners, Jung-Chul Kim, describing molecular signals and genes that may be responsible for the pathogenesis of androgenetic alopecia and therefore could be targeted with the hope of developing future medical therapies.

Along with a meeting report on the 14th Annual Orlando Live Surgery Workshop and our interesting regular features, we expect that you will enjoy reading this issue and hope that you and your patients will benefit from the information presented.

Bernard Nusbaum, MD

President's message

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Meeting in Montréal is only around the corner now and I urge you all to make the effort to attend and participate. You will definitely meet your friends, and who knows, maybe like me you will meet and get to know your competition!

Je vous vois á Montréal

Best wishes

Bessam Farjo, MD

Jimenez co-editor's message

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As I previously noted, words or terms are very important in communication. Why not just change the name of strip harvesting and make it more attractive to the public as we have done with follicular unit extraction? Now that trichophytic closure seems to have gained wide acceptance because it really works, we have a great opportunity. In my opinion, the use of the term "trichophytic harvesting" would work better and be more positively perceived than strip harvesting because it implies minimal or "invisible" linear scars. Just what patients want to hear.

In the meantime, and to change the subject somewhat, a few words of praise for Rafa Nadal, my fellow Spaniard tennis champion who this year defeated Roger Federer in Roland Garros in three straight sets. Just 22 years old and having already won 4 Roland Garros tournaments, he remains as humble and respectful toward his opponent as when he began playing the game. A true champion.

Paco Jimenez, MD

ISHRS Welcomes Katie Masini, Administrative Assistant

Katie Masini has joined the ISHRS team in a part-time capacity taking on the administrative and data-entry responsibilities for the Society. Katie comes to the Society with nearly 20 years of production and advertising experience. She has been a freelance film editor for Traditional Home Magazine, Renovation Style, and over 100 special interest titles. She is returning to work after a 5-year hiatus during which time she focused on raising her three children. Katie is eager to learn a new industry and is excited to put her organizational and professional experience to use.

Guidelines for Submitting an Article to the *Forum*

- ✓ Send submission AND Author Consent Release Form electronically via e-mail to Bernie Nusbaum, MD, at drnusbaum@yahoo.com.
- ✓ Include all photos and figures referred to in your article as separate *attachments* in JPEG or TIFF format. Be sure to attach your files to your e-mail. Do *NOT* embed your files in the e-mail itself.
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- ✓ Trademarked names should not be used to refer to devices or techniques, when possible.

Submission deadlines:
August 5, September/October 2008
October 5, November/December 2008
December 5, January/February 2009

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Notes from the Editor Emeritus

William M. Parsley, MD *Louisville, Kentucky*

Factors influencing graft survival

Progress in the field of hair restoration surgery over the past 15 years has been remarkable. Results are very natural and our understanding of full and receding hairlines is vastly improved. While outcomes are generally very good, with past reports of over 100% growth from grafts, experienced surgeons are still nagged by the inconsistencies of graft survival. Occasionally, grafts in an apparent excellent candidate will grow in far less than 100% and the surgeon usually has no good explanation. Most feel the answers lie within the basic fundamentals of hair restoration, but some believe there are some yet to be discovered factors needing to be uncovered.

X- and H-Factors

In the early 1980s, Norwood and Shiell proposed the term X-factor to describe unexplained poor survival of grafts beyond the control of the physician. They felt there was a little influence of X-factor in every case, but in 1-3% of patients it was significant. Norwood speculated that an autoimmune reaction might be involved. In 1994, Greco proposed the term H-factor to describe human errors leading to poor growth. He divided these into direct (manipulation, trauma) and indirect (drying, heat, staff fatigue) factors.

What Affects Graft Survival?

The best answer is: "nearly everything." Following are some of the primary factors to consider in graft survival:

1. Selection of patients whose donor hair is of sufficient quality and vigor to survive transplantation and future loss to baldness
2. Selection of patients with a recipient area of sufficient health to support the grafts
3. Avoidance of direct and indirect physical trauma to the grafts on the day of surgery
4. Graft size and method of preparation
5. Selection of the best storage solution (including additives) and the decision as to whether or not chill that solution
6. Creation of recipient sites so that instrument size, density of sites, and depth of sites do not damage the recipient bed to the point that they impede survival of the grafts
7. Finding the best plan of post-op care

While we are far from having the answers we seek, there are some very helpful studies and case reports to help guide us. The following is a list of categories believed to be important to survival along with pertinent reports from the literature. The holding solutions in these studies were chilled unbuffered normal saline (UNS) unless otherwise noted.

Hydration

If there is one universally accepted factor in graft survival, it is hydration. In 2000, Gandelman, et al. published an article in *Dermatologic Surgery* studying 12 patients whose grafts were subjected to dehydration and trauma. Grafts were left on a surgical glove for 3 minutes and then examined under the light microscope (LM) followed by scanning and transmission electron microscopic (EM) analysis, if indicated. Major damage was observed by all modalities after dehydration—and planted dried grafts were found not to grow. This report was followed by a study by Beehner (*Forum,* 2007) in which 60 1-hair grafts and 60 2-hair grafts were allowed to dry on a wet Telfa pad for 16 minutes before placing. The grafts were getting stiff but were not brittle. Survival for 1-hair FUs was 60% and for 2-hair FUs was 82%, suggesting larger grafts give some protection against dehydration. Wetting the dried grafts before placing did not help.

In a busy transplant setting, it is easy to lose a few grafts in each case from drying. Drying at the cutting stations, drying on the gloves, and undetected "popped" grafts continue to create a slight attrition from dehydration. The cure is persistent vigilance throughout the procedure.

Physical Trauma

The second part of Gandelman's 2000 study showed no visible damage to grafts on light microscopy following trauma (bending, crushing, stretching with forceps) and therefore EM was not performed. They admitted that LM could not necessarily rule out biological effects. Beehner found that soft crushing of the bulbs with a needle driver (rubber sleeves over the jaws) resulted in 64% survival versus a hard crush (35%). Interestingly, hard crushing of the bulge area resulted in a 0% survival for room temperature grafts versus 36% for chilled grafts, indicating that chilling provides a slight protection against physical damage.

Beehner and Frechet (2006 Annual Scientific Meeting of the ISHRS) performed a transection study on slit minigrafts (SMGs) in which intact SMGs were compared with SMGs that were transected at some point along the follicle. In Beehner's grafts, intact SMGs had a survival of 86% at 6 months, but dropped to 65% at 12 months; while transected minigrafts had a survival of only 49% at 6 months, dropping to 45% at 12 months. Frechet's transected SMGs had a survival in the range of 35%.

These studies give evidence that trauma, including transection, results in a seriously reduced survival rate.

Time Out of Body

In one of the earliest and most quoted studies on FUs, Limmer (1992) recorded the following survival rates at different times out of the body. Using at least 200 FU grafts for each time frame, the survival was: 2 hours, 95%; 4 hours, 90%; 6 hours, 86%; 8 hours, 88%; 24 hours, 79%; 48 hours, 54%. A 1% loss per hour is a rough guide according to Dr. Limmer.

While it might seem that time out of the body is a predictable critical factor, Unger's study on 4mm grafts planted within 2 minutes of removal had no increased survival over those planted after an hour, and no improvement over the survival of Limmer's FU grafts planted after 8 hours. Measuring survival at 4 months, 184 of 218 hairs (84%) reinserted at 2 minutes survived compared to 212 of 218 (97%) reinserted

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at 60 minutes (Walter Unger, presenting to AAD meeting, Dallas, Texas, 1977). Perhaps measuring at 8 months would have revealed a higher survival rate.

In an attempt to find a method for delayed graft reimplantation, Kurata, et al. compared organ culture survival (as measured by hair shaft elongation) for follicles stored for various periods of time at 4°C in Hanks solution, Dulbecco's modified Eagle's medium (DMEM), RPMI, and saline before culture with DMEM in a CO_2 chamber. The pH buffers were not identified. After 24, 36, and 48 hours storage, survival in saline was significantly lower than the other solutions; however, none of the grafts grew in organ culture after 48 hours of cold storage in any of the solutions. Ten grafts were preserved for 7days in DMEM at 4°C then planted under the panniculus carnosus in athymic mice. At 5 months, 6 grafts were still growing. It is clear that long-term storage of grafts would be a significant advancement but is still a work-in-progress.

Chilling versus Non-chilling

Using unbuffered normal saline, Raposio, et al. reported an 87% survival of chilled (1°C) versus 88% room temperature (RT) (26°C) storage of grafts for 5 hours followed by organ culture for 10 days in Williams E media. No survival was defined as loss of normal follicular architecture. The hair shaft elongation rate between the two groups was also similar.

Jiange, et al. (2005) compared chilled storage in Ringer's solution for 1–7 days at 0°C versus 4°C followed by (1) outer root sheath culture and (2) implantation under the panniculus carnosus of athymic mice. Survival following storage at 0°C was modestly better than at 4°C for all time periods of storage for both ORS cultivation and implant survival, with both categories showing no significant growth after cold storage for 7 days. Qian, et al. reported on human hair follicles implanted into athymic mice after several periods of storage at 0°C in Ringer's solution compared to 0°C in DMEM culture media. Growth after 24 hours of storage followed by implantation into athymic mice for 5 months was 84% for Ringer's versus 72% for DMEM. Results were also better with Ringer's at 48 and 72 hours, but with considerably reduced survival. No regrowth was seen after being held in either solution for 7 days. The ability to culture outer root sheath cells after 24 hours of graft storage was also better with Ringer's (95%) versus DMEM (86%).

The value of chilling is well established in general organ transplantation. Kidneys, for example, show up to a tenfold increase in survival time in chilled storage compared to room temperature storage. Hair follicles do not appear to be as sensitive to RT, but studies indicate that there is an increasing loss sometime after 6 hours. However, studies have not been continued long enough to know at what time period the break point occurs; therefore, more research is needed to determine the maximum room temperature storage time for hair follicles.

Holding (Storage) Solutions

Beginning in the late 1950s, hair grafts have predominantly been stored in unbuffered normal saline (UNS). Some of the best results reported in our field have been with the use of this solution. But is it the best solution or are grafts just pretty resilient? When compared to other storage solutions, saline has generally shown decreased survival. There have been quite a few articles written on the subject recently, but few brief comments will be made here.

pH. Being unbuffered, UNS has a variable pH, usually in the range of 5.0. Normal human serum has a pH of 7.4. Increasing acidity has a known negative effect on tissue survival. The effect of using UNS on follicular tissue pH is not known at this time. Researchers will generally buffer normal saline with phosphate (PBS) before conducting tissue studies. Plasma-Lyte A has a pH of 7.4, using an acetate buffer. DMEM most commonly contains a natural bicarbonate buffer and is designed to be used at 37 degrees *in vitro* in controlled chambers with 5-10% CO_2. In open air, DMEM can become alkaline and may not be healthy for hair grafts. DMEM used in hair studies normally contains the more expensive HEPES buffer, which works well in open air situations. Advanced intracellular balanced solutions most commonly use HEPES, particularly in those meant to be chilled as it adapts to temperature changes. It should be noted that DMEM is not specifically approved as a transplant storage media (personal correspondence with Sigma-Aldrich Co.).

Osmolality and electrolyte balance. Osmolality of normal serum ranges from 280–310 mOsmol/L. UNS has an acceptable osmolality of 308. Advanced solutions use osmotic buffers because there is a higher concentration of impermeable solutes intracellularly versus extracellularly. Membrane pumps are altered during cold storage. Adding impermeable solutes, such as lactobionate and dextran, as osmotic buffers helps to maintain the proper balance, particularly in chilled solutions.

Extracellular fluid has a high Na + and a low K + concentration, while intracellular fluids have the opposite (low Na + and high K +). With cold storage, the Na + /K + pumps and Ca2 + channels are shut down, with the potential to create ionic imbalance. Normal saline, lactated Ringer's, tissue culture media, and Plasma-Lyte A have an extracellular ionic concentration, which could potentially make grafts in chilled storage susceptible to imbalance and cell swelling. Intracellular-type preservation solutions (HypoThermosol, Custodial, Viaspan, Celsior) are quite expensive, but the small number of reports so far seems to suggest a modest benefit at normal surgical time durations compared to normal saline, and even more benefit for delayed graft insertion times.

Additives to holding solutions. A variety of additives have been included in storage solutions, some with promising results. Energy substrates and antioxidants are the most common additives. Krugluger, et al. found that DMEM containing inhibitors of inducible nitric oxide synthase (iNOS) prevented post-transplant hair shedding of grafts in 6 of 6 patients. The primary inhibitor of iNOS was aminoguanidine. DMEM containing arachidonic acid inhibitors prevented graft hair shedding in 5 of 6 patients versus 0 of 6 in controls. Both additives also demonstrated significant improvement in hair shaft elongation studies.

In 1998, Swineheart found no significant graft survival difference between storage in UNS and tissue culture media (RPMI) chilled to 9°C, with survival measured at 5 months (82% vs. 84%).

Raposio, et al. (Derm Surg., 1998) reported that enhancing normal saline with ATP-MgCl and deferoxamine showed improved graft survival. Normal saline (control) was compared to the "enhanced" saline by storing grafts in these solutions at RT for 5 hours. Half of the grafts in the control and experimental groups were then placed in Williams E

media and cultured in a controlled CO_2 chamber for 10 days. The grafts in the enhanced solution had a 98% survival rate compared to 87% for the control. The other half of the grafts was studied by hair shaft elongation, which showed no significant difference in survival. Currently, work is ongoing with ATP, which normally has difficulty crossing the cell membrane. By using liposomes, ATP is able to easily enter the cells; but because the liposome incorporates into the cell membrane, the membrane can weaken with too high a concentration. In addition, the freeze-drying of the ATP needed for this process is very expensive. For these reasons, work is being conducted to determine the effectiveness of a safer, inexpensive preparation (lipo-tripolyphosphate) topically for ATP supplementation during the post-operative period in hair transplantation.

Ischemia Reperfusion Injury and HT Grafts

During transplantation, tissues develop ischemia. In organs susceptible to IRI, upon reperfusion and exposure to oxygen, the conversion of hypoxanthine (a breakdown product of ATP) to xanthine releases free radicals and reactive oxygen species—and starts a cascade leading to cell death by apoptosis or sometimes necrosis. The free radicals released by apoptotic cell death (ACD) are particularly damaging to the double strands of DNA and the cell membrane, where they cause lipid peroxidation. This lipid peroxidation of the cell membrane releases malondialdehyde (MDA) and 4-hydroxy-alkenals (HAE), which are considered measurements of IRI. DNA breakdown during ACD can be measured by cytoplasmic histone-associated DNA fragments (HADF).

Most transplanted organs are surgically reconnected to the body's blood supply and are exposed to a sudden dramatic rise in oxygen tension. In contrast to common organ transplants, hair grafts are perfused passively for at least 3 days before being revascularized, thus not receiving a sudden "blast" of oxygen. For this reason, some question exists whether IRI occurs in hair transplantation. Cooley used the MDA assay to test 150 grafts in 7 patients. The test grafts were placed into the scalp and later removed to complete the ischemia/reperfusion cycle and then tested against control grafts that were never reimplanted. The MDA assay in test grafts revealed MDA levels elevated 200–600% over controls. Krugluger, et al. demonstrated a dramatic rise in HADF after 36 hours of culture in serum-containing DMEM culture media. In addition, HADF was significantly reduced by storage in media containing antioxidants. In yet another study, Krugluger reported better growth and less shedding after adding various antioxidants to holding solutions. While more studies are needed, there certainly appears to be reasonable evidence for the existence of IRI and ACD in hair grafts.

Platelet Rich Plasma

There is currently considerable interest in platelet rich plasma (PRP). PRP is rich in growth factors, among which are platelet derived growth factor (PDGF), transforming growth factor beta-1 (TGF ß-1), and vascular endothelial growth factor (VEGF). PRP has been used with benefit in both the donor strip and also to grafts before placement. In 2005, Uebel presented a study in which grafts were dipped in the PRP created on the day of surgery from the patient's blood. Grafts were dipped into the PRP for 15 minutes before implanting into the scalps of 23 patients. There was a 15% increase in graft survival in the PRP side compared to controls. PRP also looks promising in donor and recipient site healing. The negatives are that it is a little cumbersome and expensive to prepare.

Freezing for Long-term Graft Storage

In 2002, Adanali, et al. reported that grafts frozen for 2 weeks at –20°C (standard freezer) showed no damage under LM examination, suggesting that this might allow long-term graft preservation. In response, Jimenez performed a study of 150 grafts frozen for 1 hour, 5 days, and 7 days at –20°C before implantation. Survival after freezing for 1 hour was 20%; 5 days, 0%; and 7 days, 0%. This demonstrates the unreliability of LM to evaluate survival. At –20°C, ice crystals are constantly forming and reforming, killing the cells. Freezing tissue for storage requires much colder temperatures in order to create a "glass formation state" (no crystal movement), usually with liquid nitrogen. This is an involved process using cryoprotectants in which modifications for tissue type and timing of the freeze/thaw are critical.

Effect of Density on Survival

An important often-quoted study on 2 patients by Mayer, et al. in 2000 compared 2-hair FUs planted at various densities and measured at 8 months. Results showed the following survival: 10/cm^2, 97%; 20/cm^2, 92%; 30/cm^2, 70%; 40/cm^2, 79%. All sites were made with an 18g needle, which is quite large by today's standards. In a 2006 study, Beehner studied 2 patients using densities of 20 and 30/cm^2 into 19g needle sites and 40 and 50/cm^2 into 20g needle sites. Results showed the following: 20/cm^2 (95% patient 1, 87% patient 2); 30/cm^2 (93%, 92%); 40/cm^2 (70%, 100%); 50/cm^2 (67%, 94%). While the results are inconsistent, this study seemed to indicate that recipient site size is important. A recent yet unpublished study tends to verify this, showing 98–100% survival at densities of over 60 and 70 FUs/cm^2 while using small recipient sites.

Survival at higher densities is influenced by a variety of factors, the most important of which are the site size, tissue handling, donor hair quality, and recipient site quality. Doctors new to the field would be well served to increase density slowly.

Skinny versus Chubby

In 1997, Seager performed a study on 88 "skinny" grafts in which the trimming left the papillae with no surrounding tissue and compared them to 163 "chubby" grafts in which ample surrounding tissue was left. The survival rate was 89% and 113%, respectively. In 1999, Beehner compared survival in 60 "skinny" and 60 "chubby" grafts, but left an equal amount of tissue surrounding the dermal papillae. Result survival rates were 101% and 133%, respectively. More recent studies have not shown survivals much in excess of 100%, possibly due to better counting techniques. Regardless, it appears healthier for the grafts to leave a little tissue beyond the dermal sheath and papillae. Planting trauma and graft dehydration may be reduced with just a little extra tissue.

Intact versus Non-intact Grafts

In 1999, Beehner performed a study comparing intact FUs compared to grafts with the same number of hair follicles but containing follicles from two adjacent FUs that were subdivided. The grafts containing follicles from subdivided FUs actually had a little better survival, though not significant.

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From this study, it appears that it should be safe to divide FUs, if needed.

Lateral (Coronal) vs. Parallel (Sagittal) Grafts

In 2006, Perez and Parsley performed a study using 2-hair grafts planted both laterally (l) and parallel (p) at densities of 30, 40, and 50 grafts/cm^2. Results: 30/cm^2, 70% (p) vs. 100% (l); 40/cm^2, 86% (p) vs. 92% (l); 50/cm^2, both 105%. Sites were all made with a 19g needle. This small study, along with a general overview of results around the world, would tend to indicate that there may be no significant differences in survival using lateral versus parallel grafts.

Miscellaneous

In the July/August 2007 issue of the *Forum* (Vol. 17, No. 4), Rinaldi, et al. used a twice daily topical post-op solution containing adenosine sulfate 0.1%, taurine 1.0%, and ornithine chloride 1.0% (called 1-3 atodine). Adenosine sulfate upregulates vascular endothelial growth factor (VEGF) and follicular growth factor-7 (FGF-7), while taurine and ornithine stimulate outer root sheath growth. At 1 month, vessel diameter and hair shaft diameter were both larger than the placebo. Revascularization (using reflectance confocal microscopy) of the grafts was quicker by nearly threefold, and the follicle growth was improved.

Could one of the keys to improved graft survival reside with VEGF? Yano, et al. demonstrated that perifollicular angiogenesis correlated with upregulation of VEGF mRNA expression in murine outer root sheath keratinocytes, but not in dermal papillae cells. The role of the ORS being the primary site of VEGF upregulation was also found in a study by Krugluger, et al. Transgenic overexpression of VEGF resulted in a strongly induced perifollicular angiogenesis; resulting in increased hair growth, follicle size, and shaft diameter. Systemic neutralizing anti-VEGF antibodies resulted in poor hair growth and reduced follicle size. Because the outer root sheath is more accessible to topical therapy than the dermal papillae, it is easy to speculate that the topical 1-3 atodine solution mentioned in the previous paragraph might be effective.

General Impressions

We have looked at graft survival from many viewpoints, yet have not satisfactorily found some of the factors leading to inconsistencies in growth. In this author's opinion, part of it may lie in the recipient bed and the speed of revascularization. Grafts placed immediately after harvesting don't seem to grow significantly better than those placed several hours later. Rinaldi's use of topical 1-3-atodine solution post-transplantation, the effects of PRP, the use of inhibitors of iNOS, and the work on upregulating VEGF are all exciting. Grafts may take 3 or more days to revascularize. Anything to speed this process or support them in the interim logically might help. Preconditioning of grafts with growth factors and antioxidants while out of the body is also very promising. Additionally, isolated cases suggesting improved hair growth using hyperbaric oxygen (HBO) are encouraging, especially when one considers studies showing improved skin graft and flap survival with HBO. It should be pointed out that oxygen therapy is known to stimulate angiogenesis.

In conclusion, there is much to be learned about hair graft survival. Fortunately, interest in research is growing rapidly.

General References

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colonized or infected body sites of other persons, or (3) devices, items, or environmental surfaces contaminated with body fluids containing MRSA. Poor hygiene, crowded conditions, openings in the skin such as cuts or abrasions, and skin-to-skin contact are additional factors that can contribute to transmission.

Decolonization

Colonization indicates the presence of MRSA without illness. Colonization can occur in the nares, trachea, skin folds, rectum, or in an open wound. Decolonization entails treatment of persons colonized with MRSA to eradicate carriage of that organism. Decolonization of persons carrying MRSA in their nares has proved possible with several regimens that include topical intranasal mupirocin alone or in combination with orally administered antibiotics (e.g., rifampin in combination with trimethoprim-sulfamethoxazole or ciprofloxacin) plus the use of an antimicrobial soap for bathing. In one report, a 3-day regimen of baths with providone-iodine and nasal therapy with mupirocin resulted in eradication of MRSA colonization.

MRSA cases are likely to occur in hair transplant practice and should be suspected in any wound or post-surgical infection. Cultures should be taken prior to initiating therapy, and therapy should be guided by the sensitivity patterns identified in culture.

HCPs implicated in transmission of MRSA are candidates for decolonization and should be treated and culture negative before returning to direct patient care. In contrast, HCPs who are colonized with MRSA but are asymptomatic, and have not been linked epidemiologically to transmission, do not require decolonization.

Although decolonization is effective, high recurrence rates make routine screening and decolonization of HCP or community groups an ineffective strategy unless performed within the context of epidemic MRSA (E-MRSA). Decolonization is indicated in patients with recurrent MRSA infections and for HCPs implicated in an outbreak.

ISHRS Member Survey

To assess the current status of MRSA in hair restoration, practice surveys were mailed to 207 ISHRS members. Ninety-three surveys were returned (45% response rate). We did not have a protocol to analyze nonresponders. Fourteen MRSA cases were reported by the 93 practices. Two practices had 2 cases; two, 3 cases; one, 4 cases, and nine reported 1 case each. This suggests that MRSA infections are occurring in 9.6% of the HT practices surveyed. The 93 practices perform 24,241 hair restoration procedures per year. In the past 12 months, the surveyed practices experienced 6 MRSA cases, which is a 0.25/1000 incidence rate of MRSA infection among hair restoration surgeries. This is a low-risk occurrence rate; however, busy practices that perform 500 or more procedures per year can expect a case every four years. Certainly, if a practice were to experience two or more infections within a year, there would be cause to suspect the infections may be arising from within the practice.

We asked survey participants to describe their current screening and preventive practices. Results are summarized in Table 1.

Table 1. MRSA Practice Survey (n = 93)

	NA	Yes	No
Has MRSA occurred in practice?	0	14	79
MRSA cases within past 12 months?	0	6	87
Nasal Culture screening of employees?	5	5	83
Regular Staff carrier screening?	0	1	92
Patient screening for MRSA?	0	1	92
Hand washing polices?	0	82	11
Hand sanitizer policies?	0	64	29
Made changes in practice because of MRSA risk?	0	18	75

Very few of the practices have performed any colonization screening of staff or patients. On the other hand, most use hand washing/sanitizer policies. Eighteen of the 93 practices have made policy and procedure changes in view of MRSA. Of practices that have had MRSA cases, 56% have changed procedures to reduce risk of future cases. Measures taken have included: mandatory washing/sanitizer policies, introduction of routine pre-op Hibiclense scalp scrubs, routine use of doxycycline post-op, and use of Technicare (Active Ingredients: USP Chloroxylenol 3.0%, Cocamidopropyl PG-Dimonium Chloride Phosphate 3.0%) on the donor wound.

The hair transplant MRSA infection cases reported included donor wound infections (Figure 2), folliculitis, and impetiginous scalp lesions.

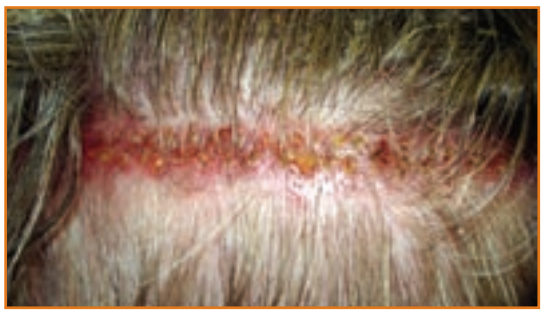

Figure 2. MRSA donor wound infection. *Photo courtesy of William M. Parsley, MD.*

Prevention and Treatment in Hair Restoration Practice

The key to prevention of outbreaks within a clinic is strict adherence to hand washing/and use of hand sanitizers. Specific and strict policies need to be in place and monitored for compliance. Compliance is facilitated by locating wash/sanitizer stations outside each treatment room. This

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practice must be accompanied by meticulous and consistent disinfection of all work surfaces and equipment.

Given the low incidence of MRSA infection in HT practice, the occurrence of two cases close together should raise suspicion that the source may be coming from the clinic. It is appropriate to screen clinical staff with nasal cultures and initiate decolonization of any who are found to be positive. Furthermore, sanitation procedures should be reviewed.

However, most hair transplant surgery–related MRSA infections will be CA-MRSA arising from individual patients who are colonized. While it is not cost effective to do nasal swab screening on all patients, it does make sense to do risk screening of all patients by including pre-op questionaires on recent hospitalizations or surgery, contact with a MRSA case, recent boils, or chronic conditions associated with open skin lesions. If increased risk is identified, pre-op nasal culture screening would be appropriate and, if positive, decolonization would be indicated.

Despite carefully adhering to infection control practices and screening for high-risk patients, MRSA cases are likely to occur in hair transplant practice and should be suspected in any wound or post-surgical infection. Cultures should be taken prior to initiating therapy, and therapy should be guided by the sensitivity patterns identified in culture. If infections are treated empirically with beta-lactams or macrolides pending culture results, patients should be followed closely.

Table 2 summarizes current recommended MRSA treatment protocols . Practitioners need to be aware of resistance patterns in their communities and use this knowledge in selecting antibiotics. Choice of antibiotic will evolve as MRSA sensitivity changes.

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Table 2. MRSA Treatment Guidelines

Colonization *(Recommended only for HCP implicated in case cluster, outbreaks, or high-risk patients.)*	• Nasal Mupiricin ointment bid for 5 days, plus, • Trimehtoprim/sulfa double strength po bid for 10 days • Or, Minocycline or doxycylcine 100 mg po bid 10 days, plus, • Providine/iodine baths for 3 days
Superficial colonization of a wound without signs of infection	• Regular cleaning with Hibiclens • Topical application of silver dressing with activity against MRSA (Acticoat or Silvasorb) or Mupiricin ointment • Close monitoring for signs of infection
Superficial skin and soft tissue infection cellulitis (HA or CA MRSA) *(Antibiotic choice should be determined by local resistance patterns.)*	• Local wound cleaning and debridement • Topical Mupiricin • Trimehtoprim/sulfa double strength po bid for at least 10 days • Or, Minocycline or doxycylcine 100 mg po bid for at least 10 days • Plus, Rifampin 300mg po bid X 5 days • If failure of above measures, • Infectious Disease consult • Zyvox (linezolid) 600mg po Q12h (monitor for myelosuppression if longer than 10 days
Complex skin and skin structure infection *(Antibiotic choice should be determined by local resistance patterns.)*	• Aggressive debridement essential • Topical Mupiricin • Trimehtoprim/sulfa double strength po bid for at least 10 days • Or, Minocycline or doxycylcine 100 mg po bid for at least 10 days • Plus, Rifampin 300mg po bid X 5 days • If failure of above measures, or known HA-MRSA • Infectious Disease consult • Zyvox(linezolid) 600mg po Q12h or vancomycin iv