Evolving Treatment Landscape of Psoriasis. More than Skin Deep.

Psoriasis is one of the most common skin ailments, affecting about 2 percent of the population, across gender, age or socioeconomic status. The impact of this autoimmune skin condition goes much deeper with raised cardiovascular risk, inflammatory arthritis and other immune system related conditions.

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The severity of the condition determines the treatment approach ranging from topical treatments to phototherapy.

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We are discussing Psoriasis treatment approaches with dermatologist Dr.

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Joel M. Gelfand.

Full Transcript:

Priya Menon: Good morning and welcome to another episode of CureTalks. I'm Priya Menon, your host and today we are discussing the evolving treatment landscape for psoriasis with Dr. Joel M Gelfand from the University of Pennsylvania. On the patient panel, bringing us the patient perspective are Howard Chang and David Stanley, a warm welcome to all. Getting on with the discussion, we have with us Dr. Gelfand, professor of Dermatology and Epidemiology at the Perelman School of Medicine, University of Pennsylvania. Dr. Gelfand, such a pleasure to have you here. I'm going to start with some very basics, to lay the foundation of our discussion. So could you please begin with what is psoriasis and some of the known causes?

Dr Joel M Gelfand: Well, fundamentally psoriasis is an autoimmune disease, where what happens is that under the influence of genes we inherit from our parents, and this is multiple genes that come together in combination, if you will, that makes our immune system sort of susceptible or primed to act in what we call an auto inflammatory or autoimmune manner. And so what happens in people who develop psoriasis is some trigger comes, in some cases it's a strep infection, and other patients that may be something that we don't even know what triggered it, and the immune system gets confused and it starts reacting to proteins that are normally made by the skin by the epidermis and thinks these proteins are foreign or abnormal. And so the way our bodies evolved over time was to say, there's something wrong with our skin, just flick it off.

Dr Joel M Gelfand: And so that's what happens in psoriasis, the immune system think there's something wrong with the skin, it releases substances, we call them cytokines, and they cause the skin cells called keratinocytes to proliferate very rapidly. So our normal skin cell takes about a month to be born and in psoriasis the entire skin will turn over in about a day or too. And that's why patients are stuck with having

these large plaques in their skin that are very thick, that can itch that could crack and can bleed.

Priya: So why I am going to be asking this is we've got a whole lot of questions on psoriasis. And one of the questions, I think a couple of them actually touch upon the genetic inheritance of psoriasis and go on to ask if psoriasis can be inherited. So is that one of the causes that people have psoriasis?

Dr Joel M Gelfand: Yeah, that's a great question. So it can run in families. About 40% of people who have psoriasis will have a family history of the disease, which means actually, the majority of people do not have a family history. And that's again, because the genetics of psoriasis are quite complicated. It's multiple genes that come together in combination to make one prone to developing this problem when some other environmental trigger comes into play, whether it be an infection, other risk factors have been demonstrated for psoriasis or things like obesity, for example. Those who are overweight, have a higher risk of developing psoriasis over time. There's been some studies showing that major stress stressful life events, a definite family divorce can also trigger psoriasis in some people who probably have some type of genetic susceptibility. For those who have psoriasis, I would like to reassure them that if they have children, it's not like the children are destined to develop psoriasis.

Dr Joel M Gelfand: The lifetime risk of parents who have children or their children developing psoriasis when the parents have it, is probably around 20% or so. And the severity of psoriasis, the inheritance of that is pretty complicated. Typically, what you'll see is maybe if the mom or dad has pretty severe psoriasis, if the child develops it, it's usually more of a mild case. And so I hope that information reassures people who were living with psoriasis, that the likelihood that their children will have to face the same degree of severity is pretty low, and also we are making so much progress in this disease that we increasingly have better ways in managing this disease over time.

Priya: So is there a typical age range for onset? Or do we see it across age groups?

Dr Joel M Gelfand: Well, psoriasis can occur at any age of life. It can come on shortly after birth, in any neonatal period. I've had patients develops psoriasis for the first time in their 80s in the setting of having a major stressful life event, the loss of a sibling. So this can occur at any point in time. Now that said, generally the disease most commonly comes on in the 20s 30s 40s and 50s.

Priya: And how different is paediatric psoriasis from adult onset?

Dr Joel M Gelfand: Well, I think biologically paediatric psoriasis is quite similar to adults psoriasis and response to treatments fairly similarly to adults psoriasis, so it is essentially the same disease. In general when the disease starts earlier in life, it tends to be more severe for patients more extensive over time, compared to those who develop psoriasis later in life, but that's sort of an average situation. Each patient's journey is highly individual when it comes down to it.

Priya: Dr Gelfand, I'm going to take a few more seconds and dig a little bit more about paediatric psoriasis because we know that we have quite a few caregivers of psoriatic patients listening in today. You are, I believe part of the team that released the paediatric psoriasis guidelines in November of this year. So can you briefly explain some of the main points of these guidelines so that listeners get are informed about this?

Dr Joel M Gelfand: Yeah, so I think there's a pretty broad guidelines and it speaks to several different issues around the care and management of psoriasis in children. They highlight for the first time, some of the comorbidities that people need to be aware of in children with psoriasis, obesity and metabolic syndrome are particularly prevalent in young people who develop psoriasis, so their caregivers should be aware of this and follow appropriate guidelines for identifying things like high blood pressure in children or tracking for diabetes or abnormal lipids the way they would in any child, recognising that the results are more likely to be abnormal in a child who has psoriasis especially when it's more significant.

Dr Joel M Gelfand: The guidelines also outline the various treatment approaches we have for psoriasis

ranging from topical medications, ultraviolet light phototherapy, pills have been used for a long time, like how to use safely things like Methotrexate and then also outline the data emerging for our newer therapies, biologics, medications like Etanercept or Ustekinumab, which had been approved in the paediatric population for use in these patients.

Priya: So how does treatment options differ for children as compared to adults?

Dr Joel M Gelfand: Well, that's a good question that I think with children, several things are more challenging in children. One is oftentimes a lot of our treatments which are quite expensive, have not been proven to work in a paediatric population or don't have FDA approval, and therefore it can be very hard to get access to some of these therapies. Second issue is that parents are rightly so are often very cautious about what treatments we're going to use in a child especially when we don't fully understand the long term safety of some therapies on a young individual. Now that being said, there's a lot of uncertainty in life in general and specifically in the world of psoriasis and so for many children who were suffering with psoriasis not treating the disease is really damaging as well.

Dr Joel M Gelfand: It has severe effects on self esteem, there's higher rates of anxiety and depression. It may interfere with their development in terms of their ability to focus in school, they have a lot of itching or sleep disturbances from their psoriasis may affect their social well-being their ability to make friends and things of that nature. And so clearly in children who have psoriasis, it's impacting them in terms of the physical symptoms or emotional symptoms or social symptoms of psoriasis. We have a variety of ways to treat the disease effectively. It's been thought that some of our therapies are probably even better tolerated in children. So methotrexate classically seems to be safer in children than in adults in terms of the effects in the liver, although that's somewhat anecdotal information and it's not definitively known to be true.

Dr Joel M Gelfand: Some of our therapies that we use in adults like a drug called Acitretin, a form of vitamin A, that could cause issues with bone development, and so we tend to shy away from using that long term in children, whereas you'd be more comfortable using that long term in adults. ultraviolet light phototherapy is often highly effective for children with psoriasis but maybe very difficult to do if the child has school or after school activities, making it hard for them to make it` to the office three times a week, but we're trying to address this issue by including children in a large pragmatic trial we're doing called the LITE Study where patients 12 and older are randomised get treatments to psoriasis with phototherapy either at home or in the office.

Dr Joel M Gelfand: Also, they're a very young child, they're five years old, they may have a hard time standing still, inside the phototherapy booth and so it may not be so appropriate in that age group. Coming the biologics now are more novel therapies things like Etanercept, Ustekinumab is approved by the FDA for use in the paediatric population. So they're very effective approaches. But we keep on making progress in psoriasis, other mechanisms actions like the IL-23 inhibitors such as Risankizumab or Tildrakizumab or IL-17 inhibitors like Secukinumab or Ixekizumab. These drugs have yet to been approved paediatric psoriasis and therefore conditions will often have a hard time accessing these therapies in that age group because they are prohibitively expensive.

Priya: So what are some of the standard of care treatments other than those you mentioned now, for paediatric population, I want to know for the adult population, and I'm sure, our panel of Howard and David will have more questions on treatments for you. But if you could just briefly just touch upon some of the standard of care treatments that adults are offered, currently.

Dr Joel M Gelfand: Yeah, so I'll talk to this but by categories, because, we've been so lucky to have so much progress in psoriasis in the last decade or so that we now have more than a dozen treatments that are considered to be standard of care. And a lot of times how we decide what treatment to use, the patient is based on shared decision making with the patient, what the patient's preferences are, what their treatment goals are, what their underlying health comorbidities are. So do they have significant psoriatic arthritis? Do they have other medical problems they've been dealing with, like have they had issues with inflammatory

bowel disease, it's pretty common in people with psoriasis or do they have a strong family history of multiple sclerosis, sometimes we see that in people with psoriasis. Have they had a recent malignancy and has that influenced the treatment approaches that they're willing to use? So broadly speaking, we have a variety of topical medications that we tend to use when disease is fairly localised, just a little bit on the elbows and the knees may be a little bit on the scalp.

Dr Joel M Gelfand: When the disease is more extensive getting to be more than 5% of the body surface area and you can think of this as the palm of your hand. The palm of your hand is basically about 1% of your body surface area. So if you have psoriasis that you would need five of your own palms to cover, it's very burdensome for patients to be able to put on topical medications regularly when disease gets more extensive. So when disease is more extensive or not responding to topical medications, we have three categories or approaches, ultraviolet light phototherapy, the most classic one being narrow band phototherapy which is highly effective. We have targeted versions of narrowband phototherapy called Excimer laser, which is very effective for localised small plaques of psoriasis. An older modality is called PUVA, where people take a pill by mouth, sensitising the sunlight and then they get ultraviolet A phototherapy with it.

Dr Joel M Gelfand: We don't use that as much anymore because it's inconvenient for patients, but in people of colour, darker skin patients, it's a very safe and very effective approach to use. Then we have pills by mouth, Methotrexate, Acitretin, Cyclosporin. And then a newer medication a premier West, and Apremilast is currently fairly popular, because you don't need any laboratory monitoring with that medication. And that makes it much more convenient for patients. Its downside to that it gets expensive so it can be hard to access. Its efficacy is sort of modest if I gave it to say 10 patients about three patients have a good clinical response the rest, not so much. And people could have some nausea or queasiness with it, some diarrhoea that could be uncomfortable, that usually goes away but some patients have to stop the medication for it. And some patients about one in 100 patients will complain of feeling depressed on that medication and then we just stopped the medication if that occurs.

Dr Joel M Gelfand: Our newer biologics injectable medications we have basically three flavours, those that target TNF, which have been around for two decades now and are especially beneficial for joint disease, psoriatic arthritis, I should say. They also could work for other conditions like inflammatory bowel disease, Crohn's ulcerative colitis. We then have things that target IL-23 either specifically, like three of them we have Rizenkuzuman, Tildrakizumab, and Guselkumab or non specifically, which will be used Secukinumab which blocks both IL-12 and IL-23. Secukinumab is also approved for treatment of Crohn's disease so often useful in these patients overlapping diseases. And then finally we have three IL-17 inhibitors. That would be a Secukinumab, Ixekizumab and Brodalumab.

Priya: Quite a lot of new drugs out there for psoriasis. Dr Gelfand, I'm going to take some audience questions now since we are on the topic of treatments and you did mention phototherapy as well. We have a question asking, is phototherapy offered as first line of treatment and who qualify for it?

Dr Joel M Gelfand: Yeah, so what we're going to learn a lot more about this as we do the LITE Study and for those are interested, you can just go to www.thelitestudy.com, where we'll have a better understanding of how clinicians and patients actually choose to use ultraviolet phototherapy. Generally speaking, it's patients who have psoriasis affecting visible areas, arms, legs, trunk. There's a lot of disease in the fingernails or the genitals or the scalp is severely involved. Phototherapy is not so great in those situations because the light can't penetrate to be effective in the nails or scalp and we tend to not treat the genitals because that could cause burns or potentially skin cancer over time in men. So generally speaking of patients who have psoriasis affecting a least 4 or 5% or more of the body surface area, in areas that are amenable to being hit by the ultraviolet light. We have special versions of ultraviolet light phototherapy where we would treat the palms and soles, those areas are often very difficult to treat.

Dr Joel M Gelfand: So we use a form of topical cover in that circumstance where we put a medication on the skin called Soroban that sits in the skin for a period of time and then we shine ultraviolet A light. And

that's a pretty effective treatment for psoriasis that affects the palms and soles. Finally, there's another variant of psoriasis called Guttate psoriasis, where people tend to be covered with these very small spots of psoriasis all over the body, that responds very well to phototherapy as well. And as you can imagine, some of you have these little tiny five millimetre sized spots of psoriasis over the body their whole body surface area may be small, if you add up all those little spots, but it's almost impossible to treat that with topical medications, but it's got so many spots all over and ultraviolet phototherapy is very helpful in that circumstance.

Priya: Phototherapy seems quite an interesting topic here because we have more questions on that from the audience. Someone wants to know, what are some of the possible side effects of phototherapy?

Dr Joel M Gelfand: Yeah, so what's this speak about what we call narrowband phototherapy. This is essentially a single wave of the light and the ultraviolet B spectrum. This wave of the light comes from the sun so we get naturally environmentally. But what we've learned from research over time is that shorter wavelengths of light, which come from the sun as well cause burning of the skin without really helping psoriasis very much and longer wavelengths of light, which could cause damage to the skin as well don't help psoriasis very much either. And so that's why we have what's called narrowband phototherapy. Now, it is ultraviolet light. So one needs to protect their eyes when they're getting this treatment so that way you don't cause a burn on the eyes or cause cataracts. Then with short term use if the doses not adjusted just right a patient could have a sunburn like reaction. That's usually pretty mild when it comes down to it. It's very rare that we need to treat that with any medical therapy beyond just some moisturizers. And then in theory with long term use of patients are being treated for years and years, and they have fair skin, they may have more premature ageing of the skin, more freckles and wrinkles, if you will, and in theory, they may have a higher risk of skin cancer, although interestingly, studies to date really haven't demonstrated higher rates of skin cancer and patients getting this type of treatment.

Priya: Thank you, Dr. Gelfand. My next question and last one before actually bring on the panel is on comorbidities. So we have evidence that shows an association of psoriasis with a number of comorbidities ranging from arthritis, depression to cardiovascular disease, sleep apnea to lifestyle linked issues smoking, alcoholism, skin cancer. I mean, like, I believe the list is almost endless. So Dr Gelfand, when I was preparing for this talk it was kind of scary. And you have worked extensively on psoriasis and comorbidities like cardiovascular events related to it. It would be great if you could talk about comorbidities and its effect on quality of life of psoriasis patients.

Dr Joel M Gelfand: Yeah, so psoriasis is a very complicated disease, where inflammation drives this condition, both in the skin and ultimately in the blood. And so as we've learned more about inflammation over the last couple of decades in medicine, we've learned that many conditions that are seemingly unrelated, actually have similar pathways of inflammation that drive them. So insulin resistance, which causes diabetes, actually, this type of inflammation that promote that, that are similar to psoriasis inflammation. Similarly, cardiovascular disease, atherosclerosis or hardening of the arteries, it's not just things like cholesterol that caused that problem, but the body's immune response to cholesterol and the vessels that results in atherosclerosis and ultimately cardiovascular events. So there seems to be some shared pathophysiology between psoriasis and some of these comorbidities that we're observing to be a higher frequency in our patients.

Dr Joel M Gelfand: I think what we've learned from the research over the last decade or so is a couple of things. One is there tends to be a dose response for people are very limited psoriasis, mild psoriasis, the rates of these comorbidities may be slightly elevated, but it's small enough where we don't think it's that clinically important. That's except of course for psoriatic arthritis where that can be common and people with mild psoriasis and be quite as severe in adjoints. That said as the psoriasis gets more severe as you have more your body surface area involved with psoriasis, you have a higher risk of developing things like diabetes or cardiovascular events or psoriatic arthritis. And so, on one level, this could sound a little bit scary to patients and those who care for them. But on the other hand, it's really an opportunity, because many of these comorbidities, we think have opportunities for prevention.

Dr Joel M Gelfand: So for example, someone has psoriasis, they know that that means that they may have may have higher rates of abnormal lipids or diabetes or cardiovascular events over time. We can prevent these things by identifying high blood pressure and treating it, treating elevated cholesterol with things like statins, early identification of diabetes and treatment. By applying what we know about cardiovascular prevention to people with psoriasis. It's like we can we can prevent a lot of these complications in our patients. But we know from a lot of work that we and others have done, that patients with psoriasis tend to be unaware of their traditional cardiovascular risk factors. And when they do have them, they tend to be undertreated. And so, to me, this is sort of like a warning signal to a patient and their care team that when someone who has a chronic inflammatory disease like psoriasis, they should be extra attention paid towards efforts at prevention.

Priya: Thank you, Dr. I think being mindful of time, I am going to bring on the panel. We have with us Howard Chang who has lived with severe psoriasis and eczema for more than 40 years. He's an active health advocate and featured columnist on Everyday Health writing 'The Itch To Beat Psoriasis'. Welcome, Howard. Before you start with your questions for Dr. Gelfand, I would like you to share your story with us and also tell our audience the three things that have helped you in managing your condition.

Howard Chang: Okay, thank you so much. Yes. Thanks so much for coming on Dr. Gelfand and to just shed some light on psoriasis and just to help answer our questions with patients and advocates. So my journey really started when I was a child and I really appreciate the discussion about paediatric psoriasis. 40 years ago treatments that I went through and everything that I've experienced since I could really relate to a lot of what Dr. Gelfand was talking about in terms of different treatments and so forth. I was diagnosed at eight years old. I had a strep throat. So we talked about how infection can be a trigger. And I had a strep throat, a high fever, and I got that guttate psoriasis just broke out all over my body.

Howard: So, we went to see dermatologists and they said it was psoriasis and then they sent me over to UCSF University of California, San Francisco to confirm that diagnosis, which they did. So, yeah, so I had psoriasis at that young age in elementary school and faced a lot of bullying, low self esteem, developed a lot of social anxiety from it, especially as a teenager, having just a lot of my skin covered with disease. And when I graduated from high school when other people were going on graduation trips and preparing for college, I went to the psoriasis treatment daycare centre near Stanford for six weeks to get this treatment called Anthralin paste and I don't think we use that anymore, but it was just a really cumbersome and not very effective treatment. So just really painful experience there. When I went to college, I started systemic treatments. I started taking pills, again, methotrexate, and back then they had me doing liver biopsies.

Howard: So, I've had the experience of doing that as I hit a certain amount of treatment with methotrexate. And then I was on Isotretinoin, which the doctor had mentioned before, but about 13 years ago, I really faced my worst flare, I was about 95% covered. A doctor had no more options. I was using secondary and tertiary treatments, third line treatments and nothing was working. I was depressed. I wanted to quit my job. I wanted to quit my life, it was just a really pretty desperate situation. So they got me back to UCSF, back where it all started for me and Dr. John Koo, he talked to me and helped me out. That was a very emotional experience, just to know that there were options. So I ended up going on cyclosporine at that time, and then later some biologics came out. I've been on 6 biologics since, some worked great. About half a year ago on a new one.

Howard: And it's been a journey of trying to heal my skin but also emotional, spiritual healing. A big part of that, for me was blogging and getting involved in National Psoriasis Foundation in volunteering, patient advocacy, speaking in Sacramento or Washington DC, just writing and joining panels and just trying to help others to redeem this experience I've had. That's been a crazy journey in terms of how the treatments have come along over 40 years as well. So it's really great to be where we are now. And I'm really grateful for all the great research and all the great work that doctors like Dr. Gelfand and other researchers have done over the years.

Dr Joel M Gelfand: Howard, I want to say your story is really inspirational to us, to me in particular and I personally have a lot of admiration for people who have to live with psoriasis, it does create a lot of

challenges for patients and patients are often misunderstood. The general public often doesn't understand what psoriasis is. There are still lots of myths out there about being contagious and things of that nature, which it absolutely is not. And so it's inspiring for us to hear your story and how you've progressed through the years. And I think we're still making lots of progress in psoriasis. There are still plenty of patients who struggle mightily with the disease, and may respond well to a biologic, but they may lose response over time. And they have to try another biologic. And so I think that those of us in the research community and the medical community are excited about the progress we've made, but know that we haven't solved the problem yet and are working diligently to move towards a cure or find better ways to treat people today on long term control.

Howard: Thank you so much. It's, it's really amazing, like I said, the advancements in the just being part of the community and seeing the dedication of the patients, the advocates and our doctors and our researchers, so thanks so much. Yeah, I think this is a story that, as I talk to other patients and other advocates that we've gone through similar journeys and they were telling me that when we used to get together way back when there was a lot of depression and just pessimism but with a lot more optimism now. Priya asked me three kind of suggestions or tips and so, the first one for me was just getting educated.

Howard: I think about back when before the internet before anything that we could get information easily as we can now, it was hard to get educated, I got templates from the National Psoriasis Foundation, I was trying to learn as much as I could. But now there's a lot of great information on the internet to learn about the condition, to learn about all the great treatments that are out there, and just the options and it's just to learn about yourself to just how your body, your condition responds to different environments, potential triggers, treatments and so forth. So the first thing for me was just to get educated and just take that stuff. So nothing to be afraid of, and the more you know, the better you can treat and just manage the condition. My second one was similar to get treated. Dr. Gelfand said a lot of people are still suffering. There are a lot of great options out there. So work closely you're your doctor.

Howard: I've had some great relationships with my dermatologist, we work closely together, and they really listen to kind of my concerns. My condition, they take my history. So just getting treated, it sounds simple, but it kind of can solve a lot of the problems just to take that stuff if you're not getting treated right now. And then the last one for me was to get connected. So for many years, again, without the internet and without being connected to a local support group or advocacy group, I was very lonely. And one of the comments that I've gotten over the years, pretty less so recently was that people saying that they thought that they were the only one they felt so alone with psoriasis, that's just a horrible way to go. And when you've got lesions in all of your body or maybe you're dealing with depression or anxiety and just feeling like there's no one out there who understands you. So I think being able to get connected. This National Psoriasis Foundation is a group that I've been a part of. There are a lot of events locally, fundraising events, they have online groups and resources. And so those, I think, help us get inspired by others who have gone before that help us connect to others who go through the similar things that we go through. So get educated, get treated, and get connected.

Priya: Thank you Howard. I think that that's really very apt and very helpful for people who are listening so Howard says get educated, get treated and get connected if you want to manage your psoriasis well. Howard, please ask your questions to Dr. Gelfand, I know you had some great questions there.

Howard: I have so many questions. We talked about treatments and biologics and I recently read about how we may have personalized biologic treatment, you could just go to a patient and know which biologic might be effective. Like, I've tried six and it was kind of a frustrating process. What is your take on the state of psoriasis treatments being tailored to individual patients? And how far away do you think we are from here? I know it's a hard question, but just kind of the research.

Dr Joel M Gelfand: So we take the question about cure first, and then we'll talk about individual treatment second. So if you were asked me, is there a chance to get cured from this disease 10 years ago I would have said, No, there's no way we could cure, these are so complicated diseases, and I don't think there's a

chance of curing it. Now 10 years later, we've learned so much more, specifically we've learned what the actual proteins in the skin are that the immune system is reacting to. So we now know it's what's called the antigen and what's inciting this problem. And we also know fundamentally that the immune pathways involved in this diseased state IL-23, which promotes differentiation of immune cells, T cells into Th17 cells, which releases a cytokine called IL-17. This pathway was barely understood 15-20 years ago.

Dr Joel M Gelfand: And now all of a sudden we have therapies that are highly effective and rapidly beneficial in patients with psoriasis. They're not cures, of course, but they are highly effective treatments for many patients. Some of the questions are, why do some patients like you're explaining your experience, why some patients respond great, and others don't respond so well? We don't know the answer to that perfectly yet. Some data suggests that in fact, most patients, close to all patients should respond well to medication, the target IL-23 or IL-17. But that people vary a lot in terms of how much of a dose of the drug they need. So one hypothesis would be that well, if you didn't do well on let's just pick a drug say execute like Ixekizumab a partial response, but unclear, well, maybe you need twice a dose, or three times a dose, a four times a dose.

Dr Joel M Gelfand: This is a hypothesis that needs to be tested. But some data suggests that and the reason why we think this is because people have done these sort of elegant studies where we take patients who had very severe psoriasis went in one of these targeted biologics, and then they only had three or four plaques left. If you biopsy those plaques and look at their genetic profile and immunologic profile that is run the mill psoriasis, there is nothing unique to it, suggesting that the issue is not enough of the biologic is getting to that particular patch in the skin to interrupt the information that's going there. Now moving on to personalised therapy. So this is certainly broader in medicine, a very eager area of investigation. Some fields are more apt to be successful in that area.

Dr Joel M Gelfand: So cancer, for example, in cancer, you will often have two or three mutations in the cancer itself that drugs specifically target. In psoriasis, it's trickier because it's often multiple genetic pathways that are driving multiple different immunological pathways and therefore it may not be sort of silver bullet, a single approach that would knock out all those different pathways inflammation that are active in an individual. So currently, the standard of care is we don't have any tests we can order to decide that we should use biologic A vs biologic B or Pill A vs Pill B. That's just not available, but there's certainly a lot of research trying to move us closer in that direction.

Howard: Now, that would be incredible. Yeah, just during this trial and error over the years, when we have to wait two or three months, and then we have to try something else, and sometimes you're getting worse. Hasn't happened to me as much recently, but over the years, I've faced that so just kind of the area is pretty interesting to me.

Dr Joel M Gelfand: Yeah, well hoping that with newer, more targeted biologics, the IL-17s and the 23s that that will be less common experience for patients. But it is so likely to be patients who still had that same experience, where it doesn't seem to work or works and then stops working. And that's the larger problem our patients tend to face now is that they do well, a biological but overtime they start losing response. And, our goal for our patients is to be able to treat them with a medication safely and have long term control their disease, so they remain in remission for many years, and we haven't achieved that goal for the majority of our patients yet.

Howard: Yes. I think another area besides biologics and kind of traditional medicines, it seems like alternative medications, especially diet is a big discussion in the psoriasis community. Can you speak to diet or supplements and do you have any advice for people living with psoriasis in terms of food intake and so forth?

Dr Joel M Gelfand: Sure. So the best data out there so far related to diet is really around weight loss. And so for those who are overweight, and by overweight, I mean a body mass index of greater than 30. And that's based on your weight divided by height. And one could just go online to calculate your BMI. Just

Google calculate my BMI and calculators will come up and you can figure out what your body mass index is. So people who have high BMI and a lot of our patients with psoriasis do and we put them in a medical category of obesity. When they lose weight, their psoriasis gets less severe. They respond better to treatments that they're on. Those effects though are relatively modest and very difficult to obtain because as you can imagine, it's very hard to lose weight and then to maintain weight loss. Patients with severe obesity when they have BMI is over 40. I often talk to my patients about considering things like bariatric surgery, because we know when those patients bariatric surgery will lower their risk of diabetes and arthritis over time.

Dr Joel M Gelfand: But there are also a good deal reports in the literature, people with bad psoriasis, who have had bariatric surgery lost a lot of weight and their psoriasis got much, much better and in my clinical experience, that's been the case as well. Now coming to specific diets, things like gluten-free diets or anti-inflammatory diets, in my view, these are largely anecdotal at this point in time, without real clear proof that they're clinically beneficial for patients. And so I don't recommend this to my patients. Most importantly, I don't want patients to feel guilty that it's their diet and how they eat that's causing their disease. I mean, ultimately, this is an autoimmune disease that was triggered. And changes in diet, really, that are geared towards weight loss, could have some modest benefits. But that alone doesn't make a major difference in patients. Other alternative health approaches have shown some evidence at a rigorous level in terms of clinical trials.

Dr Joel M Gelfand: There's some data that mindfulness meditation can be helpful for patients. There was a study done in the 1990s, by Jon Kabat Zinn, who's a world expert in meditation and a clinical psychologist. And what he showed is that patients who were listening to meditation tapes while getting phototherapy compared to patients listening to regular music tapes, that those with the meditation approach cleared faster and required fewer treatments. So there's some decent data that meditation helps and that could also help with things like anxiety, and help with concentration. So the book I tend to recommend is called Wherever You Go, There You Are, by Jon Kabat Zinn. It's a nice introduction to meditation techniques. But there's certainly lots of resources out there about mindfulness meditation that people can look at.

Dr Joel M Gelfand: The last thing I want to mention to our audience, is that over the history of the field of psoriasis we've had lots of examples of things that were thought to the herbal remedies for psoriasis, that seemed to be very, very effective. And only later were determined to be laced with the potent steroids like Clobetasol. And so we do have to caution our patients and those listening, that if you're using some that's not been approved by the FDA as an over the counter or herbal remedy, and it works really, really well, sometimes that may be because it actually has active medical ingredients in there that may not be safe to be taken on a long term basis. So I think some caution is indicated here. And it's very important to speak to your healthcare team, your doctors about what supplements alternative therapies you're trying. So we're fully aware of what's going on.

Howard: That's so helpful. There's so many different treatments, so called treatments that are out there and they hit the community. And I think people can be desperate at times when they go on to try certain medications. And so I think people can get taken advantage of. So one thing we always say is if it works for you, but doesn't necessarily work for other people, and yes, so this area, I hope, we can have a little more studies on to I feel like we've heard about a psoriasis diet ever since I was a kid. One area that's really interesting to me and my blogging and advocacy is help bring awareness to the impact of the disease on the whole person, we talk about quality of life issues, anxiety or depression or relationships, social impacts. What does current research say about how psoriasis impacts quality of life, is this something that's measurable and do you have any suggestions for those living with psoriasis? Or for those who care for them to address quality of life concerns that they might have?

Dr Joel M Gelfand: Well, certainly there's been a lot of research in this area for the last couple of decades. And I'll speak to the general terms what we learned. So one is there was a time when the broader community thought, oh, psoriasis is not a serious disease, and the data on comorbidities, and also the quality of life had dispelled that myth. There was a time when certain insurance companies would not even

cover treatments for surprises at all saying it wasn't medically necessary to treat. And so we've come a long way from those days, which were only about 20 years ago, actually. So we know that psoriasis can have significant impairment on people's quality of life, meaning, their mental and physical functioning, and that the symptoms can be as severe as other major medical illnesses like diabetes, for example. We know that younger people and women tend to be more affected on quality of life measures compared to older individuals or men, although again, that's I wouldn't want to generalise that each individual's journey is unique and different in terms of how the disease affects themselves.

Dr Joel M Gelfand: And then oftentimes, the burden of disease to the patient may not be perceived well by the physician. So, oftentimes a doctor may think the disease is mild, but the patient thinks is severe. Or the physician thinks the disease is severe and the patient thinks it's mild. And so it's very important to have that conversation between a doctor and patient where the patient should help the doctor understand, this is how this disease affects my life. I can't wear clothes, I can't go to the beach. I can't sleep at night because I'm itching. It's affecting my ability to work with someone in sales, whatever specific things that are affecting the patient, it's really important to bring it to the doctor's attention so they know the degree of urgency necessary to control those symptoms or improve them. I think the advice that you gave before, get educated; so I think knowledge is power, understanding what's going on in your body, what psoriasis is, I think is extremely empowering and necessary.

Dr Joel M Gelfand: I think getting treated – by getting treated, I mean having a care team who has expertise in psoriasis, understands your disease state, understands all the treatment options available and can make them available to you, I think is very important. I think getting connected, as you said is extremely helpful because there are over 8 million people with psoriasis in the US, over 125 million people worldwide, and that really helps a lot. People with psoriasis, because of the stigmatising effects of the disease often feel socially isolated. And that's a really tough way to go through life, a tough way to feel. I have some patients, when I asked them about psoriasis, I'll say, well, what does your wife think about your psoriasis? And they'll say, we never even talked about it. So these conversations can be very hard, even in people with their loved ones to discuss. But we know that people feel better when they are connected to others, when they're understood what they're going through. And so I think that idea of getting connected both to your family, your friends in the broader community brings a lot of relief and mutual understanding for patients.

Priya: Dr Gelfand and Howard, I want to probably bring on David Stanley, and so we have David also on the panel. David is a writer, teacher, actor, narrator and melanoma survivor and he's an advocate of skin disorders. David's book on his melanoma journey titled It Started With A Freckle is available on Amazon. So David, please join the panel and the discussion and ask your questions.

David Stanley: Sure. Thank you Priya, always a pleasure. And Howard by the way, that's just an incredible story. We need to connect because I'd love to hear more of that. But in the meantime, we can track each other down. Dr. as Priya said, my lay expertise is in melanoma but several people when I announced that I was going to be on this panel reached out to me, unrelated to melanoma issues, of course, and they were saying, well, I have scleroderma, and I have psoriasis. Could you ask if there's some relationship here? And if there's some, what sort of outcome, I guess I'm looking for a little ray of hope in what is a horrible autoimmune disease and then psoriasis piled on?

Dr Joel M Gelfand: Yeah. Well, scleroderma is a very tough condition. For those who are listening and who aren't familiar with it, a sclerosing condition, where the skin and sometimes the organs become scarred down or fibrotic and it could be really devastating to mobility or to organ function, a very challenging problem and very difficult thing to treat. And so, I think when people have two different autoimmune diseases at the same time, be it psoriasis and scleroderma, or psoriasis and lupus, or psoriasis and inflammatory bowel disease, it's very important that they be treated in a multidisciplinary environment – having a care team that understands all aspects of these disease states, so that way a treatment can be selected that benefits both diseases. So for example, a patient I just saw a few days ago, who developed severe scalp psoriasis while on Infliximab for her Crohn's disease, which was on for 10 years. And so we were able to switch her from Infliximab to Ustekinumab, which works both for Crohn's disease and for psoriasis and so now her gut is

under good control and her skin is cleared up.

Dr Joel M Gelfand: And so she's just back to her normal self at this point in time. And so that's the key, is to understand how the therapies interact with these different disease states. There are some drugs that you may want to avoid. For example, if someone has multiple sclerosis, an autoimmune disease, and psoriasis, we would avoid things like TNF inhibitors like Adalimumab, for example, which we know can aggravate multiple sclerosis.

David: I really have three more questions here that I want to toss out to you in the last couple of minutes that we have. I'm here in Flint, Michigan, you're in Philly, temperate zone, we get 102 degree temps in the summer and right now 20 degrees in the winter. Can you talk for a few minutes about weather as triggers for psoriatic flare ups?

Dr Joel M Gelfand: Weather it's certainly a trigger for many patients with psoriasis. When the weather gets colder and drier, the skin is itchier for a lot of people, scratching the skin or rubbing the skin creates a phenomena we call the Koebner Phenomenon, where essentially when we scratch our skin that's like a signal to the body's immune system that something's wrong and then it triggers psoriasis and nose patches. When the weather's warmer, especially in the influence of ultraviolet light that tends to be helpful for people with psoriasis. Now, ultraviolet light, as we talked about earlier, from the sun, is not always effective enough on its own. And we know that because we have ultraviolet centres in Hawaii and Florida. Hence we know that the medical use of ultraviolet light, where it's a single wavelength of light, what we call 311 – hat's much more effective for controlling the psoriasis. And so a lot of my patients prefer intermittent treatment, they may come in for a course of white therapy in the spring or winter to get disease controlled, but then they could stop it in the summer.

Dr Joel M Gelfand: They're pretty mild anyway with natural sunlight, and better weather. And some of my patients choose the same approach with their oral medications or their biologics.

David: Two more questions and then I'll hand it back over to Priya. My background is actually in zoology, I've done a lot of genetics work. Can you talk for a few more minutes you opened the show with that about whether or not in your view the expense involved in genetic counselling is worthwhile as a predictor for psoriasis in offspring?

Dr Joel M Gelfand: Well, I think that's important for patients to be aware of what the genetic underpinnings of psoriasis are. So one is, as I mentioned earlier, about 40% people have a family history of psoriasis – that means most do not have a family history. And so that's often reassuring to patients, but some patients feel like well, why am I the only one in my family that has to deal with psoriasis? Well, that is the nature of the complexity, the genetic patterns of this disease state, and that's a normal part of this disease experience. And then the second thing is a lot of my patients will say I'm so devastated with my psoriasis, I would never want to have a child who had to deal with the same psoriasis. And for those patients, I help them understand that one is that the likelihood that their child develops psoriasis over their lifetime is still relatively low, probably about 20% or so, that certain things can be done to lower their risk of developing psoriasis like if they maintain a healthy body weight and don't smoke, that lowers the risk of developing psoriasis over time.

Dr Joel M Gelfand: And then also typically, if one person has severe psoriasis, the children may have mild psoriasis and maybe less impactful for them. And then finally, look at all the progress we're making. My patients always like to say, I don't have my dad's psoriasis because now we have so many better options now. And so I hope my patients feel reassured that they want to have children that they should they should go ahead and have biological children that they wish to and not think of psoriasis as a limiting factor in that respect.

David: My last question. You did touch on this for a few moments, Priya mentioned this as well, that there was a big comorbidity study that was released, I think back in like October, so maybe September, about psoriasis and comorbidity. Can you speak to that and some specific kinds of cancers and what you think the

future is for that sort of medical research, that's our relationship as a predictor.

Dr Joel M Gelfand: Yes. So we covered some of that ground earlier. So I'll touch on some new points that you brought up. One is in the realm of cancer, I think generally speaking, the best data suggests that people with psoriasis probably are not more prone to cancer in general, that some of the cancers we see we pick up maybe due to other factors like obesity or smoking or alcohol use, for example. Certain types of cancers like lymphoma seem to be more related to psoriasis. We think that chronic inflammation could promote lymphoma, but that risk is pretty low and therefore patients really shouldn't be too alarmed by that information. Clinicians need to know that sometimes the type of lymphoma of the skin called T cell lymphoma, that often look like psoriasis. So we need to make sure we have the right diagnosis for our patients. But again, that's a pretty uncommon thing for people to have to worry about.

Dr Joel M Gelfand: And then, patients should take advantage of what we know helps lower the risk of complications from cancer. So, colonoscopy screening of cancer when you're in your late 40s or early 50s, mammograms for women when they're in their 50s or older, sometimes in the 40s. Those types of screening modalities can do a lot to lower a patient's risk of developing cancer that could be treated early and preventing a bad outcome.

David: This just popped in my head as I was listening to you, one of the things that's going on right now in melanoma research are RNA inhibitors, the inhibitor pathway. Do you know about any research that's going on in that sort of area with psoriasis treatments?

Dr Joel M Gelfand: Yes, there are a variety of approaches under investigation either at a very basic level, like animal web model level or starting to get towards human studies where people are looking at things like epigenetic regulation, RNA regulation of inflammation. So those are pathways that are being evaluated by companies and scientists.

David: Very cool. All right. Thank you, Dr. Priya. Those are my questions, back over to you.

Priya: Thank you, David. Thank you very much. Dr Gelfand, we can take some questions from the audience. I see many more on light therapy. So I'll pick one – how effective is balneo phototherapy for psoriasis?

Dr Joel M Gelfand: Balneo Phototherapy, which is essentially like going to the Dead Sea, for example, soaking in water and ultraviolet light. It could be pretty effective, but obviously pretty inconvenient. And so, medical phototherapy in our hands is quite effective. We published a paper in one of our journals, the Journal of the American Academy of Dermatology, where use of phototherapy was about as effective as treatment with a biologic called Adalimumab, which is a pretty effective therapy. Now of course, treatments always individual for patients and so for some patients it is not as effective as in others and the other issue is that with phototherapy, when you stop it the disease comes back. And so for some patients, it's not a great choice because some people don't want that sort of a yo-yo effect where it's like their skin is clear, but then starts coming back again and it's clear again and starts coming back. That's part of the reason why we're doing this study of home phototherapy versus office phototherapy.

Dr Joel M Gelfand: This is called the LITE Study funded by the Patient-Centred Outcomes Research Institute or PCORI to see if we can make the delivery of phototherapy more patient centred, where the treatment is done in our house using a home unit. And we think that's it's likely to be as effective and safe as was done in the office but we're, that's research is ongoing now.

Priya: Okay, thank you, doctor. We have minute more so I am going to just have a wrap up question for you, Dr. Gelfand. It would be great if you could talk about some of your research, and what the future treatments of the psoriasis look like?

Dr Joel M Gelfand: Yeah, so I think the biggest things we're working on currently is a series of clinical trials, designed to better understand the effects our therapies have on the cardiovascular system, trying to

understand what they do to the inflammation in the arteries, what they do to how our body processes cholesterol, the effects they have on atherosclerosis so that work will continue to emerge, and hopefully we'll have a better understanding over time if whether or not we're able to lower cardiovascular risk just by treating psoriasis through our therapies. A second major form of research is better understanding how ultraviolet light therapy, delivery to more patient-centred manner could work. And hopefully through that research, we're doing a study of 1050 patients across the United States. Hopefully we'll be able to shift care to be more patient-centred, so more patients could access to a highly effective therapy that can be done at home on their own schedule.

Dr Joel M Gelfand: We also continue to do these large population studies where we found people with psoriasis of varying disease severities to understand how body surface area predicts health outcomes over time, that will give patients more empowerment so they could understand well, what are my risks, given my individual psoriasis severity where I need to be concerned about. And I think more broadly the communities, continued events, work in biologics as new biologics being investigated that may have even higher efficacy compared to what we have in the market currently. They're small molecules, things that are pills that can be taken by mouth that may improve upon the efficacy of what we have currently available in the market. So, stay tuned, each week there's roughly 50 to 70 new scientific publications in peer reviewed literature about psoriasis, knowledge is expanding rapidly, and with that expanding knowledge, so is the treatment landscape we have to offer our patients.

Priya: Thank you very much. Dr. Gelfand. Dear audience, psoriasis is one of the most common skin ailments affecting about 2% of the population across gender, age or socio economic status. The impact of this autoimmune skin condition goes much deeper with as we heard, cardiovascular disease, inflammatory arthritis and other immune system related conditions. However, as Dr Gelfand was saying a lot of research is going on, new drugs are coming in, so this has made management of the condition better. Dr. Gelfand, thank you so very much for your time and all the information that you've shared with us and our audience today. David and Howard, thank you for participating and for those great questions bringing in the patient's perspective. We also thank the University of Pennsylvania and its office of clinical research. This talk will be available on curetalks.com Please visit our website for details and upcoming talks. Thank you everyone and have a great day.