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The potential role of hair transplant surgeons in treating vitiligo: A case report

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Introduction

Vitiligo is an acquired idiopathic condition characterized by patchy loss of skin pigmentation due to the absence of epidermal melanocytes. About 1% of the world's population is affected, including individuals of all ethnic groups and both genders. Fifty percent of cases begin before age 20. Vitiligo is probably determined by an autosomal gene because more than 30% of cases have a positive family history.¹

As hairs within a vitiliginous patch of skin are often de-pigmented, both the epidermal and follicular melanocytes are targets for the antibody-associated autoimmune response.^{2,3}

Cosmetics may not be able to cover vitiligo on exposed areas. When less than 10% of the body surface is involved and the patient is psychologically affected, treatment may be considered.⁴ Over the years, many different medical and surgical modalities have been developed in restoring melanocytes at the vitiliginous sites.⁵

Surgical techniques are usually offered to patients with refractory but stable vitiligo that has developed no new lesions over the past two years. Current options include cosmetic tattooing or micro-pigmentation, regional dermabrasion, transplantation of blister epidermis, autologous cultured melanocyte grafting, autologous non-cultured epidermal cell suspension, and single-hair grafting.

Transplanting single hairs for treating vitiligo was described by Na in 1998.⁶ Twenty-one patients with a mean age of 23.4 and a mean disease duration of 7.7 years were recruited for the study. From the occiput, a 1cm strip was harvested, slivered, and then divided into many single-hair grafts. The entire follicle was used for hair-bearing areas, while only the upper two-thirds was used for glabrous areas. All grafts were inserted using Choi implanters. The density of transplantation was not mentioned in the study. Follow-up was from 1-3 years.

Different patterns of re-pigmentation were observed in the two groups:

1. **Localized/segmental vitiligo:** Fourteen out of 17 patients (81%) developed peri-follicular re-pigmentation of areas ranging from 2-10mm (average 3mm) in diameter.
2. **Generalized vitiligo:** Only 1 in 4 (25%) developed a peri-follicular re-pigmentation 3mm in diameter.

In this study, all transplanted hair retained pigmentation at 12 months of follow-up. Five patients (23.8%) had re-pigmentation of de-pigmented hair in the vitiliginous areas.

At the time of this study, single-hair grafting had not enjoyed popularity as the authors described hair dissection being "tedious and time consuming" and the number of donor hairs "limited." However, most hair surgeons today are capable of transplanting thousands of grafts in a single session. With good technicians and microscopes, hair transplant surgeons should reconsider their potential role in treating vitiligo.

Case Report

In August 2001, a 45-year-old Asian male presented to DHT Clinic (Damkerng [Pathomvanich] Hair Transplant Clinic, Thailand). He requested eyebrow transplantation to an area affected by vitiligo. There had been no change in the lesion for many years. He had no other medical condition and was not taking any medications.

On examination there was a patch of vitiliginous skin along the medial two-thirds of the left supra-orbital ridge. It was rectangular in shape and measured about 1cm x 3cm. De-pigmented hairs were

Plan to Attend



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President's Message

Edwin S. Epstein, MD *Virginia Beach, Virginia*

When the ISHRS was founded, a code of ethics was adopted: principles to define the honorable behavior of hair restoration surgeons toward fellow members, and to protect our patients. An ethics committee was established to review complaints and to make disciplinary recommendations to the Board of Governors (BOG). Because of concerns that disciplinary action against a member might result in legal expenses that could potentially threaten the financial stability of the ISHRS, the BOG decided that the president should triage and respond to ethics complaints.

A few months ago, Bill Rassman revisited the topic of ethics in a *Forum* article. As president, the most common complaints brought to my attention include denigrating colleagues with the intent to injure reputation or their business, truth in advertising or marketing, and professionalism on the Internet.

Years ago, I vacated an office to move into larger space. Another hair transplant group moved into my prior space, and when patients inadvertently came to the old office to see me, some were told I didn't work there anymore. Not exactly a lie, but certainly not the truth. Now, with the Internet as our primary means of communication, I have received reports of practices acquiring similar domain names as their competitors and using other creative means to drive potential searching patients to their website. Is this creative competition based on superior internet knowledge and skills, or is this stepping into the gray zone of professional ethics violation?

It used to be said that one happy patient told one other, but an unhappy one told 10. Now they can tell millions, and a demeaning message or rumor becomes viral, and the damage is done. The Internet is a powerful educational tool, marketing forum, and an arena for patients to share their experiences, good and bad. However, accountability and the legal system are still lagging behind technology. As health care providers, we must lead the way in ethical professionalism. We must resist the opportunity to denigrate each other, or confuse the "listening" public through anonymous postings either personally, by staff members, or by hired internet monitors. Otherwise, we lose the public's trust. The public should have a forum, but we can work together with webmasters and other internet site hosts to create a healthy venue by which adverse surgical events can be discussed both openly and maturely without hostility, and thereby diffuse patient anger and fear in a healthy manner. We should not see this as an opportunity to denigrate a competitor on the Internet, but as a learning opportunity for us all, including the affected physician. Perhaps the formation of a "peer review group" composed of ISHRS members could both present surgical and treatment suggestions to an involved physician, and demonstrate to the public our response to their concerns.

The ISHRS Bylaws contain procedures for members to register complaints, as well as grounds for disciplinary action. Such grounds are most obvious when a governmental agency has disciplined a member. The ISHRS is neither judge nor jury, but can be a mediator to provide a venue for grievances to be maturely and ethically addressed before matters escalate to the legal venue. Let us all take the higher road, and I encourage all members to review the ISHRS Code of Ethics, and grounds for discipline under Article VI of the Bylaws, on a regular basis. This Code of Ethics is reprinted on page 40 for your review.

Edwin S. Epstein, MD



Co-editors' Messages

Paco Jimenez, MD *Las Palmas, Spain*



I frequently receive requests from new doctors on how best to get training in Hair Restoration Surgery. My advice is always the same: If you are seriously interested in this field and willing to spend one to two years in training, then go ahead, check the website of the ISHRS, look for the fellowship programs, and apply for one. There is no better training than a full one-year *in situ* performing hundreds of cases. Dr. Damkerng

Pathomvanich, director of one of these fellowship training programs in his clinic in Thailand, has encouraged his trainee fellows as part of their duties to submit articles for publication to the *Forum* (in this issue, it is the turn of Drs. Fatemeh Sadat and Theresa Cacas). As a *Forum* co-editor, I would like to express my gratitude for the impressive number and quality of articles received from Dr. Pathomvanich's clinic over the past two years.

I would also like to reflect on the use of hair follicle transplantation in vitiligo (a depigmenting disorder characterized by cutaneous patches with complete loss of pigmentation). This disease affects 2% of the worldwide population. A number of therapeutic options of repigmentation of vitiligo are available (topical corticosteroids, topical tacrolimus, psoralen ultraviolet light [PUVA], etc.), yet they commonly show unsatisfying outcomes. In this issue, Dr. Bertram Ng (by the way, another of Dr. Pathomvanich's former fellows) writes an article on the use of hair follicle grafts in vitiligo. It has been reported that melanocytes obtained from the hair follicles can induce repigmentation of the vitiligo patches (Vanscheidt, W. Repigmentation by outer root sheath derived melanocytes: proof of concept in vitiligo and leucoderma. *Dermatology* 2009; 218:342-343). We, as specialists in hair transplantation, are in the perfect

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Bernard Nusbaum, MD *Coral Gables, Florida*



The hair follicle has rich populations of stem cells, and, in this issue, Dr. Bertram Ng describes how follicle transplants can be utilized as a source of melanocytes to treat vitiligo, a dermatologic disorder that has significant psychological impact. Dr. Theresa Cacas and colleagues present a study on using bent needles for transplanting curly hair grafts. Dr. Fatemeh Sadat then presents data regarding differences in laxity measurements between patients of different age groups. Because improving strip donor scars is a continuous goal, and scalp laxity assessment is the hallmark for preventing tight closures, tools for measuring laxity have been developed.

Ergonomics, teaching capabilities, and quality monitoring are some of the advantages of microscopes with LED monitors. In their article, Drs. Dae-young Kim and Hyung Suk Kim demonstrate how using the most up-to-date equipment can achieve the resolution necessary to make these systems a viable option. As more surgeons incorporate this technology into their practice and gradually overcome technician resistance, it will be interesting to compare transection rates with experienced technicians utilizing these systems as compared to those who use the binocular microscope.

In her Hair Sciences column, Dr. Nilofar Farjo has written an interesting article on how minoxidil stimulates hair growth. In Review of the Literature, Drs. Marc Avram and Nicole Rogers raise our awareness regarding an etiology of scalp erythema and scaling that has not received much notice. Apparently, patients with dermatomyositis can present with clinical features that overlap between telogen effluvium and scalp seborrhea/psoriasis. This will certainly raise my index of suspicion when confronted with this constellation

of symptoms. In her Hair Sciences column, Dr. Nilofar Farjo has written an interesting article on how minoxidil stimulates hair growth. In Review of the Literature, Drs. Marc Avram and Nicole Rogers raise our awareness regarding an etiology of scalp erythema and scaling that has not received much notice. Apparently, patients with dermatomyositis can present with clinical features that overlap between telogen effluvium and scalp seborrhea/psoriasis. This will certainly raise my index of suspicion when confronted with this constellation

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Editorial Guidelines for Submission and Acceptance of Articles for the *Forum* Publication:

- Articles should be written with the intent of sharing scientific information with the purpose of progressing the art and science of hair restoration and benefiting patient outcomes.
- If results are presented, the medical regimen or surgical techniques that were used to obtain the results should be disclosed in detail.
- Articles submitted with the sole purpose of promotion or marketing will not be accepted.
- Authors should acknowledge all funding sources that supported their work as well as any relevant corporate affiliation.
- Trademarked names should not be used to refer to devices or techniques, when possible.
- Although we encourage submission of articles that may only contain the author's opinion for the purpose of stimulating thought, the editors may present such articles to colleagues who are experts in the particular area in question, for the purpose of obtaining rebuttal opinions to be published alongside the original article. Occasionally, a manuscript might be sent to an external reviewer, who will judge the manuscript in a blinded fashion to make recommendations about its acceptance, further revision, or rejection.
- Once the manuscript is accepted, it will be published as soon as possible, depending on space availability.
- All manuscripts should be submitted to both drnusbaum@yahoo.com and jimenezeditor@clinicadelpelo.com.
- A completed Author Authorization and Release form—sent as a Word document (not a fax)—must accompany your submission. The form can be obtained in the Members Only section of the Society website at www.ishrs.org.
- All photos and figures referred to in your article should be sent as separate attachments in JPEG or TIFF format. Be sure to attach your files to the email. Do **NOT** embed your files in the email or in the document itself (other than to show placement within the article).

Submission deadlines:

April 5 for May/June 2010 issue
 June 5 for July/August 2010 issue
 August 5 for September/October 2010 issue
 October 5 for November/December 2010 issue

President's Message

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CODE OF ETHICS

of the International Society of Hair Restoration Surgery

PREAMBLE: Membership in the International Society of Hair Restoration Surgery is a privilege accorded to physicians of the highest moral and professional standards, it is not a right. The ethical principals adopted by the International Society of Hair Restoration Surgery define the essentials of honorable behavior for the hair restoration surgeon.

- I. The member recognizes that a greater moral responsibility is necessary in cosmetic surgery than in many other fields because of the lack of oversight by government and/or peer review and the emotional involvement of the patient.
- II. The member acknowledges that he or she is in a position of trust and will not betray that trust.
- III. The member will not take emotional or financial advantages of patients.
- IV. The member acknowledges that he or she is in a position to affect each patient's appearance, self-confidence, and possibly the success of the patient for his or her entire life. With every treatment the lifelong effect is considered in the light of continuing hair loss.
- V. The member will recommend treatment for each patient as the member would recommend for themselves or another family member under the same circumstances. This does not mean that the treatment cannot be modified to accommodate the desires of the patient.

- VI. Members will maintain truth and integrity in their advertising always avoiding deceptive communications. If a member promotes a technique or an opinion which is not accepted by the majority of the profession as a whole, the member should acknowledge that this opinion or technique is the opinion or technique of the individual physician and not shared by the profession as a whole. Trademarking and copywriting names for common terms are discouraged.
- VII. Members will not denigrate their colleagues using false or misleading information with the intent of injuring the reputation or business of an ISHRS member by any means, either directly or indirectly to include print, radio, television, Internet advertising, Internet website activity, or any other public statement made by the member or his/her representative. Violation of this code will not be tolerated and is grounds for disciplinary action.
- VIII. A member with knowledge of an illegal or improper act(s) by another physician should report such activity to the appropriate agency.
- IX. A member shall continue to study, apply and advance scientific knowledge. A member shall pass knowledge on to colleagues.
- X. The patient's confidences shall be kept private. Information will be divulged only with the permission of the patient except as otherwise required by law.
- XI. Members will adhere to the codes of ethics of medical societies of their respective countries.

The Code of Ethics was last amended by the membership on October 17, 2003

Dr. Jimenez's Message

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position to explore alternative and feasible ways to transplant follicle-derived melanocytes into vitiligo patches.

Moreover, it is time that we start exploring the use of hair follicle grafting not only in vitiligo but also in other non-alopecia related conditions, as for example in wound healing, where there is solid evidence of the healing-promoting role of hair follicles. Clinical scientific studies are needed, and the hair transplant surgeon should play a leading role in the design of such studies. This could hopefully open a wide range of new applications and a high demand for new therapeutic procedures.

Paco Jimenez, MD

Dr. Nusbaum's Message

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of findings. In addition, they present the results of an important study that shows that the obvious may not always be true in that Latisse®, which has received much acclaim for thickening and lengthening eyelashes, was shown not to be effective in treating eyelash alopecia areata.

You'll find more on these and other topics, including the always controversial Letters to the Editors section, inside this issue. We encourage discussion and debate, so I would like to take this opportunity to ask of all members to voice their opinions and to not hesitate to submit a Letter to the Editors. We will try to publish it along with the original author's reply as soon as possible.

Bernard Nusbaum, MD

Oops... Please note a correction:

There was an error in the description of Dr. Michael Beehner's "Chubby, medium, skeletonized" study report in the January/February 2010 issue of the *Forum* (Vol. 20, No. 1, p. 1). The 3 study boxes on the left, which contained all 2-hair FU grafts, were 1.2cm x 1.2cm in square area, rather than the 1cm² that was reported. The two boxes on the right side, which contained all 1-hair FU grafts, were each 1.1cm x 1.1cm in size.

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Notes from the Editor Emeritus

Michael L. Beehner, MD *Saratoga Springs, New York*



The Good and the Not-So-Good of the Internet in Hair Transplantation

It is hard for me to fathom the changes that have occurred in our field over the past 20 years regarding how we market our services to the public and how our patients find out we exist. So much has changed. I entered the field in 1989 and for the first 10 years all I needed was an ad in the sports section of a few nearby newspapers every couple of weeks and a small Yellow Pages ad in several communities within a 175 mile radius from Saratoga Springs, and this brought me a steady stream of patients. No more! Even though we have continued with infrequent newspaper ads and remain in the Yellow Pages with much smaller ads, it is fairly rare for a new consult patient to tell me he learned about me from either of these sources. At this point in time in history, there is a large elephant in the room, and it is the Internet. Because I've been doing this for 20+ years, I'm fortunate in that around 40% of my new patients come from referrals from our past patients, hair salons who have seen my patients, and physicians (mainly dermatologists and plastic surgeons). But almost the entire other 60% learned about us through the Internet. How our patients find us there varies greatly. Many simply type into their Google search box "hair transplants + New York," or variations thereof, and then click on our website. Many others bump into one of the several prominent "hair sites" that dispense information and/or specific recommendations (products and/or surgeons) on the treatment of hair loss.

Four years ago I did an unofficial "study" of around 100 consecutive consult patients who said they found us "on the Internet," and I inquired as to what words they punched in for their search. The two overwhelming leading entries were "hair transplant" and "hair transplants." My hunch is that the modern-day prospective patient in addition punches in a qualifier word, such as the name of a city or state. Many patients mention that they "did some research" on the Internet. This usually means that they bumped into a website where I was listed or "recommended." The last I looked, there were at least nine such referral sites one could belong to. Some of these will enroll a surgeon simply upon his or her asking to be included. Others are a little selective and ask for pictorial evidence of good results and will even poll other doctors and regular visitors to the site before including a surgeon on the "recommended list." Some of these sites deal with all things hair, and have sections on everything, including hairpieces, lotions and potions, etc. In our own practice, while decreasing our expenditures in the newspapers and Yellow Pages, we have decided to participate with three of these sites, and, despite some of the risks involved, it certainly helps in our recruiting patients, especially since we practice in a fairly small population center. It helps us

reach people from outside our geographic area who for some reason are attracted to some aspect of what we do or how we do it.

I should also add that another important way the public learns about hair transplantation is from the frequently aired "infomercials" on TV, especially those by Bosley and MHR. I'm sure many of the viewers contact these respective companies directly, but a fair number just let the information sit in their subconscious and then at some future time will perhaps conduct an informal search about hair transplant providers in their area and find us. In 1995, at the Annual ISHRS Meeting in Las Vegas, I was eating breakfast with Larry Bosley and told him that we should all chip in and help him pay for his TV ads and the videos he sent out, since we all benefited from them, and he said he thought that was a great idea! We all owe a debt of gratitude to these larger companies who help make the public aware of what modern hair transplantation can accomplish. In truth, some of the hair sites play off of an "anti-large group" bias to attract the single providers so they feel they have a "union" fighting on their behalf—as a David against the Goliaths of the world.

The main "good" of the Internet is that people can find out that we exist and somehow get to our website to get a feel for our practice and what we're all about. The computer allows their "fingers to do the walking" and essentially walk into your practice and look around anonymously without having to leave their home. A good website is the one essential every hair transplant physician must have. Without it, you are dead in the water. One under-appreciated aspect of the website is that you must have high-quality photos of your results, showing both "before" and "after" photos. Some detailed views of your transplanted hairlines are important also. If you don't include them, the viewer will assume the worst, that you are hiding something you aren't that proud of. All advertising, whether it is on some referral website, a newspaper ad, or a Yellow Pages ad, must include the website prominently and try to direct patients to go there to learn more about you.

Like it or not, the various websites that list or "recommend" hair transplant surgeons have a lot of power. We are all very dependent on those webmasters running their sites in a fair and balanced manner. This is true for you, whether or not you decide to cast your lot with them, as your patients may still post positive or negative things about you there, and patients can also type in a "search" for any comments or posts relating to you. For the most part, in recent years, these "webmasters" have been balanced and fair, but there have been several very public instances in which a physician has been dragged over the coals on a long thread or two, and then removed from a site, which, as you can imagine,

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Notes from the Editor Emeritus

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seriously impacts his or her reputation on the Internet and causes much personal anguish for the individual involved. Almost every physician listed on any website has at one time or another had a disgruntled patient post a negative note on the site claiming the growth was poor or that he was unhappy with some aspect of the experience at that physician's office. In most cases in which the complaint is relatively minor, it quickly gets buried deep in the archives and no harm is done (except that it will be included in any future "search" by a patient). When the negative claims are of a more damaging or serious nature, the physician is in a tough spot. He can go on the site and try to defend himself, but often is limited in what he can say or show in photos, due to patient confidentiality. One site now makes clear to patients posting negative comments about a physician, that they must allow the physician to defend himself, even disclosing some of the facts of the case and showing photos, as long as the patient's identity is hidden. This is definitely a step in the right direction.

Most patients who at some point have an interest in possibly undergoing hair transplantation will then go to the Internet, do a little "research," and visit several websites. They then either do something about it or they don't, and then they go about their lives and leave these sites behind. But there is a core group of perhaps a few hundred individuals, either past patients or ones on the "fence" about having a transplant, who virtually live on these sites and exert a fair amount of influence upon the patients who come to these sites looking for guidance. Further muddying the impartiality of these sites are the considerable numbers of individuals who comment in posts almost daily and are paid employees of a given clinic. Often their advice to a patient is cloaked in language such as "do your research" and "don't be afraid to get on an airplane and travel," etc., but the overall effect of these constant stream of comments is to boost the visibility of several high-profile clinics and to slightly disparage less-well-known hair surgeons. This can be an intimidating thing to a physician new in our field who is trying to establish himself in the internet world. To the webmasters' credit, for the most part, they do require such individuals working for a clinic to identify themselves on each posting and their relationship to any clinic they may work for. Also to the credit of the webmasters, blatant marketing tactics by such individuals or by physicians are usually stricken off the thread.

The main negative about the Internet, whether or not you choose to be listed on any of these various referral sites, is that a single patient has the potential to totally ruin your reputation. We are all aware of patients from the past who spent years lambasting certain surgeons, sometimes due to work done 20-30 years ago when the large grafts were the only transplants used, as if that surgeon should have waited 15 years and known about technology that didn't even exist at the time. I can recall five or six instances in which a hair surgeon who did high-quality work and was respected by his or her peers was attacked on the Internet by a patient and the physician responded directly in a very persuasive

and thorough manner, such that the matter was properly defused and his or her reputation left relatively unharmed. Around a year ago I asked a highly respected colleague and friend of mine how he viewed his involvement with a given website, and he responded that he felt some anxiety every day he went to work, that the patient in his chair that day might be the one who has some unusual poor growth or some rare complication and then goes to the Internet to vent his unhappiness. I think we all can identify with this physician. I can recall three patients over the years who did this to me, one recently whom I transplanted eyebrows for as a charity case. In trying to get a little smarter each time this sort of thing happens, I'm starting to see a pattern that helps me to identify individuals who may end up as my "internet nightmare." They often have some deep psychological instability, usually due to a recent loss of some sort in their life. Some degree of Body Dysmorphic Disorder also is usually present and they have an almost over-emotional view of their hair loss problem. All three of the patients I mentioned above, during the week or two before the procedure, were nervously calling or emailing us, jumping back and forth on various preferences or even whether to proceed or not. My advice would be to not accept patients that exhibit these traits. You will be inviting problems you will not like in the future. These individuals usually are in the mode of blaming others for their problems in life and you are only lining up to be the next one for them to blame.

The ISHRS website (www.ishrs.org) is another valuable website for your patients to find you. Their search engine ranking has been pretty high and our listing there has resulted in some referrals. It is important to make sure your website, personal biography, and photo are listed there.

Positioning in the various search engines, particularly Google, is a big boon to having more people view your website. The reason some of these hair websites are so frequently visited by patients is that they are positioned high in the search engines for the various words that patients punch in to start their "research." Another option for marketing is to purchase positioned "box ads" of your practice on Google and other sites. Many of these boxes will appear periodically to viewers (e.g., every third viewing) and thus will be more reasonable in cost. It is important that you have a web server who can work with you to optimize your positioning on search engines and who can guide you as to which "key words" should be included on your home page. Having "links" to other sites on your website has also traditionally helped secure a higher search engine listing.

My final summary comment is that the Internet is here to stay, whether we like it or not. It's not going to go away, and, in fact, will probably become even more dominant as time goes on in its role of helping prospective hair transplant patients determine their physician choice. If hair transplantation is the heart of your practice, I would advise you to gain some level of presence on the Internet. Display your work, have a good website, and encourage your happy patients to post notes about their results. If you do this, then the occasional unhappy camper that we all have, when he or she does post something, the complaint will sit in stark contrast to a generally large body of favorable comments regarding what you do and the high-quality results that are your norm. ✧

Treating vitiligo

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found in this area (Figures 1 and 2). The density of the eyebrow was low in the medial one-third.

A donor strip 0.8cm x 3cm was removed. Only pigmented hairs were selected and the 2-hair and 3-hair follicular units were split into a total 169 1-hair grafts. 21G needles were used for “stick-and-place” insertion. There were 122 grafts transplanted to the medial two-thirds of the left side amongst the existing de-pigmented hairs. Forty-seven grafts were added to the upper margin of the right eyebrow to balance the density. Post-operative progress was uneventful.

Results



Figure 1. Preoperative frontal view



Figure 2. Preoperative frontal close-up view

On follow-up in January 2008 (after 7 years), there was a near complete remission of the localized vitiligo. No new lesions were observed elsewhere. The original de-pigmented eyebrow remained de-pigmented. Although the transplanted hairs retained most of the density, at least half had lost their color (Figures 3 and 4).

The patient rejected the proposal of dyeing the eyebrows as cosmetic cover-up. A second session is planned to replace the de-pigmented hairs one by one using the technique of follicular unit extraction (FUE).

Discussion



Figure 3. 7-year postoperative frontal view



Figure 4. 7-year postoperative oblique view

Sub-Populations of the Follicular Melanin Unit

Epidermal melanocytes make up 5-10% of the basal layer cell population. They produce the melanin pigment in elongated, membrane-bound organelles known as melanosomes that are packaged into granules and transferred to adjacent keratinocytes via phagocytosis.

Epidermal melanocytes originate from the neural crest, from where the melanoblasts migrate, to first populate the epidermal basal layer before they non-randomly enter the developing hair follicles. During hair follicle morphogenesis, the melanocytes reach their respective distinct anatomic compartments.⁷ Such region-specific differentiation is believed to accelerate melanoblast/melanocyte differentiation and enhance their secretory activity.^{8,9}

There are three sub-populations of melanocytes in a mature hair follicle: melanotic dopa-positive, amelanotic dopa-negative, and moderately differentiated.

Melanotic dopa-positive melanocytes are found in two sites (Figure 5):

Site 1. The basal layer of the infundibulum (infundibular melanocytes)

Site 2. The upper half of the dermal papilla. These melanogenic bulbar melanocytes transfer melanin predominantly to the hair shaft cortex, less to the medulla, and, only rarely, to the hair cuticle. Melanogenesis takes place cyclically during anagen, being switched off in catagen to remain absent through telogen.⁷ Studies have shown that bulbar and epidermal melanocytes share the same mechanism in melanin transfer and are interchangeable, yet they can be lost independently of each other.

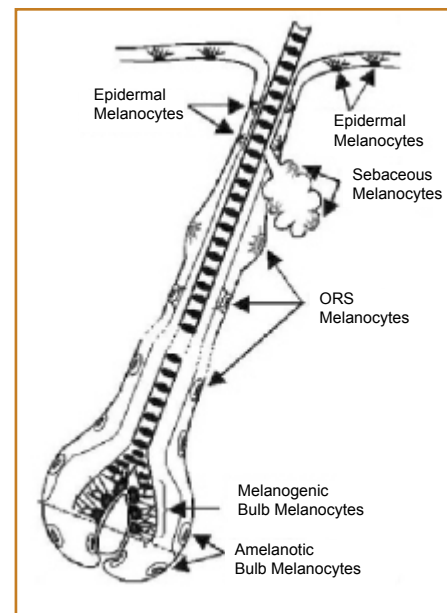


Figure 5. Melanocyte distribution in the human anagen scalp hair follicle (adopted from A. Slominski et al., Hair Follicle Pigmentation).⁸

Amelanotic dopa-negative melanocytes are found in three sites:

Site 3. The outer root sheath within the “bulge” region of the lower isthmus. These ORS melanocytes act like follicular stem cells and provide a precursor melanocyte reservoir for the skin. They divide, proliferate, and migrate upward along the hair follicle surface. On their way to the epidermis these cells mature in both function and morphology to re-pig-

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ment the epidermis after wound healing and in vitiligo.⁸⁻¹² When re-activated by signals from the dermal papilla during telogen-anagen transition, they also move downwards to differentiate into cells of the inner root sheath and hair shaft.

Site 4. The periphery of the bulb. These amelanotic bulbar melanocytes are less-differentiated and can either be newly recruited immature ORS melanocytes or bulb melanocytes that survive catagen and telogen in an amelanotic state only to undergo differentiation again in the next anagen.^{13,14} They both have the capacity to enter vacant niches, including, via migration, to the epidermis.¹⁵

Site 5. The most proximal hair matrix

Moderately differentiated melanocytes may be found in the following site:

Site 6. The basal layer of the sebaceous gland (sebaceous gland melanocytes)

Case Finding 1: De-pigmentation of the Transplanted Hair

The color of the human hair is determined entirely by the activities of the melanogenic bulbar melanocytes. The purpose of our surgery was to add pigmented hair to increase the density of the eyebrow, not to treat skin color. At least half of the transplanted hair follicles were affected by vitiligo and became de-pigmented, but the hair density remained. In this sense, the surgery was only a partial success. This finding suggests that these cells are vulnerable to autoimmune injury in vitiligo and thus are unreliable as donor.

Case Finding 2: Remission in the Vitiliginous Skin

Remission of epidermal vitiligo was an unexpected finding. Spontaneous remission is unlikely. The vitiligo autoimmune response is still active in this case judged by the de-pigmentation of the transplanted hair.

In 1983, Harrist, et al. reported that cells below the arrector pili muscle showed reduced or absent expression of class I major histocompatibility molecules.^{15,16} Westgate, et al. suggested that the hair follicle is an unusual immunologically privileged site not subject to classical immune surveillance.¹⁷ After transplantation, some follicular melanocytes, most likely the ORS melanocytes, must migrate to the basal layer and differentiate into epidermal melanocytes. They escape continuous attack from the vitiligo antibodies to maintain remission.

Case Finding 3: No Change in the Existing Vitiliginous Hairs

There are two possible explanations:

1. The ORS reservoir melanocytes are more catered for the epidermis than the neighboring hair bulbs (81% vs. 23.8% in Na's study).
2. The ORS melanocytes that migrate to the bulb are being destroyed.

Hair Follicle Transplants in Treating Vitiligo

So far it is not known whether transplanting an intact 2- or 3-hair FU would achieve a better result than splitting it into single-hair grafts. As the ORS melanocytes are the most

crucial in treating vitiligo, grafts must include the middle third (the bulge) of the follicle. Sardi transplanted the upper one-third to upper half of the hair follicles but reported that "repigmentation in vitiligo may not be obtained."¹⁸ Na observed a better result when using the whole follicle for hair-bearing areas, and the upper two-thirds for glabrous areas. This is still a very sensible approach as obviously more ORS melanocytes are included. Since the bulb melanocytes are not reliable as a donor, removing the dermal papilla will help to reduce hair growth in glabrous areas.

To save time, there is no need to remove the hair shafts during graft preparation as these can easily be plucked out a few weeks after transplantation. Any emerging hair can be ablated by various means at a later date.

Grafts can be inserted and evenly distributed using Choi implanters or forceps. According to Na, the average perifollicular re-pigmentation is 3mm in diameter (0.07cm² in area). Theoretically, 15 single-hair follicles are sufficient to re-pigment one square centimeter, so this density should be transplanted in the first session. Based on these figures, 1,000 1-hair grafts should cover an area of 65cm². As some hair transplant clinics can manage 3,000 to 4,000 grafts per case, it may be possible to cover up to 520cm² of vitiliginous area in one session. Subsequent grafting may be considered for partially re-pigmented or new areas. The technique can be combined with narrow band UVB, PUVB (psoralen + UVB), or topical corticosteroid therapies for a more rapid result.^{19,20}

Advantages of Hair Follicle Transplants in Treating Vitiligo

There are several advantages to consider:

1. When compared to epidermal melanocytes, follicular melanocytes are denser and more melanogenic. Being immunologically privileged, they may be less susceptible to immunological damage after transplantation.
2. The scalp provides an easily available source of melanocytes. Most patients can donate up to a total of 10,000 single-hair grafts.
3. Donor scars can be minimized by using FUE or the trichophytic closing technique, and are easily hidden under existing hair.
4. Hair follicle grafting does not leave any sign of residual scar in the recipient area, while conventional epidermal punch grafting may leave a cobblestoning appearance.
5. Grafting around the eyelash area or angle of the mouth is technically possible.
6. Touch-up re-pigmentation can be achieved simply by inserting more grafts.
7. The overall complications and side-effects are minimal.
8. Sophisticated and expensive equipment is not required. The procedure can be performed in any clinic set up for follicular unit transplantation where a large number of grafts can be harvested, prepared, and inserted within a short period of time.

Conclusion

Na has demonstrated that hair follicle grafting can be considered in treating localized and segmental vitiligo in exposed areas. In this case study there are two important

findings: 1) graft-induced remission can last up to 7 years; and 2) the sub-populations of follicular melanocytes have different immunological responses to vitiligo. Grafting should include the middle one-third of the hair follicle, which contains the maximum amount of ORS melanocytes. The procedure is simple by today's standards, and can be performed in any hair surgeon's office.

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