

**Dermatologic Diseases and Obesity
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Lindsey Bordone, MD, FAAD, interviewed by Sabrina Shearer, MD, FAAD

SABRINA SHEARER, MD, FAAD: Welcome to another episode of *Dialogues in Dermatology*. I'm Sabrina Shearer, Assistant Professor of Dermatology at Duke University and the Durham Veterans Affairs Medical Center. I'm super excited to be joined today by Dr. Lindsey Bordone. Dr. Bordone is a board certified dermatologist and nationally recognized expert in hair loss in complex medical dermatology. She has contributed extensively to our field, spending time at the NIH and over ten years on faculty at Columbia University. She's now in practice at Bordone Dermatology. She is joining us today to discuss the intersection of dermatology and obesity. Dr. Bordone, thank you so much for being here today.

LINDSEY BORDONE, MD, FAAD: Thank you so much for having me.

SABRINA SHEARER, MD, FAAD: Obviously, the impact of obesity really permeates our society and the way that we practice medicine, in general. It's super interesting to think about how dermatology specifically plays into that. So thinking about it at its most basic level, what are some of the ways that obesity affects the function of the skin?

LINDSEY BORDONE, MD, FAAD: I don't think you can look at the function of the skin without factoring in someone's BMI. On many levels, there is an impact of high insulin and inflammation as a result of obesity and other factors that come into play that are metabolic and how they affect the skin at every level, and the scalp, and hair growth. The primary thing that we see is inflammatory conditions of the skin as a result of chronically high insulin and chronically high BMI.—

--There's been a lot of data on this over the last two decades regarding psoriasis and more so now HS. It's critical that as part of our comprehensive approach to these diseases, we also treat obesity as the component of the condition.

SABRINA SHEARER, MD, FAAD: How has obesity changed your approach to management? So you're thinking about treating obesity kind of on one end here. And as you choose your medications to treat these diseases as far as biologics and things like that, how does obesity change your approach to managing those patients?

LINDSEY BORDONE, MD, FAAD: You cannot uncouple an inflammatory condition from obesity. Because I'll give psoriasis as an example. There is a bidirectional affect that obesity and inflammation have on each other. So if someone is obese, we know that their response to biologics is significantly less, biologics are significantly less effective in patients who are obese. So if someone's BMI is over 35, the chance of that biologic working goes down dramatically.—

--The higher the BMI, the less effective the medications are. We know that inflammation causes insulin resistance. Insulin resistance causes inflammation. So if you're using a medication that isn't that effective and you're also managing someone with insulin resistance, you're only treating half of the disease. So you're not going to get them to the successful endpoint that you're hoping for, unless you manage the other component of the condition, which is their obesity and inflammation. They go hand-in-hand.—

--And now we have effective management for obesity that wasn't available a decade or two decades ago like it is now. So as part of the management, it has to be part of the comprehensive treatment plan.

SABRINA SHEARER, MD, FAAD: As you're sort of waiting for those other medications to take effect or lifestyle modifications to take effect, do you have to adjust your dosing strategy for the

psoriasis medications or the hidradenitis medications based on the patient's weight along the way?

LINDSEY BORDONE, MD, FAAD: Yes, so if you have adiposity, especially visceral adiposity, you're producing a lot of interleukin-6 and TNF-alpha. If you are putting someone on a medication that treats high TNF levels but you have a source that's continuing to produce it, you're chasing your tail. So you treat the obesity to bring down their TNF levels and at the same time, you put them on a biologic. Because if someone has a lot of inflammation, that will make them insulin resistant and also it's very hard to exercise when you're very inflamed or you're not sweating sufficiently because you have psoriasis plaques all over your body.—

--So what you do is you treat their psoriasis but in the background, you're also treating their obesity. And the same goes for HS. HS is a little bit different than psoriasis in that it is unidirectional. The single biggest modifiable risk factor for HS is obesity. If you are able to treat their obesity, reduce their risk of things like sinus tracts, which we know are worse in patients with a higher BMI. You also reduce all of the comorbidities that go along with hidradenitis suppurativa.—

--So you obviously treat the condition, because we know how to treat that. But you treat the source of the inflammation as well, which is the obesity.

SABRINA SHEARER, MD, FAAD: It sounds like there's truly a disease-modifying role for weight reduction, as far as changing the trajectory of the disease state.

LINDSEY BORDONE, MD, FAAD: Absolutely. I think the earlier the intervention, the better. Because if you're treating someone with HS with a biologic and they're terribly insulin resistant and they're continuing to gain weight, what are we really doing for them, if we're not taking care

of the biggest modifiable risk factor. It's the same as lung cancer and smoking. Yes, you can take care of the cancer but if someone continues to smoke, what are we doing?—

--We have to address the other component of the disease and it's been like the elephant in the room. I think part of that is we haven't had the ability to address it as effectively as we do now. But there's no denying that as dermatologists, we're used to handling very complex medications and these medications are not nearly as difficult to manage as things like cyclosporin or methotrexate. So it should be part of our comprehensive care plan.

SABRINA SHEARER, MD, FAAD: So are you prescribing the GLP-1s?

LINDSEY BORDONE, MD, FAAD: I've been prescribing GLP-1s for over five years and I've had excellent results. Some of my psoriasis patients who developed psoriasis after they developed metabolic disease have been able to go off of biologics. They do stay on GLP-1s lifelong, that is the trajectory I tell them to expect. Because there are some people that just produce a lot of insulin. It's good in the right setting. It's good to be insulin resistant in periods of famine. There is a survival mechanism to it.—

--But in modern day where we have access to lots of food, that works against us. So I tell them to expect to stay on it, because even if their weight is stable but their insulin starts to climb again, their inflammation will start.

SABRINA SHEARER, MD, FAAD: Shifting gears a little bit, we also know that adiposity and hormonal changes are closely linked. Can you touch a little bit on that and how that can affect the skin?

LINDSEY BORDONE, MD, FAAD: In men and women, it's different. Women who have adiposity tend to have higher testosterone and men who have adiposity tend to have a higher estrogen. So in women in cases of PCOS, there's actually now subcategories of PCOS. There

are the lean PCOS patients that we know are still insulin resistant. And then there is the very standard PCOS patients that have all the physical manifestations like obesity and hair loss and hirsutism.—

--In PCOS, there is a known component of insulin resistance that we're not addressing. When someone is insulin resistant, their body compensates by making more insulin. So they develop hyperinsulinemia. As you develop more insulin resistance in women, your sex hormone binding globulin produced by your liver is decreased. So the amount of testosterone that that sex hormone binding globulin binds to goes down and your free testosterone goes up.—

--So these women wind up with lots of free testosterone. That causes hormonal acne, hirsutism, androgenetic hair loss. And if we're not treating that insulin resistance and we're just treating the testosterone component with things like spironolactone, again we're chasing our tail. So we have to address the metabolic component. Also something to keep in mind is that as women go through menopause, their ability to produce estrogen goes down in their ovaries, but their fat cells still produce a lot of estrogen.—

--So after menopause, these women who have high estrogen and features of PCOS need to have their uterine lining monitored. Their risk of endometrial cancer increases dramatically. So if you have a female patient coming in who is postmenopausal and has obesity and they're there for a skin check, we really should be recommending that they see a gynecologist for monitoring of their uterine lining. Many women after menopause are not making regular visits to their gynecologist, so we have to remind them of that.—

--And then the other side of it is men. So in a male patient who has obesity, your fat cells produce aromatase and it converts testosterone to estradiol. For men that have normal testosterone, that testosterone is being converted into estradiol and they have lower overall

testosterone. So obesity feminizes men and masculinizes women. We see the outcomes of that in different ways.—

--In women, it's more of the hirsutism, acne, androgenetic hair loss. In men, we see a feminization. Which is another thing that is interesting with these GLP-1s, there is a lot of data to show with gastric bypass, we see a huge increase in testosterone. That is where we see the largest increase in testosterone. Second to that is GLP-1 use. And in some men who are on GLP-1s, after they've had weight loss, they'll come in with some features of higher testosterone that they're not used to.—

--For instance, they might develop a little bit of acne along the way as their body adjusts to a new testosterone level. They might have a little bit more androgenetic hair loss. We can address these overall. Their BMI is much healthier and blood flow to their skin is improved because of insulin sensitivity.

SABRINA SHEARER, MD, FAAD: I think that concept of a lot of the things that we sort of think of to treat those problems are more like band-aids and you are really trying to get at the underlying etiology here, as obesity as like a unifying trigger for a lot of these issues.

LINDSEY BORDONE, MD, FAAD: I don't think there is a single disease in dermatology that obesity doesn't touch. The example I like to give is if you have a threshold over which you will develop an inflammatory condition and there are certain things that will push you over that threshold. Let's say that you made someone obese and gave them alcohol and gave them COVID and you put them into an inflammatory state and pushed them over that threshold, you could remove those inflammatory agents and move them back in the other direction over the threshold.—

--Obesity is such a massive component of inflammation. It's not like alcohol, where you can get a pulse of inflammation and then you don't drink for a few days and it goes away. Obesity is chronic. The same thing with diseases, you get a pulse of inflammation and then your inflammatory markers go down. There's no escaping inflammation when you are obese. It also affects everything from blood flow to inflammation to hormones, so every single aspect of dermatology is touched by obesity.

SABRINA SHEARER, MD, FAAD: You touched a little bit on this already, but when we are seeing patients in clinic and they're coming in say for that skin exam and you have the observation that they have obesity, you mentioned in that postmenopausal woman, talking about getting them into GYN and keeping up those healthcare maintenance things. What other sort of clinical signs should we be looking out for that should prompt evaluation for metabolic diseases or hormonal workups or things like that?

LINDSEY BORDONE, MD, FAAD: We are the best specialist for identifying acanthosis nigricans, skin tags, a Frank sign of the earlobes, and excess soft tissue. Other things are poor blood flow in the skin. We start to see diminished hair growth on the peripheral extremities. We know that in people who have vascular disease of their lower legs, they stop growing hair there and that's a sign of vascular injury. One of the ways in which insulin affects blood flow is it's supposed to dilate blood vessels so that blood rushes through, cells pick out the sugar, and the sugar comes down.—

--But when your insulin is always high, I give this awful example, it's like your mom always screaming at you. You stop listening, so blood vessels stop dilating in response to insulin and they stay constricted. So we'll see that in the forearms of men who are obese. They'll have loss of hair on the top of their forearms and on their lower legs. If you apply insulin to the skin of

someone who is lean, it can cause vasodilation. But if you apply insulin to the skin of someone who is obese or insulin resistant, it doesn't.—

--So in restoring insulin sensitivity, we're also improving blood flow, wound healing, and other important aspects to hair growth and skin remodeling.

SABRINA SHEARER, MD, FAAD: We have a really unique role where we can be sort of on the frontlines of identifying some of those things, it's a good call to action for us.

LINDSEY BORDONE, MD, FAAD: The other thing is patients are motivated to see a doctor when they can see issues in their skin. Most of the time, someone in their 20s is not going in because they feel like their kidneys are off or their liver is off, you don't have symptoms from that. But they can see that they have inflammation on their skin. And the skin is just mirroring what's going on internally. We do know that with hidradenitis suppurativa, people have much, much higher rates of fatty liver. So if they're coming in their HS, we should be also inspecting their liver metrics.—

--I often will order liver enzyme tests and a CBC to check a FIB-4 score in patients who have bad HS. That's very easy to do, it's just a simple calculator online where you can punch in their age, their liver enzymes, and their platelets and know whether or not they're moving into a territory of really needing some liver management. But we are the ones that will find that if we're attune to it. We're the only ones that probably patients will have interactions with in certain age groups.

SABRINA SHEARER, MD, FAAD: Sort of thinking a little bit more broadly and taking a step back as we treat the dermatologic conditions when these patients are coming in, are there specific complications or challenges with respect to treatment, specifically in obese patients?

LINDSEY BORDONE, MD, FAAD: There are complications that occur on either end. For instance, patients have atypical immune responses when they're obese. So if someone is going to have a complication on a biologic, it's more likely going to be an obese patient. On the other hand, if you mean management with a GLP-1 and complications, I think so long as a physician is well versed in maintaining very stable but slow weight loss, you can avoid 99 percent of the complications that come along with GLP-1 use.—

--But in general, patients with obesity have much higher rates of hospitalization, complications from almost any condition and have atypical responses to medications because their liver function is not as perfect as someone without obesity.

SABRINA SHEARER, MD, FAAD: What about the complications of weight loss itself? As we sort of see more patients or we're prescribing more of the GLP-1 agonists, are you seeing specific dermatologic complications of using those medications?

LINDSEY BORDONE, MD, FAAD: I haven't seen dermatologic complications. The biggest thing I've seen is when there's a fluctuation in hormone levels that people are adjusting to. For instance, when men start to have an increase in testosterone and an increase in blood flow, yes, their need for medications like Viagra and Cialis go down so you have to caution them about that. There's other things where they'll have complications like, I wouldn't even call it a complication, but there's a side effect of increased oil production for a period of time in some people when their testosterone shifts faster than their body can adjust to it.—

--But these are all very mild, minor things that we can manage as dermatologists. Overall, their improvement is pretty profound in every way. Or maybe if people do experience a telogen effluvium if they lose weight rapidly, but I tell my patients you want to lose one to two pounds per week max and if they're prone to shedding, stick to one pound per week. The way that the

medication was recommended to be dosed when it first came out because of the clinical trials was you increased the dose every month, as tolerated.—

--So if someone wasn't nauseous or having some issue with symptoms, you would just keep escalating the dose. That is not the way it's dosed anymore. And that has helped us to avoid a lot of the complications of GLP-1s, where you dose it slowly. If someone is losing one to two pounds per week, no, you don't go up on the dose to the point of tolerance, you leave them there. That avoids getting gallstones. It avoids blood pressure issues. It avoids shedding that occurs with rapid weight loss. I think patients do much better when you stick to low and slow.

SABRINA SHEARER, MD, FAAD: In the back of my mind throughout this discussion is sort of the context that patients are coming to us in really this very vulnerable state. They're already really self-conscious about their cutaneous disease, so we don't want to amplify the insecurity. But weight counseling, it sounds like it's really an essential part of patient care. So as we sort of think about lifestyle modifications and our ability to treat patients holistically, how do you approach that conversation with patients?

LINDSEY BORDONE, MD, FAAD: I approach it from a very scientific point of view. We know that insulin is directly inflammatory and we know that insulin causes weight gain and that weight gain causes inflammation. What I tell patients is I don't care what your weight is, I care about your disease and your health. If you were at this weight and you didn't have excess inflammation or excess insulin, then we would leave it, there's no problem. But if this is contributing to a disease state that will ultimately shorten your lifespan, I want to address it.—

--I think it's important to tell them it's not their fault. If someone has high insulin, good luck in not being obese. It's very rare to have high insulin and not be obese. So I think a lot of times they have been told just exercise and diet. You're not going to exercise and diet your way out of insulin resistance in many cases. For instance, in postmenopausal women, we know that insulin

resistance goes down pretty dramatically with loss of estrogen. Postmenopausal women have always talked about gaining weight in their midsection and fat redistribution.—

--And they're exercising and they're doing all the stuff. So I think it's really important to tell patients, "Look, this is a downstream effect of chronically high insulin and metabolic changes that we evolve to have and it's not working for you. So if we address this, it's going to make your disease better and make you live longer. And yes, the side effect of these medications in addressing your high insulin is weight loss. But the important part is that we're going to control the high insulin levels and the inflammation that comes as a result of that."

SABRINA SHEARER, MD, FAAD: That's a really great approach, thank you for that. I think having those words is super useful. Again sort of thinking about the patient holistically, we know that obesity is affecting patients on many levels. Obviously not just in their skin, all of their organs are being affected. Who else do you think should be brought into the conversation when you start getting into that, should we be going on a GLP-1 or what else can we do to sort of control that insulin resistance piece?

LINDSEY BORDONE, MD, FAAD: I work with so many different specialists. For instance, I end up ordering a lot of primary care labs and imaging because people just don't have access these days. So in a patient that I have who is obese and if it's a male that's obese and 45 or older, I'll order a calcium score on them. I do lipid panels on them. I'll send them for a stress test, an EKG with a cardiologist.—

--But sometimes just to get a baseline understanding of their health and to make sure that they're not waiting on finding a specialist to get those labs or that imaging done, I just order it myself. A calcium score is easy to order, it's about \$100. In women that are perimenopausal, I order a DEXA scan. They're inexpensive if they go to an outpatient facility, sometimes it's as

low as \$60 cash. If a woman has high estrogen because she's obese in a postmenopausal state, I send her to a GYN.—

--I work with urology because there are hormonal issues that occur in men and they have some of the downstream effects of that, like erectile dysfunction and they're being treated for those with certain medications that they're going to need to potentially come off of. The other big one is blood pressure. If you have high insulin and your blood vessels aren't dilating in response to insulin, what does your body have to do to push blood through those vessels? It has to jack up the pressure, right?—

--So people in response to high insulin will have high blood pressure. Also, you have all this adiposity putting pressure on blood vessels, yet another source of high blood pressure. You have to monitor someone's blood pressure as their weight comes down and work with a cardiologist or a primary care doctor to start shaving off medications. The same goes for high cholesterol. I've had patients who have had a significant dyslipidemia, with very high triglycerides, very high LDL, low HDL. That starts to self-correct over the time that a patient is losing weight.—

--Rates of anxiety and depression go down because a lot of patients have this chronic food noise or they have sad feelings about their body. So I've had patients go off of some of those meds. So I think when we talk about other systems of the body, we're looking at more medication reduction than medication addition. When I see patients every six months on these meds, we reevaluate what they're on, we discuss it, and then I will tell them to see their primary care or the doctor prescribing that medication, to talk about dose adjustments or discontinuation of drugs.—

--I will say that this has become very difficult to do in modern medicine. Because reimbursements have gotten very low, administrative costs have gotten very high. To have this

time with patients, it's so precious and difficult. So it depends on your level of comfort and time and your overhead costs, but it's something that if dermatologists had all the time in the world to do and they were motivated to do it because they could afford to, I think more than any specialty dermatologists would excel at this.

SABRINA SHEARER, MD, FAAD: I think that that's a direction that we all hope to get to as we move forward. I do think that we're nearing the end of our time together. But before you go, do you have any last thoughts that you'd like to leave with our listeners?

LINDSEY BORDONE, MD, FAAD: I think that dermatologists are so smart. It's the hardest specialty to get into. Patients come to us because of physical changes that they're not happy about. I think more than any other specialty, we are the ones that have the opportunity to intervene and really help these patients. So go for it.

SABRINA SHEARER, MD, FAAD: This has been truly a fascinating conversation and I think something that we really need to think about more intentionally in order to effectively treat our patients. So thank you so much, Dr. Bordone, for sharing your pearls today and for taking the time out to join us. And thank you all for tuning in to another episode of *Dialogues in Dermatology*.

LINDSEY BORDONE, MD, FAAD: Thanks for having me.