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A recently characterized, underdiagnosed cause of female androgenetic alopecia and polycystic ovarian syndrome: non-classical 21 hydroxylase deficiency

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If you harken back to medical school, to recall the complex steroid pathway controlled by enzymes that catalyze production of various steroid hormones from cholesterol, you may remember the pathologic entity of 21 hydroxylase deficiency—but probably don't expect to see it in your clinical practice. Classical 21 hydroxylase deficiency is genetically inherited and, though it is the most common autosomal recessive disorder, affects only 1:10,000-23,000 live births depending on the ethnicity of the population.¹ Gene mutations can occur and result in only 0-5% of normal 21 hydroxylase enzyme function, which

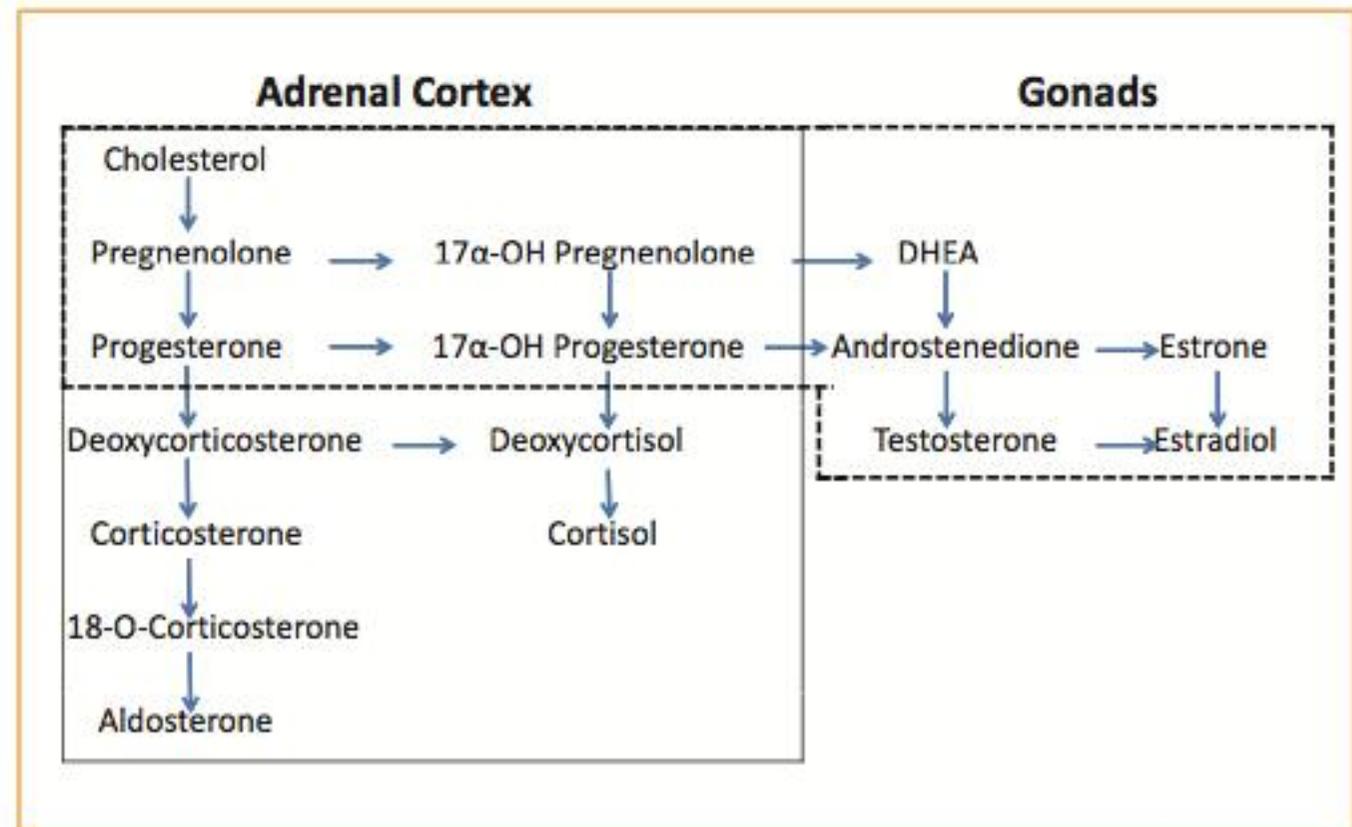


Figure 1. Steroid pathway.

prevents cholesterol from continuing down the path to form cortisol and mineralocorticoid (aldosterone). Instead

Questions for Dr. Lorenzo

Q. If a surgeon is uncomfortable with defining the surgical plan and its "safe zone" based upon the patient's willingness to take medication for the rest of his life to prevent the progressive nature of balding, could he instead define a conservative "safe zone" and extract only from it for procedure 1?

First, I always try to guess the safe area, whether the patient is stable or not. Of course, when a patient's hair loss is stable, I feel more comfortable in defining that area. Second, I do operate on young patients who have tried medications and have had to stop treatment because of side effects; I would prefer, however, not to operate on patients who do not want to take medication for concern that my estimation of "stable" and future hair loss is inaccurate. I try to use clear logic as a protocol and that appears to give me good results.

Q. Following donor healing, the surgeon would then know whether the patient is going to heal acceptably like Patient 1 or whether he'll heal with the, in my opinion, disfiguring scarring of the donor of Patient 2 (Figures 10 and 11). Based upon this, is the surgeon justified in harvesting into areas that cannot be determined as safe or unsafe?

I've never seen poor healing with small punches. In Patient 2, the disfigurement is caused by the use of a large punch (1 mm or greater) and not by the patient's healing characteristics. A surgeon must always extract from areas considered safe according to the visible signs of developing androgenetic alopecia (AGA). There is the concern, of course, of that what appears "safe" can later

transected or divided *in vivo* (splitting). When we do the frontal area, we need to have more singles than when we repair the crown. For that reason, I increase the diameter of the punch when I harvest for the crown to avoid the transection, and I try to yield 10, 12, or 15% of singles when I work in the frontal area. If I don't have the singles I need, I decrease the punch diameter at the end of surgery to divide the follicular units *in vivo*. For me, the transection rate is not as important as the number of hairs per follicular unit. I try to keep 2.2 hairs per unit in the front and try to reach 2.5 hairs per unit at the crown. "Splitting" is the action of separating with the punch *in vivo* (or *in situ*) a portion of the follicles in a grouping (follicular family or follicular unit). The extracted graft will contain fewer follicles than are in the group. Splitting can be produced deliberately or unintentionally.

Q. Do you feel it is the small size of the punch, the transection that masks the scar with subsequent hair growth at the extraction site, or both that are important for the superior cosmetic effect?

Transection and splitting to hide the scar is more important than small punches, both the small punch size with splitting have an additive effect.

Q. Do you have thoughts about the use of ACell or other growth factors to promote growth of the transected follicles in both the donor and recipient areas?

I had my experience with ACell one year ago (40 patients). I didn't see any change in survival or any circumstantial evidence of regeneration or auto cloning of the hair. What I saw was a

Same bag... two different concepts

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I think we are putting in the same bag two different concepts; to me, the use of the safe/unsafe area and the overdepletion of the donor site are clearly not the same.

First, the use of the safe area. We can define the safe donor area as that portion of the scalp that contains follicles not affected by balding. Regarding this concept, we will have lifelong discussions about if the safe limits that we accept the day of the procedure will be equally safe in 10 or 20 years. But the answer is not about how to predict the evolution of alopecia; the answer is in the protocols that we must have to carry out a procedure, whether by FUT or FUE. In my protocols, the best indication for surgery is the hair loss stability, either by age (40-45 years with a defined pattern of alopecia), or by medication (finasteride in patients under 40 years old). In the patients under 40 who cannot be under treatment due to side effects, it is important to be more careful and conservative with the safety margin in their limit areas. To me, a young patient who voluntarily does not want to take medication is not a candidate and should expect to clarify his bald pattern. The unsafe area represents less than 10% of the harvestable zone, and in case that patient's alopecia evolves despite previous concepts, the use of small punch diameters (0.75-0.9 mm) will prevent the visible traces (white dots) from becoming visible in the future. Finally, and quoting Dr. Cole, while this 10% of follicles are in the recipient area, they will be fulfilling the goal of the patient, which is to cover the recipient area, not the donor.

I think the second concept has greater significance. Indeed,

extraction in a possible second or third procedure. We know that the use of small punches increases the range of transection and splitting, and this improves the recovery of the donor area. The big punches remove more material around the follicle, possibly including stem or resting cells even though we have not been able to prove it. But patients that we are currently seeing after large FUE surgeries are confirming what we reported previously.

As an example, about 4 months ago, I saw two patients with similar characteristics: both had light brown hair, 50 microns of hair thickness, and both had had a previous FUE procedure. The breakdown for the first patient (Patient 1) was as follows: 3,101 FUs, 0.75mm punch, 2.37 hair per units, 7,353 hairs, and 83.3% of 2-, 3-, and 4-hair FUs (that means 16.7% singles = close to transection rate).

When I divide a surgery in two sessions, I always wait 5 months for the second (which is the necessary time needed for good recovery of the donor site). Figure 1 shows the comparative at 5 months. The second patient, Patient 2, had undergone a 3,500 FU procedure with another surgeon in 2010. Unfortunately, we don't have the statistics, we don't know the size of the punch, and we don't have his prior photos, but Figure 2 shows him prior to the second procedure.

The recipient area (result), however, is not the issue. Both patients are cases of advanced alopecia needing many units. We are going to focus on the status of the donor area after removing more than 3,000 units.

Patient 1 retained a good donor area, so we planned a second procedure of 3,000 FUs to cover the crown. Patient 2 had a pretty depleted donor area, so we couldn't plan more than 2,000 FUs. In the procedure, we obtained 2,151 FUs.