Hair Sciences

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In this article we have asked dermatologist Rodney Sinclair of Melbourne, Australia, to give some of his opinions on female hair loss. He has collaborated on this with his senior scientist Dr. Nick Rufaut. We have chosen some more clinically based rather than purely scientific questions for this edition. It is interesting to read his method of diagnosis and first line treatment of female pattern hair loss as this differs from that which some of us follow. Dr. Sinclair's clinical grading system seems more comprehensive than the traditionally used Ludwig scale (see Figure 1). Some of the more recent work on genetics is discussed also. This is an area of some very interesting developments: not only will we be able to give patients a prediction of their likelihood of developing AGA but also the understanding of the mechanisms involved in the balding process itself may lead to novel treatments.

An interview with Dr. Rodney Sinclair on female pattern hair loss

Rod Sinclair, MBBS, MD, and Nick Rufaut, PhD *Department of Dermatology, St Vincent's Hospital, Melbourne, Australia*

1. What is your first line of treatment for women with androgenetic alopecia?

Oral spironolactone 100-200mg per day, as lifelong therapy.

2. Do you think that minoxidil 5% is more effective than minoxidil 2% in women? Once a day vs. twice a day?

I think that twice daily 5% minoxidil has a more rapid onset of action than twice daily 2% minoxidil; however, the difference after 12 months of continuous use is probably negligible. I believe that once daily 5% minoxidil is probably equally effective to twice daily 2%. I advise my female patients to begin treatment with the 5% solution twice a day for the first 6 months and then cut back to once daily use. The data for once daily use is purely anecdotal, but most women find twice daily use difficult, and I would rather they use it once daily than not at all.

3. Many patients complain about itching with the continuous use of minoxidil. How do you manage this common complaint?

The 5% foam for men is better tolerated than the lotion. Once daily use is better tolerated than twice daily. The 2% solution is less irritating than the 5% solution. Daily shampooing, especially with an antidandruff shampoo, can help. Occasionally I resort to topical steroids. If all else fails and the patient has been a good responder to topical minoxidil, and there are no relative contraindications, I use very low dose oral minoxidil, such as 2.5mg daily. I generally stop the spironolactone first.

4. In which female patients would you use antiandrogens and for how long?

I would use it in women with female pattern hair loss (FPHL). I ask them to use it for as long as they want hair.

5. What type of antiandrogen works best for FPHL—diane 35/yasmin, androcur, finasteride, or spironolactone?

I find spironolactone to be equally effective to cyproterone acetate, and somewhat more effective than finasteride. The contraceptives Dianne and Yasmin are useful adjuncts to therapy, but I rarely use them as monotherapy.

6. There are some anecdotal reports of the use of finasteride in premenopausal women. Would you recommend it and at what dose?

I generally avoid finasteride in women who may become pregnant. It has a very long biological half life and so even if a woman stopped it immediately on discovery that she were pregnant, there is still a risk of birth abnormality. I also find it less effective than spironolactone.

7. What do you think about the role of vitamin supplements, such as biotin or others, in FPHL?

Nutritionally or genetically mediated biotin deficiency can cause alopecia, among other symptoms that include dermatitis. Deficiencies of other vitamins such as vitamin A or zinc may similarly cause alopecia; however, these are dif-

Figure 1. Dr. Sinclair's clinical grading system.

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ferent entities from FPHL. Similarly, hypervitaminosis A causes hair loss.

8. What do you personally think about the role, if any, of ferritin levels in female androgenetic alopecia?

Reports of correlations between low ferritin levels and FPHL or other forms of hair loss are equivocal, and are complicated by debate as to what level of ferritin can be considered normal.[1,2] Similarly, the benefits of iron supplementation are unclear.[3,4] Individual women may vary in their sensitivity to ferritin levels with respect to hair follicle behavior.[5] Low ferritin levels may be a risk factor for hair loss, rather than a primary cause.

9. What is your opinion of low level laser therapy for FPHL?

This is an over marketed modality. I am yet to see any convincing trial data.

10. What is the lab work-up that you normally use for the female patient who comes to your clinic complaining of hair loss?

I often do no investigations. If I plan to use spironolactone, I like to confirm normal renal function. If the pulse rate is below 60, I do thyroid function tests. If the patient is a vegetarian, I order a serum ferritin. If the patient also has menstrual irregularity or hirsutism, I investigate for polycystic ovarian syndrome and screen for diabetes and hypercholesterolaemia.

11. What kind of devices do you use for examination of patients with hair loss: just visual inspection, phototrichogram, photographic documentation, or something other?

I use my clinical grading scale to score the hair loss (Figure 1).[5a,5b] If visual inspection does not enable a diagnosis, I take a couple of 4mm punch biopsies and have those both sectioned horizontally.

12. Why do you think that the hair loss pattern in women is more diffuse than in males?

In males, all follicles within a follicular unit are miniaturized in affected regions of the scalp. In females, however, it appears that only some follicles within each follicular unit are miniaturized, so that at least one terminal hair remains.[6] The affected and unaffected follicles may equate, respectively, to the lateral and central primary follicles seen in other species.[7] Why the later-developing lateral follicles should be more susceptible to miniaturization is unclear.

13. Male pattern hair loss has been clearly linked to the effects of dihydrotestosterone. Do you have any theories regarding the etiology of FPHL at the molecular level?

FPHL is responsive to oral antiandrogens, suggesting a role for androgen signaling.[8] However, the response is variable. This could indicate either that the antiandrogens we are using lack potency or that there is disease heterogeneity. I suspect both to be true. In some women, I suspect estrogen is also toxic to the hair and that estrogen signaling may prove to be involved in the etiology of FPHL.

14. There are two chromosomes recently found to be linked to male pattern hair loss and prediction of the severity of balding. Do you think the genetics in women is similar or completely different and does this explain the difference in patterns that we see?

Genes encoding the androgen receptor,[9] 5α-reductase type 2,[10] ornithine decarboxylase,[11] and an unidentified gene on chromosome 3q26[12] have been found to be associated with male pattern hair loss. The first two are involved in androgen metabolism or signaling. One study, albeit small scale, has found an association between FPHL and polymorphism in a CAG repeat in the androgen receptor gene,[13] however, we have not been able to conclusively confirm this association in a larger study of over 500 women. Difficulties proving the association arise because the androgen receptor gene is on the X chromosome and women have 2 X chromosomes, one of which is randomly inactivated in each cell due to lyonization.

Our research, however, has yielded 2 other candidate genes with a strong association with FPHL that suggest similar genetics, to the extent that our genes are involved in androgen and/or estrogen signaling (manuscript submitted, but not yet accepted for publication). Conceivably, differences in the relative contribution of androgen and estrogen signaling may underlie the differences between male and female follicle miniaturization patterns.

15. In my experience, nothing works for frontal fibrosing alopecia. Is there any treatment pearl that you recommend?

I use plaquenil and topical minoxidil and intralesional triamcinolone to arrest further progression.

16. How frequent do you see patients with chronic telogen effluvium and how do you manage them?

They account for around 40% of my patients who present with increased hair shedding,[5b] but no loss of volume over the mid-frontal scalp (stage 1 on my clinical grading scale). I photograph them and watch and wait. I review them every 6 months. After 3 or 4 years they come to the conclusion they are not going bald despite the fact that they are shedding vast numbers of telogen hairs.

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Rodney Sinclair is currently the Professor of Dermatology at the University of Melbourne, Director of Dermatology Services at St Vincent's Hospital, and Director of Research and Training at the Skin and Cancer Foundation. He is Immediate Past President of the Australasian Society for Dermatology Research and Past President of the Skin and Cancer Foundation of Victoria and the Australasian Hair and Wool Research Society.

Professor Sinclair is the co-author of the section on dermatology in the Oxford Textbook of Medicine and the chapter on Hair Disorders in Rook's Textbook of Dermatology. He has written 7 textbooks of dermatology, published over 150 research articles in scientific journals, and contributed more than 50 chapters to multi-author medical textbooks.

His main research interests are the biology of the hair follicles and its related structures, skin stem cell research, gene discovery, and cell based therapy.