

Proceedings & Key Messages from the AHRS Scientific Session

Cicatricial Alopecia: The Experts' Opinions

A stimulating debate on the similarities and differences of LPP, FFA, CCCA, and others. Webinar Program held on Saturday/March 27, 2021

Victoria Ceh, MPA, Executive Director, American Hair Research Society, with scientific take-home points contributed by the presenters

Introduction

The American Hair Research Society (AHRS) has a long-standing tradition to hold one of its annual scientific meetings each year as a luncheon meeting in conjunction with the American Academy of Dermatology (AAD) Annual Meeting. With the cancellation of the 2021 AAD Annual Meeting due to the COVID pandemic, AHRS held its 2021 Annual Scientific Meeting as a Zoom webinar on March 27, 2021. Although the typical sociable chatter while enjoying a lunch to-



gether did not occur, there was a friendly and dynamic interactive session on the topic of cicatricial alopecia. As is always the case, it was wonderful to see old friends and welcome newcomers.



Faculty of 2021 AHRS Scientific Session on Cicatricial Alopecia

Demographics

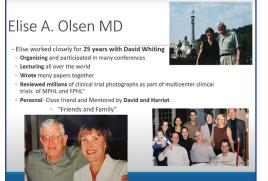
Of the 180 attendees, 72% were members of the AHRS. Geographically, the top regions were as follows: 46% from North America, 24% from South and Central America, 17% from Europe, and 7% from Asia. In terms of number of years in the hair field, 36% had 5 or less years, followed by 22% having 6-10 years, and 13% having 11-15 years. Combined, those having 16-35+ years was 29%. As self-identified with selecting all categories that apply, the audience included 75% physicians, 26% researchers/scientists, 3% allied health professionals, 8% in-training, and 4% industry.

Welcome and Sponsor Acknowledgments

The meeting kicked off with a warm welcome from AHRS President, Dr. Antonella Tosti. She thanked the corporate sponsors—Canfield Scientific, Inc., Concert Pharmaceuticals, Inc., Pfizer, Samumed, and TrichoLAB—for their generous contributions and continuous support of the AHRS and its mission. The sponsors are greatly appreciated, especially during this rough economic time globally. The audience was reminded of a wonderful "Did You Know?" handout with easy-to-read information about the sponsors including what clinical trials and products they are involved in. Dr. Tosti went on to thank Bosley, Nutrafol, P&G, Pfizer, and Viviscal, plus the many AHRS members who made voluntary individual donations to the AHRS Grant Fund, which supports research, mentorships, and educational initiatives. The audience was alerted to the AHRS 2021 Virtual Mentorship Program, noting that applications would open the following week.

The AHRS Seal of Recognition program was mentioned. It was noted that the Seal of Recognition Program was created to inform physicians and consumers about products whose quality and effectiveness are beneficial in some aspect for promoting healthy hair or scalp, diagnosing or treating hair or scalp disease, diagnosing or treating hair loss, or for stimulating or inhibiting hair growth. The program is strictly voluntary. There are certain requirements that must by met, and every product is evaluated for specific attributes selected by the company by an independent third-party testing lab and/or by the Seal Scientific Review Panel. The current two products that have earned and maintained the Seal include Lexington's HairMax LaserComb and Atlantic Coast Brands's Keranique Lift & Repair Treatment Spray.

Dr. Tosti thanked the corporate supporters of the AHRS website including Canfield, Cassiopea, Concert, Nutrafol, Pfizer, and Samumed. She welcomed non-members to consider joining the AHRS, and she encouraged all of the audience to continue to be involved.



2020 David A. Whiting, MD Leadership & Research Award

Presented to Elise Olsen, MD

A personal and touching presentation was made by Dr. Wilma Bergfeld honoring colleague Dr. Elise Olsen, who was presented with the 2020 David A. Whiting, MD Leadership and Research Award. Witnessing the accolades were not only her colleagues, but also several of Dr. Olsen's dear friends and family, including her children, and Mrs. Harriett Whiting.

Cicatricial Alopecia Overview

Jerry Shapiro, MD

The scientific session launched with an overview of the treatment approaches to cicatricial alopecia given by Dr. Jerry Shapiro. Take-home points included the following:

- Scarring alopecias are trichologic emergencies that must be treated promptly.
- Frontal fibrosing alopecia (FFA) is an epidemic that involves systemic, topical, and intralesional therapy.
- FFA is a form of lichen planopilaris (LPP).
- Hair transplants can be problematic and can worsen scarring alopecias.
- Antibiotics are the best treatment for folliculitis decalvans and oral retinoids for dissecting cellulitis.

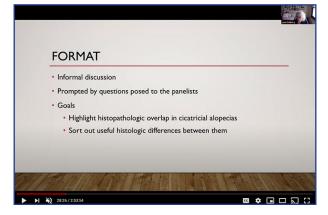
Dermpath Debate

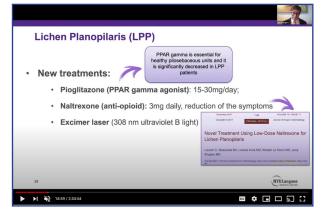
Lynne J. Goldberg, MD; Wilma Bergfeld, MD; Len Sperling, MD; John Seykora, MD, PhD

Dr. Lynne Goldberg moderated a discussion session on the dermatopathology of the cicatricial alopecias that included four esteemed dermatopathologists: Drs. Wilma Bergfeld, Len Sperling, John Seykora, and herself. The following discussions and take-home points resulted:

1. Can you answer the question "LPP vs. CCCA" in a scalp biopsy without clinical information?

• You can favor one over the other, but ultimately the correct diagnosis relies on clinicopathologic correlation.





- Premature desquamation of the inner root sheath in non-inflamed hair follicles favors central centrifugal cicatricial alopecia (CCCA).
- Active LPP tends to have more perifollicular inflammation with increased numbers of CD8+ lymphocytes.

2. Do you think you can reliably distinguish discoid lupus from LPP? LPP from FFA?

- Discoid lupus can often be distinguished from LPP, but some cases can be problematic.
- In discoid lupus there is typically a more robust interface dermatitis, thickening of the basement membrane zone, deep perivascular inflammation, and interstitial rather than perifollicular mucin.
- LPP and FFA can be indistinguishable histologically, although prominent lichenoid inflammation in the outer root sheath is more common in LPP.
- 3. Can you distinguish folliculitis decalvans from dissecting cellulitis?
- Most of the time, these can be distinguished in a deep punch biopsy.
- Folliculitis decalvans is typically more superficial, with neutrophilic or mixed neutrophilic, plasmacytic and lymphocytic interfollicular and perifollicular inflammation and fibrosis.
- In dissecting cellulitis, the inflammation is deep and diffuse, at times mixed with granulation tissue.
- 4. Do you feel you get adequate clinical information from clinicians? Adequate biopsies?
- In dissecting cellulitis, the inflammation is deep and diffuse, at times mixed with granulation tissue.
- All pathologists unanimously agreed that a deep, 4mm punch biopsy is optimal.

Science Snapshot and New Treatments, Cellular Targets

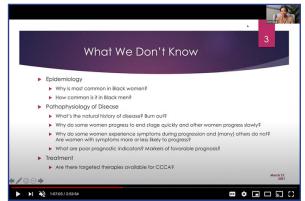
Eddy Hsi Chun Wang, PhD; Crystal Aguh, MD; Lindsey Bordone, MD

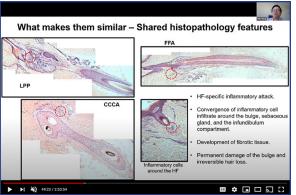
Dr. Eddy Hsi Chun Wang provided a snapshot on gene expression pathways in cicatricial alopecia, including the following main take-home points:

- Computational analysis of gene expression pathways in PCAs revealed indistinguishable molecular signature between subtypes but highly different compared to other inflammatory hair loss disease such as alopecia areata.
- LPP, FFA, and CCCA share a core set of dysregulated gene expression pathways including downregulation of cholesterogenic pathways, PPARg pathway, and upregulation of fibrosis pathways.
- LPP, FFA, and CCCA showed a prominent mast cell gene signature and was validated with histology.

Following Dr. Wang's thorough overview, Drs. Lindsey Bordone and Crystal Aguh reviewed new treatments and cellular targets. Take-home points included the following:

- Dr. Aguh discussed the overexpression of fibroproliferative genes in patients with CCCA.
- She noted that if CCCA is approached similarly to other fibroproliferative disorders, future therapies should be aimed at minimizing even mild inflammation (such as those seen in seborrheic dermatitis), folliculitis, and other sources of scalp irritation as these can spur additional fibrosis.
- In addition, it was noted that medical therapies aimed at reversing fibrosis, rather than just inflammation, should play a larger role in future therapeutic approaches.



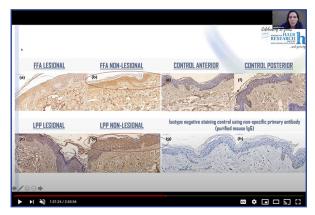


Environmental Factors

Isabella Doche, MD, PhD; Maryanne Makredes Senna, MD

Drs. Maryanne Senna and Isabella Doche presented about possible environmental factors that may be related to certain cicatricial alopecias. Take-home points included the following:

- Dr. Doche showed some preliminary findings on increased expression of AhR (aryl hydrocarbon receptor) in the epidermis of nonaffected scalp skin from patients with LPP and FFA compared to affected and healthy scalp areas, using immunohistochemistry techniques. This may suggest a possible role of this receptor, dioxins and dioxin-like substances in the pathogenesis of these diseases.
- Dr. Senna discussed the recent worldwide epidemic in scarring alopecia cases and reviewed the increase in hair



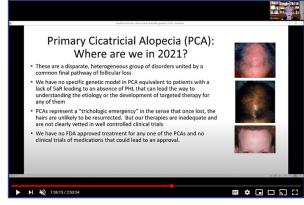
product consumer complaints to the U.S. Food and Drug Administration (FDA) in recent years. She also discussed studies including one done at Massachusetts General Hospital that showed an increased rate of allergic contact dermatitis to personal care products used on the head and neck in patients with LPP and FFA. Allergen avoidance led to an improvement in scalp itch and redness in patients. This may suggest a role for environmental allergens in this patient population and more research is needed to better elucidate this relationship.

The Path Forward

Elise Olsen, MD; Maria Hordinsky, MD

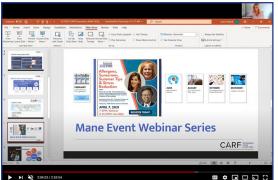
Dr. Elise Olsen reviewed the future of clinical trials in cicatricial alopecias, making the following key points:

- In order to move forward with developing new and effective therapies for the various types of cicatricial alopecias, we need to:
 - 1. Create standardized methodology for clinical trials and registries
 - 2. Collect and analyze aggregate data in clinical trials and registries
 - 3. Integrate biobank and clinical data on individual patients



Dr. Maria Hordinsky provided evolving technology snapshots and reviewed two imaging technologies that can aid with the diagnosis and assessment of treatment efficacy. The two devices discussed were Hair-Metrix (Canfield Scientific Inc., www.canfieldsci.com) and TrichoLAB Studio (https://tricholab.com). Key takeaways included the following:

- The use of these devices offers location-specific hair fiber quantitative data that does not require hair clipping or tattooing.
- Both devices provide data on terminal to vellus ratios and other quantitative measures.
- The HairMetrix technology offers patients and physicians immediate objective information to assess treatment efficacy and scalp health.
- This technology is the future of alopecia clinical management.



Patient Support and Advocacy

Jean Pickford

Ms. Jean Pickford, Executive Director of the Cicatricial Alopecia Research Foundation (CARF), a patient support and advocacy organization, reviewed the new initiatives and growth of the organization. She invited participants to take part in a webinar series entitled, "CARF's Mane Event." Clinicians were encouraged to provide their patients with CARF as a resource. Both clinicians and researchers were also encouraged to join CARF and to get involved at http://carfintl.org/.

Discussion and Questions & Answers Sessions

Angela Christiano, PhD; Maria Hordinsky, MD; John Seykora, MD, PhD

Dr. Angela Christiano, AHRS Secretary-Treasurer and Program Chair, led the discussion session with a late-breaking announcement about the 2021 AAD Hair Loss and Alopecia Initiative in Research (HAIR) Grant Program. The HAIR research grants will be offered to dermatologists, researchers, and trainees in the United States for the completion of basic, translational, and/or clinical research projects that address gaps in hair disorders research, with a particular emphasis on hair disorders in diverse populations. The one-time grant program will offer the following:

- One \$200,000 USD grant for research on CCCA
- Multiple grants ranging from \$10,000 to \$100,000 USD on CCCA, hair disorders in skin of color, racial differences or disparities in care, androgenetic alopecia in women, FFA, LPP, the role of nutrition in hair loss, and environmental/genetic factors in hair loss

Applications may be submitted to the AAD from May 14 through August 31, 2021, at the link above.

Drs. Maria Hordinsky and John Seykora next moderated a lively Q&A session. Some highlights include the following:

• For treatment of LPP/FFA, it was noted that some physicians are adding oral minoxidil with good results. Dr. Shapiro noted he uses topical minoxidil and says that he is unsure of whether oral administration adds any extra benefit. Participants discussing this thought that it was a great idea to try it orally. Studies comparing oral to topical have been done showing no difference but were based on 1mg dose only.



- Dr. Shapiro uses finasteride as his androgen blocker but feels for fibrosing alopecia of a pattern distribution, he'd like to use two anti-androgens and would consider the addition of spironolactone. Dr. Bergfeld noted that she uses spironolactone as a first-line therapy with good results.
- Dr. Shapiro noted that other than spironolactone, all of the treatment modalities noted in his presentation could be used on men with FFA.
- Next, a question was asked as to the best location for taking a diagnostic biopsy. Dr. Bergfeld noted, and Dr. Sperling concurred, it should be where there is hair, or at the edge of hair, and where it is acceptable to leave a scar. Dr. Bergfeld noted that often more than one biopsy is necessary because of the many possible causes of hair loss. The preferred punch size is 4mm. Dr. Bergfeld also suggested there is value in biopsy of normal area as well for "unobserved" inflammation. Dr. Doche noted that in a LPP study they found 60% of "normal" appearing areas of scalp were actually affected, thereby affirming the need for biopsy of normal areas as well.

- Regarding the description of the lichenoid inflammatory infiltrate in LPP vs CCCA, Dr. Seykora noted the infiltrate tends to be more lichenoid/cytotoxic in LPP than CCCA. LPP has been shown to have a higher percentage of CD8+ T cells, which are typically cytotoxic, than CCCA, which has a higher percentage of CD4+ T cells, which are typically not cytotoxic.
- Dr. Senna noted that patch testing should be done properly and comprehensively to be helpful in the management of patients with LPP.
- In the discussion on photography, an interesting note by Dr. Natasha Mesinkovska was that a data model is only as good as the person inputting the data.
- Dr. Olsen then went back to the discussion on anti-androgens and stressed the importance of taking a medical history of post-menopausal women to determine if they have any kind of breast cancer history themselves or in their family because elevated, unopposed estrogen increase can raise the risk of breast and uterine cancers. Dr. Bergfeld concurred that using anti-androgens in post-menopausal women needs to be done judiously.

Closing Remarks

Victoria Ceh, MPA

Ms. Victoria Ceh, AHRS Executive Director, wrapped up the 3-hour meeting by thanking the presenters, the audience, and the supportive corporate sponsors. The recorded session is available to all registrants and members of AHRS. She reminded the group of the next two meetings of the AHRS including virtual scientific sessions at the 2021 RADLA (Reunión Anual de Dermatólogos Latinoamericanos, or Annual Meeting of Latin American Dermatologists) and 2021 SID Virtual Meeting (Society for Investigative Dermatology).