New and Emerging Therapies (Hidradenitis Suppurativa)

So Yeon Paek, MD, FAAD, interviewed by Steven Chen, MD, MPH, FAAD

STEVEN CHEN, MD, MPH, FAAD: Welcome everyone to another episode of *Dialogues in Dermatology*. This is Steven Chen. And I'm so thrilled to be joined by Dr. So Yeon Paek, who is going to be talking about New and Emerging Therapies for Hidradenitis. She gave a wonderful talk in Vancouver and so I'm excited to be able to follow up and to chat a little bit more about all of her expertise. Welcome, Dr. Paek, how are you doing?

SO YEON PAEK, MD, FAAD: Wonderful. Thank you so much for having me, Steven, it's exciting. I listen to *Dialogues* all the time, so it's exciting for me and an honor to be able to be on a podcast episode.

STEVEN CHEN, MD, MPH, FAAD: Well, trust me, the honor is all mine. I love learning from our interviewees on *Dialogues*. So if it's okay, we'll jump right in and get started. Since we're talking about hidradenitis, I thought maybe if it's okay with you, we would just start with a baseline understanding of the disease, so that we're all on the same page. So before we even talk about therapeutics, I think we all learned in residency, now I'm getting up there in age I feel like, so I feel like I learned it in residency that it was about like follicular occlusion and there's that triad and the tetrad.—

--But really, it's not as simple as that anymore. So what's our current understanding of what hidradenitis is? What's going on under the skin? How can we target all of that?

SO YEON PAEK, MD, FAAD: I don't know if I can give a simple answer either, because our current understanding is really complex. We do think of the disease as more multifactorial. Follicular occlusion is still a key event in the pathophysiology of the disease or our understanding. But the series of events and the different players or the factors at play is very complex. We think of it now as more of an immune-driven or immune-mediated autoinflammatory condition.—

--It's unclear whether there is some sort of immunological priming that occurs first, then that leads to kind of a dysbiotic microbiome, and then follicular occlusion as a secondary phenomenon. Or, as more traditionally thought, it kind of starts with that follicular hyperkeratosis and dilatation, which leads to follicular rupture, then a series of acute and chronic inflammatory events. Probably it's a combination or kind of an interplay of all of that.—

--And there's been an explosion of research in the last five to ten years in both basic science and clinical, which I think is very exciting to kind of help us understand this disease more and to help our patients. But different inflammatory cytokines have been identified. There's in the acute inflammatory phase, the Th1 and Th17 pathway cytokines, TNF-alpha, IL-17, IL-1-beta. And then in the chronic inflammation phase, they're more pro-fibrotic cytokines which have led to the development of scarring and more of those architectural changes that you see in severe, advanced HS.—

--Then there's also the role of course of other factors, like a genetic susceptibility. There have been several genetic mutations that have been identified. But it's unclear what kind of role they play because not all HS patients demonstrate the same sort of phenotype that has been identified in these genetically-susceptible individuals. And then we know there's a role for the microbiome, bacterial dysbiosis. There's probably some aspect of hormone irregularity. And then other sort of, I call them maybe more minor players but the friction, the smoking, obesity, etc. So it's a complex interplay of all of those factors that's probably going on with our HS patients.

STEVEN CHEN, MD, MPH, FAAD: And with all of those factors playing a role, I imagine that's why so many of our treatments are reported to work, not completely but partially, because we're targeting one of such a complex interplay that's happening under and on the skin. Do you mind sharing with us what your typical therapeutic ladder might be? It doesn't necessarily have to go in order but just thinking about the different buckets that you can kind of draw from when we're

talking about targeting all of these different potential mechanisms that might be driving how HS is working. At least from a medical management perspective, what are the different options that you think about with your patients?

SO YEON PAEK, MD, FAAD: Absolutely and you said it perfectly. I rarely use any treatment monotherapy for patients unless they have very mild disease, because I see these different aspects at play. And I think it also helps to frame the disease this way to patients. Because often, I get referred patients who are like, “Well, all I’ve been given are these oral antibiotics. I don’t want to be on another oral antibiotic.” And then I have to explain the role for oral antibiotics in their disease. For example, it’s not a cure but it can help control this aspect.—

--So when I identify patients with HS after staging them, I think that’s important as referenced, so you know kind of which therapies may be more effective for that patient. Identifying the role for the inflammatory, the immune system, the role for bacteria, role for hormones, and then the role for that like follicular rupture and scarring I think is really important. Because each patient, I take an individualized approach and I kind of ask a lot of questions about what they feel may be impacting their quality of life and their disease, more than the next patient in terms of do I notice perimenstrual flares, then I’m going to be focusing on more hormonal therapy.—

--But that being said, all of my patients are put on some sort of topical antibacterial therapy, a topical antiseptic cleanser for daily use, topical antibiotics. I often reach for a topical clindamycin but we know that monotherapy builds resistance quickly, so making sure they use it in combination with something like benzoyl peroxide. Topical resorcinol, which is utilized more in Europe, I’ve started to use that more. I think it’s good as a keratolytic and maybe as an alternative to topical clindamycin.—

--And then those patients are given some sort of prescription, whether for immediate use or maybe for flares for oral antibiotics. And I do explain that this is because there is a role for bacteria in the

microbiome dysbiosis, so it's not a cure but it can help with flares and it can help maybe reduce some of that inflammation to a certain degree. And then, depending on the patient, we are kind of using antibiotics more p.r.n.—

--I think I mentioned the hormone imbalance earlier and I'd say a vast majority of my young female patients are on spironolactone. I find it to be highly effective actually to control those perimenstrual flares. And overall, I find it to be a pretty easy medication to take and to administer. So that would be additional adjunctive therapy for some patients. And then if I identify a patient as having more inflammatory burden, depending on what that inflammation looks like, I do have a low threshold to start systemic therapy that targets more of the inflammatory aspect.—

--I do utilize biologics, TNF-alpha inhibitor, of course the one that's approved for HS, Humira, adalimumab. And this year we're going to be seeing a lot of biosimilars for that. And then starting to reduce that inflammation. Because similar to how I think of a patient with scarring acne, for example, I really want to try to aggressively treat that acne before it gets to the scarring stage.—

--I'm kind of thinking along that process and hopefully I can kind of adjust the course of the disease before it gets to that scarring stage. So I think, and given our increased understanding of the role of the immune system, I'm trying to reduce that inflammatory burden. Beyond the TNFs, there are several other cytokine mechanisms that have been identified, the IL-17 inhibitors will probably be here, there's good data on those now, and you'll probably be hearing about some of those being approved for HS in the near future.—

--And then there's different mechanisms that are also being explored currently, which I think is very exciting because we need more treatment options for our patients. And then finally, sort of the last aspect that I had mentioned, the follicular rupture, scarring, and anatomic changes, unfortunately there's been a lot of medical development but none of those medicines are really going to eliminate the tunneling or the scarring that's already happened. So I think for patients

with more advanced disease, I do take a combined medical and surgical approach to try to optimize their treatment therapies.

STEVEN CHEN, MD, MPH, FAAD: That's wonderful, thank you for taking us through that. I have to briefly ask, because I feel like it's something that we're all learning in residency and we always think about, clinda rifampin as a combination I feel like is the old school oral antibiotic option. Still something that you use or it sounds like you really use oral antibiotics on a p.r.n. basis at this point?

SO YEON PAEK, MD, FAAD: And you're right. All of the guidelines have clindamycin and rifampin as sort of like probably second line after doxycycline. But we have several ID colleagues, infectious diseases colleagues in the HS sort of research world. And they have demonstrated to us that using that combination may not be great for antibiotic stewardship because of the way that rifampin induces the metabolism of clindamycin. And by about 10 to 14 days, the patient is essentially kind of on a rifampin monotherapy and they don't like that for multiple reasons.—

--So I've actually shifted away utilizing that specific combination. Clindamycin, I do use monotherapy or combinations of different antibiotics. I started to use a little more of the amoxicillin clavulanate or Augmentin. There's doxycycline, sometimes I also use oral dapsone as more chronic therapy. So there's different combinations that I've turned to. But for the reason that I stated, I don't actually utilize clindamycin or rifampin together much anymore.

STEVEN CHEN, MD, MPH, FAAD: That's super helpful. Obviously, antibiotic stewardship is something that I think has appropriately gotten a lot of attention, especially in the dermatology sphere and literature. Since we've been using it, many think overusing it, for the treatment of acne. And so I think it's great to know that tidbit about clinda and rifampin and the opinion of those infectious disease colleagues, which is very helpful. You mentioned this earlier. So let's say

there's a new HS patient who is coming to see you. Obviously, staging them, getting their Hurley stage is important to quantify or somewhat quantify their disease activity.—

--But I'm just curious, what other considerations do you have when you're seeing a new HS patient? How might you kind of figure out what to target, if you're able to at all? What other thoughts are going through your mind when you're seeing someone new?

SO YEON PAEK, MD, FAAD: I think it goes along with kind of taking the individualized approach to the patient. There have been several different subtypes that have been described in the literature for HS, including the follicular subtype, the axillary mammary or gluteal subtype. And I'm kind of thinking about in the background maybe all patients don't really fall in absolute categorizes like that. It would be great if they all did, but they don't. So I'm thinking about that in the sense that if I see a patient who appears to have more the follicular subtype, I would call it even more like the follicular acneiform subtype, then perhaps I'll utilize therapies that we use more in the acne population.—

--I have to admit, I don't usually use isotretinoin to treat classic HS, I just have not found that to be very effective. I do sometimes use acitretin. But for the follicular acneiform subtype, I do find that that can be quite helpful for some patients. Maybe there's a slightly different process going on for those patients. But in addition to that, I think staging patients in terms of severity, really identifying whether they have scarring or not, the tunneling or not, can be helpful because then you are kind of early on talking about combination medical/surgical therapies and trying to find ways that they could improve their quality of life.—

--Sometimes with medical therapy, I find there's a limitation because of the recurrence within these tunnels where there may be a biofilm that continues to cause disease flaring. Those patients, if medically they seem to be doing well except recurrence in a specific area, then those

areas are perfect surgical targets. Once we approach those areas specifically surgically, then patients are much happier with their quality of life.

STEVEN CHEN, MD, MPH, FAAD: Thank you for also confirming what my own teaching that isotretinoin really doesn't seem to work that well for HS patients. I feel like it's such a natural medication that we reach for a lot of times with these acneiform types of eruptions. But I'll keep it in the back of my mind that acitretin might be helpful for particular subtypes. Now, you've talked about surgery a couple of times. Obviously, that's primarily what we want to chat about today.—

--But I would love to know, it's obviously an option for our HS patients, but when do you actually pull the trigger to offering surgery for HS patients? Is it only after medical management has failed? It sounds like for you it's more of an adjunctive measure, it happens with medical management. How do you go about choosing the right time to offer surgery for your HS patients?

SO YEON PAEK, MD, FAAD: I think this is always about patient-centered care and really having the patient involved in their own disease management. So at the get-go, I'm talking with them about which areas bother them, like how their disease flares, what it looks like on a day-to-day basis. A lot of times, patients are able to verbalize like, "Well, I'm really bothered by this one area." Many come with questions about surgery from the get-go.—

--But often, if there's a patient with what appears to be clear or very high inflammatory burden, I do explain that I think it makes more sense for us to really try to medically manage and to reduce that inflammatory burden, so that we can have more successful outcomes if we do decide to do procedures in the future. Jumping into surgery, sometimes that may be essential for certain patients with either localized disease, it could be very helpful without necessarily having to aggressively medically manage.—

--Or in the other case of having patients with just an area that just is so tunneled that it appears like medically it probably won't touch that anatomic location very much, then we are kind of talking about it from the get-go. I guess the other part of it is I actually try to do a lot of these procedures myself in-office. I find that sometimes it's hard to get patients to see surgeons, whether the patients are hesitant or the surgeons are hesitant. In our HS population, access to surgeons is sort of an issue because surgeons have certain criteria.—

--They have to have patients with only a certain BMI or they have them stop their medical therapy and particular biologics pre and postoperatively. For multiple reasons, I'm actually trying to address the surgical concerns or these procedural issues myself in clinic, it's much easier. Patients can remain on medical management. It's a local procedure, the downtime is generally less. I found then the patients to be very happy when they're co-managed.—

--That being the case, once a patient has kind of expressed that they're interested in surgery, we could maybe think about it conjunctively at the same time as we're really pushing their medical management. But in general, I do request patients to really think about medical management first, to make sure that inflammation is under control. And then if there are residual areas, then we can consider surgery. Just because I think that immune aspect, the inflammatory aspect cannot be ignored.—

--We've learned over time that HS is not a surgical disease. Historically, that's how it used to be treated but then all of these patients came back with recurrences within their surgical scars. So I try to emphasize that because of the different aspects of the disease, we should think of it as a whole.

STEVEN CHEN, MD, MPH, FAAD: Before we dive more into the surgical approach, one thing that you mentioned made me kind of think a little bit more. You mentioned BMI. In terms of lifestyle modification, which obviously is one of those core tenets of HS treatment: weight loss, smoking

cessation, all those things, is every single HS patient that you're seeing kind of getting some advice on lifestyle modification or is it just for particular patients? How do you incorporate that into your treatment algorithm?

SO YEON PAEK, MD, FAAD: That's a great point. A lot of times, patients come to me saying, or they've been referred or self-referred and they say, "Well, my last doctor, all they talked about was me losing weight and I did not find that to be helpful." I try to balance the amount of time I spend talking about lifestyle modifications, unless the patient seems very interested in dietary changes and then we kind of delve into that a little further. The way I approach it, actually I have a handout that I have for patients that outlines a lot of these frequently asked questions, including lifestyle modifications, weight loss how it can be beneficial for your disease, no smoking, etc., or how smoking can exacerbate the disease.—

--In that handout, patients are going home and I actually assign them reading that as their homework. I find that that does address a lot of their questions unless they have more specific ones, then we do talk about that. I try to make the bulk of the visit, because of course these HS visits can be very long and detailed, I'm trying to focus on what will be able to really address their concerns. But medically what we should try to do to treat their disease and get that disease under better control.—

--So if it does, if it's a patient with milder disease, like stage 1 disease, and I think different lifestyle modifications or conservative therapy like laser hair removal if I think that would be more beneficial, we're probably going to be talking about those things more. But if it's a patient with more severe disease like stage 3, I say, "These are certain things you can consider, here's a handout. Go home and read it." But honestly, we're going to be focusing on how to reduce that inflammation for that more severe patient. So it has to be tailored, I think. But everyone does get homework to take home and it includes information on lifestyle modification.

STEVEN CHEN, MD, MPH, FAAD: So let's get more into the surgical approach. You gave a great talk at the Innovation Academy in Vancouver on a new surgical technique for HS specifically. Could you tell our listeners a little bit more about the MODES procedure?

SO YEON PAEK, MD, FAAD: The MODES procedure, which stands for Modified Deroofing With Scar Excision, it's sort of a unique outpatient surgery that we've done now in a cohort of patients in our HS referral center. It involves an initial deroofing procedure, followed by exploration of surrounding areas or tunnels. Marsupialization of those involved areas. And then excision of the involved scar tissue and fibrotic tissue.—

--So we're taking the initial concept of a deroofing, a traditional deroofing, which I utilize quite a bit in my clinic, generally very effective for individual tunnels or sinus tracts, and expanding that. So taking a little more of the area around it and taking a lot of the scar tissue. The idea for how this could be quite beneficial is that that fibrous tissue adjacent to tunnels may be the source of a lot of the recurrences that happen with just traditional deroofing.—

--So you're kind of combining an excision with a deroofing. And it seems like such an easy concept and it has been described in the literature before, but just coined as modified deroofing. And I found that terminology is actually quite confusing for both patients and providers. You're like, "Well, how is that different from a deroofing? Isn't it the same thing?" It's a little more extensive. So these procedures are taking a larger area and removing the scar tissue.—

--But it's different from a wide local excision because you're not marking out just a specified area and excising that and then closing it up or leaving it to heal by secondary intent. You're actually identifying these tunnels as you go during the procedure and then taking as much of that as possible during that one procedure, under local anesthesia.

STEVEN CHEN, MD, MPH, FAAD: So what's that look like for the patient? What does the downtime look like? Are you usually closing or are you leaving open to heal by secondary? Just curious in terms of if this is something that some of our listeners want to potentially think about for their own practices, what does that setup kind of look like in terms of patient counseling, scheduling, all of that kind of nitty-gritty stuff that we always have to worry about?

SO YEON PAEK, MD, FAAD: We actually did publish this recently in the *Journal of Cutaneous Medicine and Surgery*. So if there is interest, that article is accessible and I'm happy to share that, as well. Any listeners are welcome to email me for a copy of that. Essentially, what we're doing is if there's a patient who we've identified as a good surgical candidate, we talk about the different surgical techniques that I do in the office. From traditional deroofing; wide local excision, which by local excision to me implies that I am going to actually close it and do a repair and have sutures.—

--And then the MODES procedure, for the vast majority of patients it is left open to heal by secondary intent. So similar to a traditional deroofing process, unless there is an area that I think would benefit from maybe a partial closure, but it's not closed completely with sutures. I think that's part of the reason why it may be more beneficial is that secondary intent healing allows for lower recurrence for HS patients.—

--But this procedure can be done to any extent, so any patients. It's generally stage 2 or 3, because those are the patients with tunnels, but sometimes in a patient with more stage 1 but maybe one area that's stage 2, this can also be considered. Once that area has been identified, the MODES procedure is a pretty simple in-office procedure. I can do it within 30 minutes now. Sometimes at the beginning it may take a little longer, just depending on the extent of the surgical area it may take a little longer.—

--But the idea is to identify the main tunnel, which will be the starting point. And then the surrounding tunnels, we kind of get a sense of that, that entire area we are going to anesthetize locally, lidocaine with epinephrine, and then just utilizing a simple scalpel and a sterile probe which we have in our clinics already, so no new devices are required. Essentially, the surgical technique itself is already one that we're familiar with.—

--It's kind of incising into the main tunnel and then using that probe to follow and then removing the scar tissue as you go. The technique is fairly simple. The procedure does not take very long. I schedule these in a regular surgical block in my surgical schedule. So it's pretty easy for providers to incorporate this into their practice and hopefully it will be an additional option that is offered.—

--From the patient standpoint, it's fairly easy as well, because it's local anesthesia. It does not require much in terms of surgical prep. It could be done regardless of patient stage or BMI. And they may remain on their medical therapy the entire duration. So the downtime, it varies by patient and it varies by location, because you are leaving the area to heal by secondary intent. So I find that certain areas heal faster, like the axilla, and I think that's actually a prime location to do this procedure.—

--Sometimes the MODES procedure in the groin, buttocks area may not heal as quickly. I do find that there may be more infections in that area, simply because of the anatomic location, like postop infections. But the average time for healing, the way I explain to patients is four to eight weeks. Often my younger, healthier patients by four weeks, the area is almost completely healed.—

--Some patients, certain locations if it was a more extensive area that we treated, then it may take up to eight weeks, but on average four to eight weeks.

STEVEN CHEN, MD, MPH, FAAD: I was just going to say, I'm looking at your paper now, it's pretty clearly delineated how the procedure goes. So for any of our listeners who are interested, there's some nice photos in the article as well that can really highlight how to do this. So Yeon, you've been so generous with offering assistance with your email address. I won't make you announce your email address to all of our *Dialogues* listeners but I'll encourage everyone to download the paper, so that you might think about incorporating it into your own practice.—

--Before we end our session, since we're getting to that time, any last minute thoughts or tips that you have for our listeners?

SO YEON PAEK, MD, FAAD: I see a lot of HS patients through our referral center. Too often, I think I see patients who are frustrated because they haven't really – maybe they've been given multiple oral antibiotics over and over and they haven't really be given other options for treatment, I just want to encourage all dermatologists out there that these patients really need our help. I think procedures like the MODES procedure can easily be incorporated into a daily clinical practice, to be able to provide additional treatment options for our patients.—

--And to kind of think about how we can help improve their quality of life and help reduce their disease burden. So I just wanted to encourage all listeners out there that it isn't too difficult to manage HS patients, there are lots of options out there now and there will be more to come. And hopefully, we'll be able to all together as a specialty really be able to help our HS patients.

STEVEN CHEN, MD, MPH, FAAD: That's wonderful. I love what you said, too, about the MODES procedure in particular. These are all skills that we already have, it's just putting them in the right order, doing it for the right patient, knowing the indications, and knowing when to use it is so critical. So for our listeners, obviously they have the option of searching PubMed for your paper on the MODES procedure. But since you've so generously offered it, do you mind sharing your email address?

SO YEON PAEK, MD, FAAD: Absolutely, happy to.

STEVEN CHEN, MD, MPH, FAAD: Where listeners can directly get the paper from you.

SO YEON PAEK, MD, FAAD: The easiest way to contact me would be through my email which is Doctor.Paek@gmail.com. And that's spelled out D-o-c-t-o-r, dot, P-a-e-k @gmail.

STEVEN CHEN, MD, MPH, FAAD: Thank you for signing up for tons of emails inquiring about the MODES procedure. I'm sure our listeners appreciate it. Thank you so much for joining me and joining our listeners today on this episode of *Dialogues in Dermatology*, specifically looking at New and Emerging Therapies for Hidradenitis Suppurativa. Thanks to our listeners for joining and listening in. Until next time, thanks again.

SO YEON PAEK, MD, FAAD: Thank you.

Commentary

Samip Sheth with Benjamin Stoff, MD, FAAD (ed.)

In this episode of Dialogues, Dr. So Yeon Paek gives an update on new and emerging therapies for hidradenitis suppurativa (HS).

HS is considered a multifactorial disease. While follicular occlusion is a key event in the pathophysiology of HS, the current understanding is that of an autoinflammatory condition. For example, there may be immunological priming that occurs first, which leads to a dysbiotic microbiome, and then follicular occlusion. Or, as more traditionally thought, HS may start with that follicular hyperkeratosis and dilatation, which leads to follicular rupture, and then a series of acute and chronic inflammatory events. While various subtypes have been described in the literature for HS, including follicular or acneiform, axillary, mammary, or gluteal, not all patients fall in a discrete category.

Research on HS has advanced markedly in the last 5 to 10 years in both translational and clinical realms. In the acute inflammatory phase, the Th1,Th17, TNF-alpha, IL-17, and IL-1-beta pathways have been found to play a role. In the chronic inflammatory phase, pro-fibrotic cytokines lead to the development of scarring and other architectural changes characteristic of advanced HS. While several genetic mutations have been identified in HS, their role remains unclear. Likewise, the interplay of genetics with the microbiome, bacterial dysbiosis, obesity, smoking, and other lifestyle factors in HS patients has not been well-elucidated.

For medical treatment of HS, monotherapy is rarely offered unless there is very mild disease. For almost all patients, topical antibacterial therapy (e.g., clindamycin) and a topical antiseptic cleanser for daily use is initiated. Oral antibiotics are often used for flares. A majority of Dr. Paek's female patients are on spironolactone. If a patient has a higher inflammatory burden, systemic immunomodulatory therapy, including the TNF-alpha inhibitor adalimumab, is often deployed. For HS patients with tunnelling or scarring, a combined medical and surgical approach is best.

Surgery as the initial treatment may be appropriate for certain patients with either localized disease or with tunneling so extensive that medical treatments will not penetrate. There may be access issues for patients to see non-dermatologic surgeons. Surgeons have BMI restrictions or request patients stop their medical therapy pre- and post-operatively. For those and other reasons, Dr. Paek often performs HS surgery herself in clinic.

For example, the MODES procedure, which stands for Modified Deroofing with Scar Excision, is a unique outpatient surgery for HS. It involves an initial deroofing procedure followed by exploration of surrounding tunnels, marsupialization of those areas, and then excision of the involved scar tissue. Fibrous tissue adjacent to tunnels may be the source recurrences that occur with traditional deroofing. MODES is different from a wide local excision because a pre-specified area is not marked out and excised. Instead, during the procedure, dermatologists identify the tunnels as they go and then excises as much as possible.

References

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