

## IN THIS ISSUE

What's New in Robotic Hair Transplantation

Does the use of implanters affect the quality of grafts?

What is a hair transplant megasession?

In Memory of Dr. Jonathan L. Ballon

## The Role of the Scalp Microbiome in Health and Pathogenesis

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### INTRODUCTION

There is significant scientific and industrial interest in human-associated micro-organisms, the “human microbiome,” even being listed by the World Economic Forum among the “Top 10 Emerging Technologies – 2014.” Furthermore, the skin microbiome is increasingly implicated in many common diseases, with global direct/indirect costs estimated as >\$20 billion USD. The consumer skin and hair care markets of >\$350 billion USD/year are also strongly affected by skin microbiology. On careful consideration, a significant fraction of all consumer care markets are impacted by the skin microbiome—the surfactant and softeners deposited on clothing fabrics, the lining of diapers, both cloth and disposable, and all soaps and detergents, at a minimum. Understanding the skin microbiome therefore represents both a chance to improve human health and a compelling economic opportunity.

So far, limitations of sampling skin and the genetic complexity of eukaryotes (including fungi) have limited human microbiome investigations primarily to gut and bacteria, leaving the skin microbiome, and particularly the eukaryotes, poorly understood. This crucial knowledge gap needs to be addressed, as fungi have key roles in common skin conditions such as seborrheic dermatitis (likely *Malassezia*) and diaper rash (*Candida*). Importantly, skin fungi metabolize lipids and considerable data implicate lipids in skin homeostasis and disease. This makes the face, scalp, breast, and central back high potential sites for unfavorable conditions generated by the lipid metabolizing skin microbiome.

“Dandruff” and “seborrheic dermatitis” are disorders characterized by flaking and itching of scalp.<sup>1</sup> More than 50% of adults are afflicted, and everyone harbors the *Malassezia*, which cause the problems.<sup>2,3</sup> The anti-dandruff shampoo business alone is >\$10 billion USD per year. Dandruff research is in the midst of a resurgence, re-invigorated by the discovery of the causal fungal species (*Malassezia globosa* and *restricta*) and recent availability of multiple complete *Malassezia* genomes.<sup>3</sup>

### WHAT IS DANDRUFF?

Normal scalp has few flakes and healthy appearing, smooth skin. Dandruff is characterized by loosely adherent flakes and itching. Specifically, dandruff has no inflammation and is confined to the scalp, while seborrheic dermatitis has yellowish, piled adherent flakes that can extend beyond the scalp to beard, moustache, and eyebrows accompanied by visible inflammation.<sup>1</sup> Seborrheic dermatitis is more than superficial flaking, including hyperproliferation, excess lipids, and poorly differentiated corneocytes across the scalp.<sup>4</sup> Dandruff requires three factors: fungi (*Malassezia*), sebum, and individual susceptibility. While there remains much debate in the current medical literature, upon review, the vast majority of evidence points at the very least to a fungal “initiator,” most likely *Malassezia* fungi.<sup>5</sup>

### The microbiome

The role of microbes has been defined by “Koch’s Postulates,”<sup>6</sup> developed in 1890 to guide researchers to understand the role of microbes in disease, as the following:

1. The microorganism must be found in abundance in all organisms suffering from the disease, but should not be found in healthy organisms.
2. The microorganism must be isolated from a diseased organism and grown in pure culture.
3. The cultured microorganism should cause disease when introduced into a healthy organism.



Check out more memories from the beginning of the ISHRS— pages 121–123.

## TABLE OF CONTENTS

91	President's Message
92	Co-editors' Messages
93	Notes from the Editor Emeritus: Dr. Jerry E. Cooley
96	Does the use of implanters affect the quality of FUE grafts?
100	What's New in Robotic Hair Transplantation
102	Controversies: What is a hair transplant megasession?
104	Literature Review
105	Cyberspace Chat: Platelet Rich Plasma (PRP) and Its Use in Hair Restoration
109	Letter to the Editors
111	Hair's the Question: Calculations in Hair Transplant Surgery: Part II
114	Ask the Fellows
119	Meeting Review: SILATC
120	A Life Cut Short: Jonathan L. Ballon, MD, FISHRS
121	The ISHRS Is Turning 25: A Look Back to Where It All Began
124	Message: World Congress Program Chair
125	Messages: Surgical Assistants Chair and Vice Chair
126	Message: World Live Surgery Workshop Chair
128	Classified Ads
131	Calendar of Events

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## President's Message

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A popular daytime talk show in the United States, "The Dr. Oz Show," ran a piece entitled, "Oz Investigates: Hair Restoration Scams: How Far Would You Go to Reverse Your Thinning Hair?"

(May 9, 2017). The show had originally been working with the ISHRS to construct a meaningful episode, but, inexplicably, chose to run the episode using nonmember physicians. Although the show emphasized the ISHRS message of the dangers of the growing number of hair restoration surgeries performed by unlicensed individuals around the world, the overriding tone of the program was one that portrayed our specialty in a very poor light.

Despite the fact that the program used information, and actual images, provided by the ISHRS, there was no acknowledgment of the role of the ISHRS in the field of hair restoration or of its presence as a resource for patients or physicians. Instead, the field of surgical hair restoration was presented in a fashion that made it sound wantonly inferior to other areas within organized medicine. While our cooperation with the show stressed the role of the ISHRS in providing a foundation for education,

establishment of best practices and ethics in hair restoration, this was not acknowledged by the producers of the episode.



We recently sent correspondence to Dr. Oz to voice our concerns and to offer the ISHRS's expertise in producing a follow-up piece. In an effort to keep you informed, we have reprinted a copy of the letter that was sent, which can be found on page 113. We encourage you to review our response and to feel free to contact

See page 113 for a reprint of the ISHRS's letter to Dr. Oz.

us if you have questions concerning this television episode or the ISHRS's response to the program.

We will continue our outreach to media around the world and are grateful for the support from our members. Together, we are hopeful that we will be able to deliver the message to all prospective hair restoration patients that there are highly trained, educated and ethical physicians in our field who have their best interests at heart. ■

Follow-up: On May 15, 2017, Dr. Oz acknowledged the ISHRS's concerns.

See posting: <http://www.doctoroz.com/page/statement-international-society-hair-restoration-surgery>.

## Co-editors' Messages



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For hair growth, a healthy scalp is like the fertile ground. A balanced bacterial and fungal environment may be important. Thomas Dawson's article describes the current knowledge about the role of the microbiome, especially

*Malassezia* fungus. Perifollicular micro-inflammation has been found in more than one third of biopsies in androgenetic alopecia. Increased biomarkers of inflammation and impaired skin barrier have also been found in dandruff and seborrheic dermatitis. These conditions cause itching and may potentially affect hair growth. There are some studies indicating a positive impact of anti-dandruff shampoos on hair loss. It may be smart to add them to the pre- and post-op routine even if no signs of dermatitis are present.

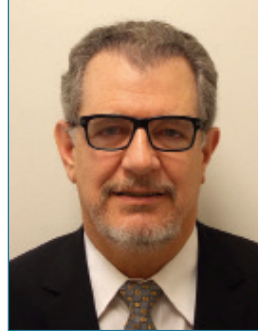
The article by Drs. Rassmann, Pak, and Knudsen aims to quantify the size of a megasession in FUT and FUE. The maximum graft yield certainly depends on many individual factors. A healthy scalp also involves a good blood supply, especially in large sessions. Could it be true that sometimes less is more, and a gradual approach with several smaller sessions may be wiser? Especially in progressive hair loss and with respect to a cosmetically acceptable donor harvest and the optimum growth in the recipient area? Or is a megasession on a virgin scalp the better approach? What are your opinions on this controversy?

Can we "fertilize" the scalp with PRP? In Cyberspace Chat, experienced users share their opinions.

Regarding new tools, improvements of robotic graft harvesting are described by Drs. Bernstein, Wolfeld, and Krejci. And a study by the von Albertinis nicely evaluates graft quality when using sharp implanters. For both devices, we need studies comparing their results to those of manual techniques.

This issue is complete with very helpful advice from our fellows, a literature review, smart calculation tasks, meeting reports, and great memories from 25 years ago.

It concludes with an exciting outlook to the workshop in Poland and the World Congress in Prague, the Golden City, where you may feel like a Bohemian when sitting in a café reading your own *Forum* article or comment. Send them to [forumeditors@ishrs.org](mailto:forumeditors@ishrs.org). ■



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I would like to thank all the authors and columnists who contributed to this issue. Tom Dawson gives us a fascinating look at the role of microorganisms, the "skin microbiome," that reside on and can affect our working surface,

the scalp. I was surprised to read that 50% of adults have dandruff or seborrheic dermatitis and everyone harbors the fungus that causes these problems. Maybe we should think more about scalp health before surgery. In Ask the Fellows, Steven Gabel discusses his routine for perioperative scalp cleansing. Special thanks go out to the all the ISHRS Fellows who took time out from their busy schedules to answer.

The von Albertinis present a well-designed study that examines the ways a sharp implanter can affect grafts when used by an experienced team. Although not the popular, implanter into pre-made incisions, it portrays sharp implanters in a positive light and adds to our knowledge concerning implanters in general.

Science is full of controversies particularly at its frontiers. Rather than being a bad thing, the debate and eventual resolution of controversies often contribute to the advancement of science. In Controversies, Rassman et al., give their view on the seemingly eternal FUT vs. FUE controversy.

The ISHRS was incorporated exactly 25 years ago on April 29, 2017, so we have officially begun our 25th year. The Jubilee celebration is continued in this issue with more recollections of the 1993 Dallas meeting and thoughts on how our specialty has changed over the years. We are fortunate that we can get insights from, and celebrate this anniversary with, many of the founders of our society.

Make sure to leave some room in your suitcases for souvenirs on your visit to Prague. Marionettes and puppetry have been part of Czech culture for centuries with puppeteers travelling from village to village to entertain the locals. Puppetry has a part in the folk arts of many European countries but it is the Czech Republic that has embraced it the most deeply in terms of the skills involved and its place in the nation's social fabric. Bohemian crystal is glass produced in the Czech Republic and it has a centuries long history of being internationally recognized for its high quality, craftsmanship, beauty, and innovative designs. Champagne flutes, ornaments, figurines, and other glass items are among the best known Czech exports and immensely popular as souvenirs. For more information about restaurants, tourist attractions, and happenings in Prague, check out [www.expats.cz](http://www.expats.cz). Don't even think of not coming to Prague.

California here we come! Please mark your 2018 calendars for the 26th ISHRS World Congress, scheduled for October 10-14 in Los Angeles, California, at the Loews Hollywood Hotel in the heart of Hollywood. ■



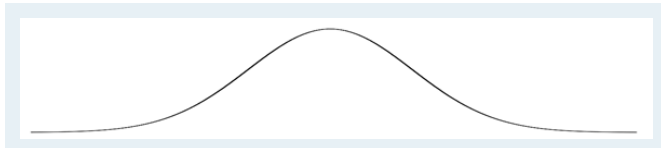
## Notes from the Editor Emeritus, 2005–07

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One of my favorite quotes is from Oliver Wendall Holmes, who said, “I would not give a fig for the simplicity this side of complexity, but I would give my life for the simplicity on the other side of complexity.” But what does this really mean? An essay by entrepreneur

Jon Kolko does a nice job of explaining how this can be applied.<sup>1</sup>

Imagine a bell curve. Moving from left to right is understanding, and the vertical axis represents complexity. When new to a particular area, we reside on the left, we have a sense of the complexities ahead of us. Without experience and knowledge, we may have simplistic beliefs that are based on faulty assumptions, inadequate evidence, and various types of biases. We don’t know what we don’t know, and we may be dangerous at this point if we are dogmatic in our opinions. One clue that we are at this point is that our communications to others about the topic are confusing and contradictory.



As knowledge and experience grow, we climb up the complexity curve and our understanding does in fact in-

crease. We are beginning to have a thorough grasp of the subject matter and may start to be viewed as experts. But we can’t necessarily communicate this information clearly to others, especially those further to the left of the curve. Unfortunately, this is in fact when many experts try to teach and lecture about the subject matter. Some may remain stuck here indefinitely.

But some may continue progressing to the right, achieving greater understanding through more experience, through an open-minded and dynamic relationship with the subject matter, and by interacting with others who have progressed to “the other side of complexity.” At this point, you not only have a clearer grasp about the subject matter and what your beliefs are, but you’ve been able to distill complex ideas into a coherent message that can be clearly communicated to others who are beginning at the other end of the curve. Many of us can recall teachers, professors, lecturers who, while brilliant and evidently in grasp of complex subject matter, had a special gift for communicating this subject matter to us in a clear, concise, and understandable way. And this helps shortcut our journey to the other side of complexity. Certainly a worthy goal for all of us, whether our goal is to become better educators to our colleagues or, more practically, to become more effective in communication with our patients.

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1. Kolko, J. Simplicity on the other side of complexity. 2016. <http://www.jonkolko.com/writingSimplicityComplexity.php> ■

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4. The microorganism must be re-isolated from the inoculated, diseased experimental host and identified as being identical to the original, specific causative agent.

Koch's postulates led to a renaissance of discovery and understanding and provided the framework for modern microbiology. However, new genomic technology and informatics have upped the game, unlocking a world of unknown complexity, including "unculturable" organisms and insight into interactions between both each other and the host. This complexity has led to difficulties with application of Koch's original postulates.

### **Fungi—the "forbidden kingdom"**

One difficulty with Koch's postulates is with fungal infections and fungi as "opportunists." Fungi can be benign or even helpful, and other times can cause disease.<sup>7</sup> One example of broad import is *aspergillus*. While *aspergillus* is ubiquitous as airborne particles, and we are all exposed with every breath, very few healthy individuals develop chronic or invasive pulmonary *aspergillosis*. However, few would argue that *aspergillus* is "causal." Fungi are also notoriously difficult to meaningfully culture, and their similarity to human cells makes design of antifungal treatments complex. Hence, research into fungi and disease lags behind that of bacteria and infection.

### **Malassezia**

The vast majority of evidence supports a role of *Malassezia* in scalp health. While all humans, and all warm-blooded animals surveyed, have a complex microflora including *Malassezia*, a series of experiments in the 1960s and early 1970s clearly support fungal involvement. Nystatin, a specific antifungal with low antibacterial activity, was compared to neomycin or tetracycline, both specific antibacterials. These papers showed removal of fungi decreases dandruff, removal of bacteria does not, removal of both is equally as good as antifungal treatment alone, and reintroduction of a resistant *P. ovale* (likely *Malassezia globosa*) causes the dandruff to return. The studies revealed the following:

- Subjects treated with a combination of both antifungal and antibacterial agents showed a significant decrease in scalp flaking.<sup>8</sup>
- The effect of a separate antibacterial (tetracycline), an antifungal (nystatin), or a combination was tested for efficacy.<sup>9</sup> Application of nystatin plus tetracycline was similar to before, but nystatin alone reduced flaking while tetracycline alone did not. Further, application of a suspension of *P. ovale* (likely *M. globosa*) in the presence of tetracycline actually increased flaking.
- A final study was conducted where individuals were treated to remove all microbes (fungi via nystatin, bacteria via Neomycin). As expected, flaking dramatically decreased. Then, while continuing the antimicrobial treatment (both nystatin and neomycin), a nystatin-resistant *P. ovale* was applied. The resistant strain induced flaking.<sup>10</sup>

Collectively, these data support the role of *Malassezia* in dandruff and fulfill three of four of Koch's postulates. Only his first postulate is not fulfilled, as all humans carry *Malassezia* as part of their commensal microflora. Even Koch him-

self learned that the first postulate could remain unfulfilled, as he observed in asymptomatic cholera carriers.<sup>11</sup>

It is worth mentioning that a contemporaneous study conducted with another common antifungal agent, amphotericin B, did not improve flaking.<sup>12</sup> It was only much later that many *Malassezia* were shown to be resistant to amphotericin B,<sup>13</sup> and that in the Kligman study the antifungal treatment may have been ineffective.

A possible counter to the antifungal hypotheses is steroidal antiinflammatory agents, such as clobetasol propionate Clobex<sup>®</sup> shampoo. While effective and not antimicrobial, this does not subvert a fungal hypothesis of dandruff genesis. Removing the fungi removes the inflammatory insult, thereby improving dandruff. Inhibiting the inflammatory response is effective, it is intervention downstream of the original insult.

### **Individual susceptibility**

An oft-cited confounder in the *Malassezia* dandruff hypothesis is that they are found on all humans but not all are affected. As for *aspergillus* and pulmonary *aspergillosis*, the most parsimonious explanation is a host susceptibility difference. The host susceptibility hypothesis is supported by a study where dandruff and non-dandruff individuals were treated with a dandruff-initiating *Malassezia* metabolite,<sup>14</sup> oleic acid.<sup>5</sup> Oleic acid applied to the scalp induced dandruff-like flaking in susceptible individuals, but not in non-susceptible individuals. This provides evidence supporting an underlying "susceptibility" predisposing the development of dandruff, as well as a direct role of fatty acid metabolites.

### **Sebum**

Sebum is implied to be required by several reasons: 1) a temporal correlation with sebaceous gland activity, including scalp flaking during infancy (cradle cap), little dandruff from infancy to puberty, and an increase with puberty, 2) dandruff occurs exclusively on sebum rich areas, and 3) an animal model of dandruff shows a requirement for both sebum and *Malassezia*.<sup>15</sup>

Human sebum is a complex mixture of triglycerides, fatty acids, wax esters, sterol esters, cholesterol, cholesterol esters, and squalene.<sup>14</sup> When secreted, sebum consists of triglycerides and esters, which are broken down by microbial enzymes into glycerides, monoglycerides, and free fatty acids. Sebum is also responsible for the stress and hormone-related increase in dandruff, it being well known that they effect sebum secretion and impact dandruff.

### **OTHER SCALP DISORDERS AND THE MICROBIOME**

Multiple other scalp and skin disorders are likely affected by the microbiome, exacerbating the lesions if not being causal. Atopic dermatitis can affect many body sites, and a recent study showed that the skin microbiome is altered in affected individuals even when not expressing overt disease (between "flares"). Bacteria including *staphylococcus aureus* as well as two species of *Malassezia* are changed in susceptible subjects.<sup>16</sup> It has also been shown that a profile of the skin microbiome can be predictive of healing or non-healing progression in wounds,<sup>17</sup> and that the fungal community in wounds correlates to a non-healing phenotype.<sup>18</sup>

Of particular relevance to the hair restoration surgery community is the role of scalp microbes in a recent report of scalp infection post FUE surgery.<sup>19</sup> There are few reports of infection post hair transplantation, but management of the skin environment could be beneficial in minimizing folliculitis that can be caused by *Malassezia* inhabiting the deep follicle.<sup>20,21</sup>

## MAINTAINING SCALP HEALTH

Dandruff is best treated by antifungal shampoos, including pyrithione zinc, selenium sulfide, or ketoconazole. In severe or refractory cases, this can be supplemented by anti-inflammatory agents, but usually only for a brief initial period followed by maintenance with antifungal shampoo. We must understand that as *Malassezia* are commensal, they are essentially impossible to permanently remove. Hence, for maintenance of the best scalp health, chronic therapy is required. Even short-term use of an effective antifungal scalp therapy may potentially promote scalp health during and after scalp surgeries, but further study would be required to understand if the benefit would be useful and reproducible.

## SUMMARY

The vast majority of clinical evidence supports the hypothesis that scalp *Malassezia* negatively impact scalp health, breaking down sebum into toxic unsaturated fatty acids that induce flaking and inflammation in susceptible individuals.<sup>3,22</sup> This should lead to their classification as “pathogens” in the recent “Damage-Response Framework”<sup>23</sup> or as “commensal opportunistic pathogens” in classical microbe/host literature.

It will be necessary to conduct significantly more research into the scalp microbiome and *Malassezia* in particular to fully elucidate the role of the microbiome and the host immune system in multiple microbe-mediated diseases. As new pathways are elucidated, new intervention targets will arise. The new, groundbreaking research in microbiomes, commensalism, and pathogenesis will enable new treatment technologies that may not depend fully on broad spectrum antifungals.

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