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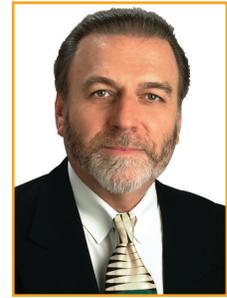
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President's Message

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It is hard to believe that we are nearly half way through the year. Your ISHRS Continuing Medical Educational Committee along with Dr. Robert True, this year's Annual Meeting Chair, are working hard to offer you an Annual Meeting that meets your needs as defined by both the ISHRS Membership Needs Assessment Survey and the post-meeting evaluation surveys from the Bahamas Annual Meeting. Meeting your educational goals is the ISHRS's primary mission.

One of the ISHRS Needs Assessment Survey questions reminded me that from time-to-time each of us needs to reassess our accomplishments, goals, and general direction of our professional lives. In the survey question, "Do you see yourself in the field of hair restoration surgery five years from now? If not, why?" 86% of the respondents (n=266) said "yes." It is interesting to me that only 40% of those who responded with "no" were planning to retire. Over half of the "no's"—60%—were fearful that their ability to practice hair restoration surgery in five years would be limited by either changing technologies or unscrupulous market forces outside of their control.

So I would like to use this communication to directly address a problem, a difficult problem, that is troubling a great many of our members. At the risk of ruffling a few feathers and becoming unpopular, the problem is that of the delegation of critical-to-quality surgical tasks to unlicensed hair restoration surgery technicians. Although few of us are participating in this activity, we know it is going on all over the United States. We feel helpless about how to deal with this unethical behavior that often puts patients at risk for poor outcomes and intra-operative safety.

I ask you to please reflect for a moment on character, and the enhanced character expected by both the public and the profession from a physician. Physicians have since the days of Hippocrates been expected to put the well being of their patients ahead of all others, including themselves. Since the time of Luke, they have cared for the sick, often at significant risk to their own safety. They sacrifice evenings and weekends to be available for their patient's problem call. They cooperate with each other to be sure that their patient is not abandoned in their absence. All because of the character expectation of the physician is to serve the patient's best interest before their own.

But what is "character"? Simply stated, character is: "Doing what is right when no one is watching, regardless of the personal cost." How does one measure character, or identify the nature of a person's character? Consider the 4F's of character evaluation: Flees, Follows, Fight, and Faithful. If applied to one practicing medicine, does one flee away from unscrupulous behaviors? Does one follow individuals of integrity? Does one fight for the patients one serves? Is one faithful to the virtuous principles of the medical profession?

I am reminded of the character of Dr. Samuel Mudd, the physician who took care of the broken leg of John Wilkes Booth, after Booth shot U.S. President Lincoln. He was a physician who did not allow politics to interfere with helping a patient in need. For that action he was torn from his young family, and spent years in a miserable federal prison on the Island of Grand Tortuga, southwest of Key West. Yet, in spite of this unjust treatment, when the island was immersed in a Diphtheria (or Cholera I can't remember) epidemic, he was faithful to his virtues of the medical profession and did all he could to care for guards and prisoners alike, all at significant risk of getting the disease himself.

So what sacrifices have you made for your patients? Do you have the character to always put patients before profits? To stay intimately involved in the management and care of your patients, and not delegate critical-to-quality tasks, such as recipient site creation or FUE graft harvesting? If not, now is the time to reassess your position. We all must work together to relieve the concerns of our peers that "unscrupulous market forces outside of their control" are destroying the future of the profession by putting patients at unnecessary risks. As I write this, Dr. Bob Leonard and the ISHRS Ethics Committee are working hard to review and update the ISHRS Code of Ethics (see page 113 for the full Code). I am confident the entire membership will benefit from the ISHRS's new ethical platform as a forum from which to develop their personal ethical positions.

Co-editors' Messages

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Complications in hair restoration don't occur very often, but when they do, it gives me a reason to educate myself. One such complication occurred in a patient undergoing an FUE procedure a few weeks ago. The problem he developed was intra- and post-operative hiccups. Although I was aware of this side effect with surgery, and knew that it was thought to be a side effect of drugs, I wasn't sure about exactly what the mechanism was that was occurring. I must say that after some investigation I am not much the wiser.

The case itself was very straightforward: 2,500 grafts over two days in a man in his late 30s with no medical problems and on no medications. The patient was pre-medicated with 10mg diazepam and 35mg prednisolone orally. Intra-operatively drugs used included lidocaine 1%, bupivacaine 0.5%, and triamcinolone with epinephrine 1:100,000 in a tumescent solution. Vital signs were normal throughout. It was noted on the first day at the patient's lunch break that he had intermittent hiccups. These were not distressing to him and continued after his food and after drinking water. At the end of day 1, the hiccups still persisted intermittently and on returning the next morning were still occasionally present. The second day progressed in much the same manner as the first

day. On the third day at check-up hiccups were still present; however, the patient reported no problems with sleeping. As the patient was not in any distress and was due to fly overseas to his home country, I decided not to treat with medication but to wait to see if they resolved spontaneously.

Persistent hiccups are described as lasting 48 hours or more and intractable as lasting more than 1 month. A hiccup is an involuntary contraction (myoclonic jerk) of the diaphragm that may repeat several times per minute. The medical term is synchronous diaphragmatic flutter or singultus, which is Latin for the act of catching one's breath while sobbing.¹ A reflex arc causes a strong contraction of the diaphragm followed about 0.25 seconds later by closure of the vocal cords, which results in the classic "hic" sound. At the same time, the normal peristalsis of the esophagus is suppressed.

On looking at the hair transplant literature, there was not much information on the cause and treatment of this condition as it relates to hair transplant surgery. It is reported as being a side effect most commonly of diazepam and associated occasionally with irritation of the vagus nerve in strip surgery.² In the past, we have had a very rare occasion where a patient has developed hiccups during the course of the procedure, but this has always been a short-lived event with no specific treatment required. A case report of herpes zoster, as described by Cotterill, also had hiccups as a complication.³

⇒ page 80

William H. Reed, MD *La Jolla, California, USA* editors@ISHRS.org



Resolved: There is an increased risk of overharvest of the donor from FUE relative to a strip harvest in a young person showing evidence of developing more advanced stages (Norwood IV+) of balding.

Okay, now that I have the hair standing up and blood pressure elevated on some and others at least reading beyond the first sentence, let me state my position that rarely are issues such as this black and white. However, from the donor perspective, FUE, as with any recent evolutionary process, evolves new risks in addition to the evolution of its positives. I propose that the donor is one such potential risk where the nuances and management of over-depletion need clarification, and the sooner the better.

If we are going to learn from the Fathers of our field, we should pursue the stated goals of the ISHRS—to educate, communicate, and interrelate—in order to avoid the mistakes they made of overharvesting the donor with their plugs with, among other things, resultant unsightly donor depletion. With the increasing automation of FUE, the practitioner can exert a power of extraction that outruns the learning curve of his exercise of judgment.

It appears to me that a strip excision, and the associated avoidance of over-depletion of the donor, is easier to teach than is the over-depletion of the donor with FUE. With strip excision, keep the strip narrow for reasonable closure tension and the scar is going to be reasonably acceptable. If not, then FUE can soften the contrast of the scar with the surrounding donor. With FUE, however, how do those experienced in the technique teach the

variables involved in overharvest of the donor in order to avoid over-depletion? If the young patient needs only a small number of grafts, then donor depletion is not a concern...at least over the short term. But what if this young patient needs more grafts over the next decade before the "safe zone" can be confidently ascertained? Do we resort to doing a strip excision during this period or do we generate a depleted "safe zone"? The "safe zone" has to be defined conservatively due to the patient's age and undeterminable degree of future balding. It seems the FUE practitioner has to either ignore the "safe zone" or risk generating a wide band of depletion within the "safe zone," which is ringed above and below by high density "unsafe" donor. How do those experienced in FUE deal with this situation? How do they teach us how to deal with the multiple variables that are much more important with FUE than with strip excision due to the wide zone of depletion versus the strip scar? These variables include donor density, fiber diameter, curl, color contrast of donor hair to skin/scar, and the possibility that the patient may want to style his hair differently in the future in a way that is incompatible with the wide zone of low density generated by a given degree of donor depletion.

I've asked half a dozen of the practitioners who have contributed mightily to our specialty to address this issue. I apologize for not asking some of you who are equally as qualified but ask you to please write a letter to the editor to share your knowledge and experience regarding this issue. I asked Russell Knudsen to comment and edit the responses in his "Controversies" column and am indebted to all of you for helping move our field forward with forethought and utmost concern for our patients by participating in our efforts to educate, communicate, and interrelate. ♦

INTERNATIONAL SOCIETY OF HAIR RESTORATION SURGERY

Vision: To establish the ISHRS as the leading unbiased authority in hair restoration surgery.

Mission: To achieve excellence in patient outcomes by promoting member education, international collegiality, research, ethics, and public awareness.

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- 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 editors@ishrs.org.
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- 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).
- We CANNOT accept photos taken on cell phones.
- Please include a contact email address to be published with your article.

Submission deadlines:

June 5 for July/August 2013 issue
 August 5 for September/October 2013 issue

Farjo Message

from page 79

In the wider literature, causes of hiccups have been attributed to several things: phrenic/vagus nerve stimulation, drugs, metabolic conditions, electrolyte imbalance, direct stimulation/irritation of the diaphragm (e.g., in intra-abdominal surgery), infection, CNS disorders, arrhythmias, coughing, and alcohol.¹ The incidence in hair transplantation is very low having been described in one case series as 0.2%.⁴ In the general population, incidence is described as equal amongst the sexes but intractable hiccups are more common in men for unknown reasons.¹

Treatment of choice for sustained hiccups is chlorpromazine, a potent anti-psychotic that also has anti-emetic properties. Side effects of chlorpromazine include sedation and for this reason I chose to wait and not treat this patient as he was flying overseas. It was not an ideal situation to be sending the patient on a plane

under the influence of a strong sedative and carrying anti-psychotic drugs into another country. Instead I gave the patient the name of the drug and told him to contact his own physician if the hiccups hadn't resolved in a couple of days. Fortunately, at follow-up after 4 days, the patient reported resolution without treatment.

References

- Wilkes, G. www.emedicine.medscape.com/article/775746-overview. 2 August 2007.
- Unger, W., et al. *Hair Transplantation*, 5th edition. Informa Healthcare, 2011; p. 418.
- Cotterill, P. A case of shingles (herpes zoster) post hair transplant. *Hair Transplant Forum Int'l*. 2012; 22(6):223.
- Salanitri, S. et al., Surgical complications in hair transplantation: a series of 533 procedures. *Aesthet Surg J*. 2009(Jan-Feb); 29(1):72-76. ♦

Notes from the Editor Emeritus

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Is it getting harder to say NO to patients?

I have previously shared my thoughts about the Empowered Patient, but have not specifically addressed what, if any, implications this has on our ability to say NO to patients.

Given that the provision of cosmetic procedures is a discretionary, healthy-patient-initiated contract that doesn't fully conform to the traditional medical model, the patient has a lot of say as to what they want. If we were to treat them as customers (or clients), then the concept of "the customer is always right" might apply, as it does in business. If, however, we apply the medical model, particularly keeping in mind the *primum non nocere* dictum ("first, do no harm"), then the right to vary or refuse certain requests becomes inherent in the negotiation of any treatment plan.

When dealing with men with male pattern balding or women with female pattern hair loss, the fact that these are progressive, lifelong conditions, arguably deserving lifelong medical management, makes a case for primacy of the medical model over the client model. However, in static conditions (e.g., sparse eyebrows, congenitally high hairlines) there is a blurring of which model might best apply.

The easiest example of the need to say No is when you suspect Body Dysmorphic Disorder (BDD), which is more prevalent in our patient base than in the general population. If in doubt, refer and delay any decision regarding surgical treatment. It is my experience, however, that any patient I suspect of having BDD does not welcome the suggested diagnosis and is hostile to the concept of referral to a psychologist for evaluation. This does, however, leave us with an easy "out" if they refuse the referral.

With male pattern balding the three most common scenarios that make saying No possible are:

1. Inappropriate hairline requests: If the request is "unnatural" we must say NO.
2. Unachievable expectations of density/coverage in extensive balding.
3. The very young, "panicked" patient who refuses medical stabilization therapy.

The first two scenarios have always been with us and are rather straightforward, but the third is somewhat more complicated. While we always should slow down the panicked patient who is making a hasty decision, the patient certainly has the right to refuse medical stabilization and in theory this should not absolutely determine their suitability for surgery.

Those of us who performed standard punch grafting will remember the (hopefully) rare outcome of operating on a young, desperate patient who returned to us 10 years later wishing they had never undergone the surgery as they no longer cared about balding and were left with a visually unnatural outcome in their frontal scalp. Does the switch to follicular unit grafting change the suitability of operating on young patients? What about the

young patients who tell us they want hair for the next 10 years but will then likely shave their head rather than continue with further treatment?

This last scenario seems to be coming more frequent with the development of FUE convincing some young men that there is no "downside" in making the decision to proceed with surgery. They can "shave their head sometime in the future with no visual consequences." Even if this was true (and it cannot be guaranteed), would this be regarded as acceptable decision making? If they are an "educated client," then perhaps so. If we apply the medical model, where does that leave us? Confused?

Consider the patient who wants surgery but tells you he will shave the grafted hairs as he intends to wear a short crewcut as his hairstyle. Do we have any advice to give this patient? I suspect many colleagues, like myself, would find this a matter of judgment, particularly regarding the maturity of the decision making of the patient. Our responsibility is to educate prospective surgical candidates as to the consequences or outcomes expected by proceeding, but they must take ultimate responsibility for the decision to proceed. Documenting your discussion in their medical record would seem wise.

With cosmetic eyebrow grafting it seems to be a fairly straightforward wish-fulfillment scenario. However, I once saw a 23-year-old female who wanted to have grafting to the area superior to her actual eyebrow as this was where she had tattooed a new, preferred shape and wanted to avoid further tattooing. She was epilating her original, normal eyebrow hairs at the same time! What was my advice? I encouraged her to think further about a future requiring BOTH epilating of normal eyebrow hairs and trimming of grafted hairs and she never returned for a second consult. I like to think no colleague agreed to her request...

With females requesting lowering of a congenitally "high" hairline, a stable hairline scenario, then the decision to proceed must rest on the appropriateness of the hairline desired. In males requesting hairline lowering, then younger patients must be expected to have to deal with possible future male pattern balding, and this scenario must be discussed and planned for. The 20-year-old patient's suggestion that he wants an age-normal hairline for the next 10 years and then might shave his head if balding occurs is not, in my view, an appropriate decision that makes me comfortable to proceed. Others may have an alternate view.

If there is doubt in my mind about the wisdom of the patient's request, then I apply the medical model. I will not be an agent of potential harm to my patients.

I usually suggest they think some more and return for a second consultation.

The increasing patient view that FU grafting, and FUE in particular, leaves them with the ability to have a "temporary" hair result, with no downside, does increasingly challenge our previous views about saying no to our patients. ♦

AGA and POS

[from front page](#)

History and Molecular Characterization of NC21OHD

A Nobel Prize was awarded in the 1930s for the contributions of Reichstein and Kendall who first isolated adrenal steroids.³ Although varying degrees of disease severity for classical 21 hydroxylase deficiency had been recognized, the first report of the distinct clinical entity of NC21OHD was published in 1979, and in 1986 the gene responsible for production of 21 hydroxylase was identified. Since that time PCR techniques have helped identify over 100 genetic mutations impacting the gene to cause both classical and non-classical 21 OH deficiency.⁴

The CYP21A2 gene, as mentioned previously, is a member of the cytochrome P450 (CYP) family and it controls transcription of enzymes that hydroxylate steroid precursors in the adrenal cortex to form corticosteroids and the mineralocorticoids. It is located on Chromosome 6 in the class III region of the major histocompatibility complex (MHC)(6p21), and is near an inactive pseudogene (CYP21P) that contains several inactivating mutations that can be transferred to the active CYP21A2 gene by gene conversion or deletion. Mutations can result in minimal or severe symptoms depending on the degree of the resultant enzyme production deficiency, and asymptomatic patients may be complex heterozygotes. The clinical phenotype in such cases has been observed to correlate well with the less severely mutated allele, resulting in activation of the allele that produces the higher level of 21 hydroxylase.^{4,5} Because a divergence between observed phenotype compared to genotype has been observed in some patients, other factors such as the effect of androgen sensitivity related to CAG repeats in the androgen receptor (AR) gene are thought to be potential contributing factors.⁵ The number of CAG repeats on the N terminal of the AR gene has been shown to be inversely related to androgen receptor binding, so that smaller numbers of CAG repeats appear to result in a greater sensitivity to androgen hormones.⁶ In the case of NC21OHD, a patient who is either more or less sensitive to their androgens would be expected to be more or less sensitive to increases in androgen produced by this condition. It has been speculated that other genetic polymorphisms that influence the quantity and activity of steroid enzymes or hormone response may also be able to influence phenotype variability.^{2,5}

Frequency and Prevalence of NC21OHD

The CYP21A2 gene is felt to be one of the most highly polymorphic. The estimated incidence of mutations in the population causing NC21OHD is much higher than classical 21-OHD, at 1:500 to as high as 1:100 in various population surveys.¹ As previously noted, certain populations have been found to have a much higher incidence, such as Ashkenazi Jews at 1:27 (1:3 are allele carriers), Hispanics at 1:40, Slavs 1:50, and Italo-Americans at 1:300.^{4,15} A recent assessment of the CYP21A2 gene dosage by real-time PCR in 144 individuals randomly sampled from the Spanish population identified that 12% were mutation carriers for NC21OHD.¹ Similarly, in Greece, a random sampling of 494 infants were genotyped, with findings of mutations for NC21OHD in 7.44%.⁷ It seems likely we will continue to identify at-risk populations as more and larger gene surveys are performed.

Clinical Features of NC21OHD

First it must be appreciated that not all people with NC21OHD will be symptomatic; for example, symptoms of mild hyperandrogenism are not generally noticed in males. Depending on the degree of enzyme activity, patients may be identified in childhood due to premature pubarche (early findings of body hair: <8 years in females, <9 years in males; apocrine odor) or accelerated linear growth and skeletal maturation, which results in a taller than average child for age, but ultimately shorter adult stature, due to premature closure of epiphyseal growth plates.^{2,4} Symptoms in adolescence and adulthood are more likely to identify affected females as they relate to unexpected hyperandrogen symptoms, with the most common being hirsutism, oligomenorrhea, and cystic acne. Decreased fertility has been ascribed to this condition; however, a recent survey showed only 12% of affected women experienced difficulty with fertility, indicating most had normal fertility.^{2,4,8} From a hair restoration surgeon's perspective, it is important to be aware of a case report of male pattern baldness in an affected young woman as a sole presenting symptom, and severe androgenetic alopecia (AGA) with marked virilization has been seen in older women.² While no published reports specific to the frequency of hair loss or thinning as part of the NC21OHD entity were found, the prevalence of associated gene mutations in women with clinical evidence of hyperandrogenism has ranged from as low as 1% up to 33% depending on the area of the United States or Europe where the survey occurred.² Polycystic ovaries have been found in about half of women with NC21OHD, and, furthermore, estimates are that among women with polycystic ovarian syndrome (PCOS) about 10% have NC21OHD.⁴ Previous studies have shown a correlation between adrenal androgen excess and ovarian cyst formation, though the exact mechanism for why this occurs is not clear; amplification of FSH receptors, and disruption of cyclical gonadotropin release have been proposed as causal factors.⁹

Diagnosis of NC21OHD

Elevated 17-OHP concentrations are diagnostic in classical 21-OHD, but may be within the normal range for individuals with NC21OHD. Serum cortisol levels are also usually normal,^{2,4} and while other androgens such as testosterone and DHEA have been elevated in some surveys, it is also reported that normal basal androgen levels and clinical presentation cannot be used to screen or diagnose,^{10,11,12} as DHEA and androstenedione may only be elevated with ACTH stimulation.¹³ It seems reasonable to expect that androgen hormones would reflect the degree of enzyme insufficiency, where lower levels of 21 hydroxylase enzyme would cause a reduction of cortisol and stimulate more ACTH, which in turn would stimulate more precursors (DHEA, androstenedione) down the androgen path to produce higher levels of androgens. However, no publications or surveys correlating androgen levels with 21-OH enzyme levels have been found to test this supposition. Because symptoms can occur even when basal androgen and 17-OHP levels are within the normal range—and have not been seen to correlate with hirsutism, acne, or alopecia¹¹—the acute ACTH stimulation test remains the gold standard to confirm decreased 21 hydroxylase activity. This test involves collection of a baseline blood sample, followed by synthetic ACTH injection with a second sample collected 30-60 minutes later, which reveals a marked elevation

in 17-OHP among NC21OHD patients. Because of the expense associated with genetic testing, and even ACTH stimulation tests, unstimulated AM levels of 17-OHP in the follicular (pre-ovulatory) phase of the menstrual cycle with levels of 170-300ng/dl as a screening tool is recommended. A positive screening test then indicates the need for ACTH stimulation to make the diagnosis. Once a biochemical diagnosis is confirmed, genetic analysis may be helpful in identifying other affected family members or carriers.¹ For the CYP21A2 gene, a panel of 9 common mutations and deletions detects between 80-98% of disease causing alleles in affected individuals and carriers.¹⁴

Treatment Considerations

Goals of treatment depend on the age of the patient. For adults, treatment goals are focused on symptomatic relief or improving fertility where this is a problem. As hair restoration doctors, we will not likely be evaluating children where the goals of therapy will be to achieve a normal rate of skeletal maturation. If we do see patients with NC21OHD, it will be related to hair loss/thinning, and clues to the diagnosis may include ethnicity and concomitant hirsutism, obesity, history of a diagnosis of PCOS, or cystic acne. Use of anti-androgens (flutamide, cyproterone acetate, or finasteride) may help women with hirsutism and AGA. Among women with NC21OHD, the use of cyproterone acetate compared to hydrocortisone was more effective in treating hirsutism.² Other studies have shown that irregular menses and acne can be reversed with glucocorticoids (0.25mg of dexamethasone at night) within 3 months, while hirsutism took 30 months to resolve on this regimen. Cystic acne caused by NC21OHD has been reported to be refractory to antibiotics and retinoic acid therapies.⁴ Although infertility apparently afflicts a relatively small percentage of affected patients, glucocorticoid therapy has been shown effective to restore normal fertility and obviate the need for more expensive fertility therapies. This works by restoring normal menstrual cycles. Specific recommendations for hair loss in the various publications were not provided; however, in women with the genetic predisposition to AGA, it seems likely that controlling androgen levels by treating overstimulation of ACTH, and/or providing androgen blockade, would be helpful. The fact that not all female patients with NC21OHD develop hair loss indicates other factors are necessary to make the hyperandrogenism result in hair loss—possibly other genetic factors related to the androgen receptor gene and the polygenic entity of AGA.

Conclusion

Non-classical 21-OHD is a relatively common autosomal recessive disorder that can present at any stage in life, and is asymptomatic in some. The surprisingly high population incidence of this entity, which includes female hair loss as a symptom, should make this diagnosis part of our differential diagnosis. Women with single or multiple symptoms of hyperandrogenism, such as hirsutism, oligomenorrhea, cystic acne, hair loss and/or PCOS, should be screened with a prefollicular, A.M. 17 hydroxy progesterone level. A high index of suspicion or elevated basal level should be followed with an ACTH stimulation test. Referral to an endocrinologist for further evaluation and therapy is indicated.

References

1. Parajes, S., et al. High frequency of copy number variations and sequence variants at CYP21A2 locus: implication for the genetic diagnosis of 21-hydroxylase deficiency. *PLoS One*. 3(5):e2138. 14 May 2008.
2. Witchel, S.F., and R. Azziz. Nonclassic congenital adrenal hyperplasia. *Int'l J Pediatr Endocrinol*. 2010; 2010:625105.
3. Huynh, R., et al. The clinical and biochemical spectrum of congenital adrenal hyperplasia secondary to 21 hydroxylase deficiency. *Clin Biochem Rev*. 2009(May); 30(2):75-86.
4. New, M.I. Non-classical 21 hydroxylase deficiency. *J Clin Endocrinol Metab*. 2006(Nov); 91(11):4205.
5. Krone, M., and A. Wiebke. Genetics of congenital adrenal hyperplasia. *Best Practice & Research Clinical Endocrinology & Metabolism*. 2009; 23:181-192.
6. Shah, N., et al. Association of AR-CAG repeat polymorphism and PCOS. *J Clin Endocrinol Metab*. 2008(May); 93(5):1939-1945.
7. Dastamani, A., et al. High carrier frequency of 21 hydroxylase deficiency determined by genotyping in Hellenic population. *Endocrinol Rev*. 2012; 33 (Meeting Abstracts).
8. Bidet, M., et al. Fertility in women with nonclassical congenital adrenal hyperplasia due to 21 hydroxylase deficiency. *J Clin Endocrinol Metab*. 2010(Mar); 95(3):1182-1190.
9. Guran, T., et al. A giant ovarian cyst in a neonate with classical 21-hydroxylase deficiency, with very high T levels demonstrating a high dose hook effect. *J Clin Res Pediatr Endocrinol*. 2012; 4(3):151-153.
10. Moran, C., et al. 21 hydroxylase deficient nonclassic adrenal hyperplasia is a progressive disorder: a multicenter study. *Am J Obstet Gynecol*. 2000(Dec); 183(6):1468-1474.
11. Dewailly, D. Nonclassic 21 hydroxylase deficiency. *Semin Reprod Med*. 2002(Aug); 20(3):243-248.
12. Ghizzoni, L., et al. Relationship of CYP21A2 genotype and serum 17 hydroxyprogesterone and cortisol levels in a large cohort of Italian children and with premature pubarche. *European J Endocrinol*. 2011; 165:307-314.
13. <http://www.endotext.org/pediatrics/pediatrics8/pediatrics8.htm>
14. Nimkarn, S., and M.I. New. 21-hydroxylase deficient congenital adrenal hyperplasia. NCBI bookshelf, www.ncbi.nlm.nih.gov/books/NBK1171/. 24 August 2010.
15. Nimkarn, S., and M.I. New. *Genetic Diagnosis of Endocrine Disorders*. Congenital Adrenal Hyperplasia, Chapter 15. 2010; 165-171. ♦

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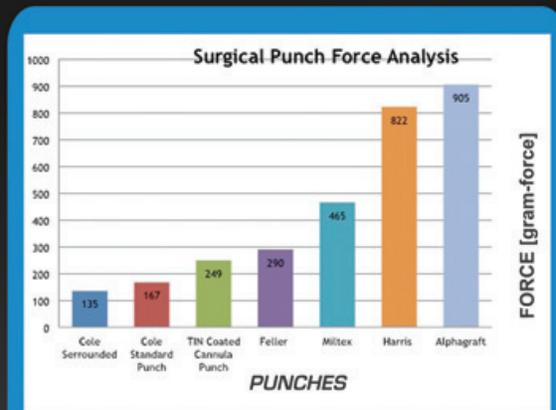
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FUE Research Committee Chair's Message

Parsa Mohebi, MD Los Angeles, California, USA pmohebi@ushairrestoration.com

ISHRS FUE Research Committee

This page is dedicated to the recently created FUE Research Committee and its goals. The Committee's intention is to increase and promote quality research in the field of FUE hair transplantation, as well as to disseminate the findings of the new FUE committee activities.



Inaugural meeting of the FUE Research Committee during the ISHRS 20th Annual Scientific Meeting in Paradise Island, The Bahamas (left to right): Drs. Bradley R. Wolf, Alex Ginzburg, Melike Kulahci, Bijan Ferudini, Márcio Crisóstomo, Jose Lorenzo, Jennifer Martinick, John P. Cole, James A. Harris, Paul T. Rose, Ken Williams, Robert H. True, Jean Devroye, and Parsa Mohebi

The emergence of new techniques in transplantation has led to significant transformation in follicular unit extraction (FUE) surgical procedures in recent years. Among these techniques are automated and robotic extraction devices. The goal of these innovations is focused on improving the quality of FUE hair transplantation while minimizing the invasiveness of the procedure. There are also new studies that clarify how FUE grafts should be handled for maximum survival during an FUE procedure. This information can assist in the better planning of FU extraction and implantation during a FUE procedure, thus leading to improved overall results.

The International Society of Hair Restoration Surgery established the FUE Research Committee at its 20th Annual Scientific Meeting. The new committee was founded to focus on understanding different aspects of FUE hair transplant procedures and the techniques that could be utilized to improve the quality of these procedures.

The FUE committee will examine the traditional and modern methods of FUE procedures and also conduct comparison studies with other current hair restoration procedures. The ISHRS's FUE Committee is comprised of several internationally known figures in hair restoration with distinguished backgrounds in research and medical innovations.

As members of this committee, we are committed to this significant effort in setting up studies and multi-center research projects to achieve the goal of this society.

ISHRS FUE Committee Initial Goals

The initial goals of this committee include:

- To investigate the previous studies and publications regarding FUE transplantation and evaluate the scientific significance of those studies;
- To standardize the language used in the field of FUE and to set proper terminology that scientists and hair transplant physicians can utilize in their research efforts; and
- To coordinate the design and implementation of studies on FUE transplantation for improving the current techniques of FUE hair restoration.

The hope is that the FUE committee can achieve its goals and improve the quality of hair transplant procedures and set new standards in the field of hair restoration surgery. Three interdependent subcommittees are established within the FUE Research Committee to achieve its goals:

1. Literature Review Subcommittee
2. Terminology Subcommittee
3. Future Studies Subcommittee ♦

Founding Members of FUE Research Committee of ISHRS (Divided into their 3 Subcommittees)

Literature Review

Chair: Bradley R. Wolf, MD, USA
Melike Kulahci, MD, Turkey
Paul T. Rose, MD, JD, USA
Ken Williams, DO, USA
Jae Pak, MD, USA

Terminology

Chair: Jose Lorenzo, MD, Spain
Jean Devroye, MD, Belgium
John P. Cole, MD, USA
Robert H. True, MD, MPH, USA
Carlos Puig, DO, USA

Future Studies

Chair: James A. Harris, MD, USA
Parsa Mohebi, MD, USA
Alex Ginzburg, MD, Israel
Bijan Ferudini, MD, Belgium
Jennifer Martinick, MBBS, Australia
Márcio Crisóstomo, MD, MS, Brazil