TRANSCRIPT

S2.E8 Hypopigmentation

Dr Blake Mumford: *I knew it was going to be a problem when I'd just finished lunch with a friend and she said, "You have something on the side of your mouth." I was working in New York City as the entertainment reporter. I was 26 in the biggest city at the biggest station and on the top-rated newscast. There wasn't any food on my mouth it was my skin.*

Welcome to Season Two of The *Spot Diagnosis*, a podcast about all things dermatological. Brought to you by the Skin Health Institute in Melbourne, Australia.

I am Dr Blake Mumford education and research fellow at the Institute. I have a new co-host with me today, Dr Aaron Robinson, who will be filling in a few episodes for Associate Professor Alvin Chong. Dr Aaron Robinson is a Consultant Dermatologist at the Skin Health Institute and an adjunct senior lecturer at the University of Melbourne working in both public and private dermatology clinics. Welcome, Aaron.

Dr Aaron Robinson: Thanks, Blake. Today's episode will focus on skin disorders which cause skin hypopigmentation and depigmentation. The opening quote comes from a journal article, Vitiligo: Patient stories, self-esteem, and the psychological burden of disease. It's a patient story of an African American newscaster who was diagnosed with vitiligo. It highlights the devastating impact the disorders of pigmentation can have on a person's career and wellbeing.

Our guest speaker today is Dr Michelle Rodrigues. Michelle is the founder and director of Chroma Dermatology, a dedicated dermatology center that specialises in the treatment of skin pigmentation problems and for those with skin of colour. She's the co-founder of the Skin Health Institute's Vitiligo Clinic and a senior lecturer at Melbourne University. She's also a senior consultant at the Royal Children's Hospital and has published extensively in journals and dermatology textbooks in this field and lectures both locally and internationally.

Recently, Michelle was awarded the International League of Dermatology's Young Dermatologist Achievement Award in 2019 in recognition of her contribution to dermatology globally, and for her work with underserved communities. Michelle, welcome to The *Spot Diagnosis.*

Dr Michelle Rodrigues: Thanks for having me on, Aaron.

Blake: Michelle, to start us off, we'd like you to share with our listeners a fun obscure dermatological fact they might not know. Does anything come to mind?

Michelle: Yes, sure. Michael Jackson did have vitiligo. This is actually an auto-immune condition that causes spots of white skin to develop and it's likely that he developed his first spot on his hand, and this is probably why he wore that famous glove.

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Blake: Disorders of hypopigmentation and depigmentation have troubled humans for millennia. Depigmenting macules were first described more than 1500 years BC by the ancient Egyptians. Hippocrates gave the first European description of vitiligo but failed to identify leprosy as a separate disease entity. Sadly, this was not an uncommon mistake and people who suffered from vitiligo were often shunned in the same way as lepers. This is an issue that still persists in some communities today. Different people have different skin tones, some are darker while others are lighter. Michelle, what gives the skin its colour?

Michelle: Well, melanocytes are small cells that actually make melanin or pigment. The number of melanocytes is actually consistent amongst racial groups. Melanosomes store and transport this pigment and it's actually the size, the density, and the distribution of melanin within the melanosomes that actually give skin its colour. The melanosomes in those with lighter skin are generally small, they're clustered in groups and they're really quickly degraded. The melanosomes in those with darker skin are actually generally larger, they individually dispersed, they're dense, they're oval and they degrade slowly, and they're actually located throughout the entire epidermis.

Aaron: Michelle, can you please explain to us why different people have such different amounts of melanin and what's the purpose of melanin in the skin?

Michelle: Well, there are a whole heap of theories, Aaron, but the most widely accepted modern-day explanation of skin colour is the Vitamin D Sunlight Theory. It's assumed that Homo sapiens emerged from East Africa and that melanin actually developed as an evolutionary mechanism to protect the skin, the hair, and the eyes actually from irradiation and from skin cancer.

Research has actually helped to solidify this because it's shown that the distribution of melanosomes in sun-exposed deeply tanned skin is actually very similar to the distribution of melanosomes in black skin. In terms of the second part of your question, which is the purpose of colour, it really is, in addition to providing protective effects, the source through which many of us find our identity. It can be viewed as an indicator of health and when things go wrong with pigmentation, it can actually lead to significant psychological and social problems, particularly in those with skin of colour.

Aaron: You mention skin of colour, what does this mean?

Michelle: Skin of colour is a term that was coined in North America to describe patients with non-Caucasian skin types. It includes a wide variety of patients with Chinese skin, Indian skin, African skin, Pacific Islander skin. It even includes Middle Eastern, Hispanic, and Indigenous patients. It's a broad group but it's important to differentiate these because patients with skin of colour do have biological, functional, and structural differences in their skin.

Blake: Skin has some ability to adapt to changes in the amount of exposure to UV radiation. Can you tell us what the skin's response is?

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Michelle: Well, this is a pretty complex question, I guess, Blake, because there are many different effects on all different cells within the epidermis and dermis from UV radiation. These can actually be broken up into effects from UVA, UVB, UVC, visible light, and infrared light and each of these affects the epidermis and dermis in different ways, but from a pigmentary perspective, the degree of sun exposure actually correlates with the aggregation of melanosomes and skin that is more sun-exposed will have less aggregated melanosomes compared with non-sun exposed sites.

Ultraviolet light definitely causes increased melanin synthesis and redistribution of melanosomes, but, ultraviolet light A and visible light seem to cause more sustained darkening of the skin, particularly in those with skin phototype four, five, and six. I guess the other important response that the skin has is its response to UV radiation in the synthesis of vitamin D. Vitamin D3 is a pre hormone that's really essential for proper bone formation and has a functional role to play within our immune system. The main way of providing the human body with vitamin D is actually its synthesis in UVB exposed skin.

Aaron: Unsurprisingly, there are skin disorders which can affect the skin's pigmentation. Some make the skin lighter and others can make the skin darker. In this episode, we're focusing on disorders which make the skin lighter. Now, our listeners may not realise that there's a subtle difference between hypopigmentation and depigmentation. Michelle, do you mind explaining what these terms mean and how they're different?

Michelle: Sure. Look, while textbooks will often discuss melanopenia versus melanocytopenia, to make things simple I think we can define things as hypopigmentation if there is a state in which there is a decreased number of melanocytes and or melanin, whereas depigmentation is a state in which the skin has a complete absence of melanocytes.

Differentiating between hypo and depigmentation is really important because it helps us decipher one condition from another. Figuring this out is pretty easy in those with skin of colour, but for lighter skin, it can be quite difficult. In such cases, it's really helpful to use a tool such as a Wood's lamp which actually will shine an area more brightly white if there is an absence of pigment.

Aaron: Thanks, Michelle. Let's start with hypopigmentation first. Can you tell us what sort of skin disorders cause hypopigmentation?

Michelle: Hypopigmentation can result from many skin conditions ranging from fungal infections and eczema, which cause inflammation in the skin, and afterwards, we see post-inflammatory hypopigmentation through to primary cutaneous issues such as sarcoidosis or even iatrogenic things such as topical steroid use or the incorrect use of a particular laser or a particular laser setting. This generally happens because inflammation can block the transfer of melanosomes to keratinocytes and the melanosome congested melanocytes actually result in the dilution of colour that we see on the skin.

Blake: I think it's time we gave our listeners a bit of a quiz now. I'm going to read a clinical vignette and then we'll give you a little bit of time to try and guess what you think the diagnosis is. Are you ready? Tyler is a 25-year-old male who works in the construction industry. He's an avid bodybuilder and attends the gym most days. Summer has just rolled around, and his girlfriend has noticed some

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white-coloured spots appearing on his back. When examining him, you note several patches of hypopigmented skin with some slight scale. Okay, listeners, you have until the end of the countdown.

Michelle: Blake was describing pityriasis versicolor. This is caused by a fungus, Pityrosporum ovale, also known as Malassezia furfur. It's actually a superficial skin infection that causes white spots to develop mainly on the trunk, the arms, the neck and the face. It can appear pretty scaly too. Anyone who gets it is usually people who live in warmer climates, people who sweat a lot, people like Tyler who actually work out a lot. It's really easy to diagnose clinically in most cases but if there is doubt, a skin scraping can be taken. With a little bit of potassium hydroxide preparation, you can see under the microscope this pretty neat spaghetti and meatball appearance.

Blake: What can Tyler do to try and get rid of these spots?

Michelle: There are various ways to treat this, but I think a topical anti-fungal shampoo, cream or lotion is a really good place to start. Commonly we use Ketoconazole, starting at about 2% for 10 to 15 minutes before rinsing it off daily. This can be done for about a week. It's really important to educate the patient on making sure that they do some kind of maintenance treatment, perhaps weekly for at least a month.

If they're prone to swimming, they work out a lot or recurrence is common, then it might be relevant to consider maintenance on a longer-term basis. Sometimes topical anti-fungal agents can be used in addition to the shampoos. Occasionally systemic therapy is also needed. Things like Itraconazole, could be considered for really extensive or recurrent pityriasis.

Blake: I take it when it gets to that point, you're probably wanting to refer to a Dermatologist, is that right?

Michelle: Indeed, that'll be a good thing to do.

Aaron: Thanks, Michelle. You've just discussed pityriasis versicolor. What's pityriasis alba and how is this different?

Michelle: Pityriasis alba's not actually a fungal infection. It's a common self-limiting eczema kind of condition that affects mainly young children with skin of colour. It's characterised by little white or white to tan macules and patches with really indistinct margins and some fine white scale on it. Occasionally kids will describe a bit of itch but it's often asymptomatic. It can be associated with atopy, things like eczema, asthma, hay fever.

No tests are generally needed to diagnose it, it's a clinical diagnosis. Rather than using topical antifungals, of course, because it's not a fungal infection, we can actually treat this very reasonably with gentle skincare, soap substitutes, good amount of moisturiser, very rarely mild topical steroids or calcineurin inhibitors are needed but that's mainly for the patient group that has that itch or visible inflammation within their spots.

Blake: Are these hypopigmented patches permanent or does it self-resolve?

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Michelle: Generally, the lesions will self-resolve over years. They won't leave permanent scarring at all.

Aaron: Michelle, you mentioned vitiligo before, vitiligo would be the disorder most of our listeners would recognise as a skin disorder which causes depigmentation. Michelle, what do you look for when you suspect that someone might have vitiligo?

Michelle: The main difference with vitiligo and other disorders of pigmentation that we've discussed earlier is really that vitiligo is a true disorder of depigmentation. Meaning there's a complete absence of melanocytes in affected skin. Vitiligo usually presents with depigmented patches on the skin. The first lesions are usually seen on the face, on the hands and on the feet. Really visible sites. It can also involve the lips, the genitals and the hair. It will present often for the first time in children or adolescents and occasionally young adults.

I generally like to use a Wood's lamp in making that diagnosis if a patient has lighter skin types as we mentioned earlier. In terms of vitiligo itself, I think it's really important to look for those other potential autoimmune conditions that can be associated with vitiligo. We know that vitiligo is an auto-immune disease. In that respect, it's no different to, say, Type I diabetes, rheumatoid arthritis or even coeliac disease. In this, the autoimmune cells actually cause destruction of the melanocytes, turning the affected skin and sometimes even hair completely white.

As mentioned before, I tend to look for potentially other autoimmune conditions in this group as well. About 15% of patients with vitiligo will have autoimmune thyroid disease. I firmly believe that we should be checking thyroid function tests in all patients with vitiligo. It's also associated with other autoimmune diseases too. It's important to ask the patient about symptoms of things like autoimmune joint disease, lupus, diabetes, coeliac disease, anemia, pernicious anemia as some examples.

Aaron: Michelle, how do you confirm a diagnosis of vitiligo?

Michelle: The diagnosis is usually a clinical one, rarely a biopsy may be needed to differentiate it from other causes of hypo or depigmentation. In general, clinical, plus or minus a Wood's lamp, is really all we need to do.

Blake: What treatment options are available currently and are there any new treatments that might be available in the near future?

Michelle: Blake, this is a really good question. I guess before we get into this, I just wanted to highlight something very important for the listeners. It's really important for us as clinicians to take time out to find out how the vitiligo is actually affecting the individual.

I think early in the introduction, Aaron did mention that disorders of pigmentation can often cause things like depression and difficulties in social and everyday life. It's true for vitiligo that things like depression, adjustment disorders, anxiety and self-esteem issues all result from vitiligo and they've been well-documented in the literature. I think it's important for us to find out how the vitiligo is affecting the individual.

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Also appreciating that in some cultures, till today, it's a really highly stigmatised skin disease and can have real and devastating effects on everything, from employment opportunities through to marriage prospects. I think once we've delved into that and that certainly is part of the management plan of the patient, topical steroids mainly strengths that are moderately potent or potent and above, calcineurin inhibitors, vitamin D analogues, and phototherapy are all really mainstay treatments for patients with vitiligo, particularly if it's widespread.

There are localised laser treatments available called excimer lasers and this can be used for very early localised lesions. The main issue here is access to treatment, although we have an excimer laser at the Institute, it would mean that the patient would need to be able to come in and have this treatment multiple times a week. Unfortunately, it's not rebated under Medicare. Occasionally for progressive rapidly aggressive disease, we can use systemic immunosuppression. That can control the progression of the disease.

In terms of new treatments, this is a really really exciting time for those of us that are interested in the area of vitiligo because the last five years has been especially exciting. We've had things like JAK inhibitors like Tofacitinib and Ruxolitinib which have demonstrated in research papers to improve not only stability of the lesions but also re-pigmentation. We need further research in the area to confirm how these can be used, and more importantly, how we can attain more durable responses.

I think these durable responses are likely to come in the future from IL-15 blockers. I'm really excited to see how these new treatments can really help us Dermatologists and add to our treatment armamentarium.

Finally, I'll say that there are some patients who do present with really extensive disease. They have small islands of normal pigment left behind. They can often desire to have a more even skin tone. In these very rare cases, we can actually use depigmenting agents in the form of a cream called Monobenzylether of hydroquinone. To depigment someone is a very big process psychologically. This needs to be entered into with absolute caution and complete discussion with the patients from all aspects of their condition.

Blake: Wow. Sounds like there's some exciting new treatments on the horizon for vitiligo. Michelle, if I'm a GP and I've got a patient who I think is presenting with new vitiligo, at what point should I consider referring to a Dermatologist?

Michelle: I really think, Blake, that it's important to refer early because without treatment and without the correct treatment or the correct combination of treatments, most patients will experience progressive worsening of their skin. The longer the duration of vitiligo, the more treatment-resistant the lesions can become. Occasionally there are conditions that look very similar to vitiligo as we've discussed. Missing that diagnosis and treating with topical antifungals for example, may change the course of disease completely for that patient.

I think a key point to take from our podcast today is that really early treatment, ideally within the first 12 months, will actually give the patient the best possible chance of re-pigmentation. More importantly, it can give us time to optimise their psychological and social well-being.

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Blake: That sounds like good advice, Michelle. Finally, do these depigmented areas in vitiligo, do they spontaneously regress or get better on their own or is it more that you see a progressive course?

Michelle: In most cases, Blake, it's progressing. I have seen a few cases where patients have described a spontaneous repigmentation, but I rarely think this is spontaneous. It's probably a result of incidental ultraviolet light exposure outdoors, plus or minus other environmental factors that might play a role in some very small, mild lesions but the majority are unfortunately progressive without treatment.

Aaron: Michelle, just briefly, what are some of the other skin conditions that can also cause depigmentation?

Michelle: Well, there are many of these Aaron, and the vast majority of other depigmenting conditions are actually congenital, meaning people obviously are born with these from birth. There are some other ones to consider. Nevus anaemicus is a primarily vascular anomaly, which can occur mainly on the chest of the individual or the upper back area and it can look quite depigmented. One of the clues is that the area surrounding it will have an area of hyperemia or erythema.

The second one is naevus depigmentosus and naevus depigmentosus generally speaking, will look similar, but at closer inspection, will actually be hypopigmented rather than depigmented, so the name is actually a bit of a misnomer and can get confusing. There are other conditions as well to think about, sarcoidosis can look very similar to vitiligo in some rare cases and T-cell lymphoma of the skin can also look similar sometimes. There are many differential diagnoses. We've mentioned a few just now, but there are many to consider.

The other one of course is albinism, which people will know and recognise that this is a congenital condition with the absence of melanin, but vitiligo is acquired not congenital.

Blake: Michelle, finally, just before we let you go, can you tell us a bit about the outreach work that you and your clinic are involved in and perhaps give us some examples of disorders of depigmentation and hypopigmentation that you might see in these communities?

Michelle: So, we were really fortunate in 2016 to be able to undertake a trip out to these rural villages within India. I mustered the courage to ask a couple of colleagues, Dr. Celeste Wong, who's now a colleague of mine at Chroma Dermatology, Dr. Gary Raj, who's a Dermatologist in New Zealand, and a local pharmacist, Manisha Cor, and we got together and planned a trip, a series of visits out to rural communities and did a couple of things.

Number one, we provided on the ground clinical services from a dermatology perspective to these communities. We saw all sorts of things, fungal infections, scabies, pityriasis, vitiligo, and other inflammatory conditions like eczema and psoriasis, of course, as well as other very rare infections. Secondly, we were able to provide education to the local community village workers, and these people were very critical in providing on the ground assistance to their villages, they're very respected members of the community, and what we did try to do is work with them to discuss with them how scabies, for example, is contracted, how it can be treated, how patients can be looked

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after if they do develop these things or entire villages, and we also tried to bust some of those myths surrounding pigmentary disorders, in particular, things like vitiligo and melasma.

What was really interesting was that many of these communities have firmly fixed beliefs on how and why things like vitiligo and melasma can occur. We heard stories like people believing that vitiligo was a curse from God, right through to people feeling that vitiligo was contagious, and perhaps this goes back to the fact that leprosy looked very similar back in the day and there still is that misconception if you will. We really enjoyed the trip to India, and I must also give kudos and thanks to the American Academy of Dermatology who provided a substantial grant for us to be able to provide that education and preparation.

The second project was actually out in Fiji and that was last year. We partnered with Pacific Dermatology Limited, and this was an organisation created by an incredible Dermatologist, Dr. Margot Whitfield in Sydney, and she partnered with the ministry of health in Fiji to basically come up with a program that trained and supported local doctors in their journey to becoming Dermatologists.

At the moment, there are no qualified Dermatologists within the Pacific islands, but this program aims to change that and change it sustainably. Being able to be a part of this in some small way has been fantastic. We've been involved through delivery of lectures on pigmentary disorders, pregnancy issues, and we also continue that despite the COVID restrictions on travel, we continue that in an online virtual forum and there too in Fiji there were some interesting pigmentary disorders.

One was hyperpigmentation as a result of drinking Kava, which is a local drink, and it's called Kava dermopathy and it causes dry, itchy, brown, scaly skin to develop. It's a quite an interesting and novel condition for us to see and treat, but of course, there was an abundance of melasma given the climate and the abundance of outdoor work that people over there undertake. Again, it was a good opportunity to hopefully educate and shed some light on these disorders and to bust some of those stigmas and myths surrounding pigmentary disorders.

Blake: Sounds like quite a challenging but rewarding experience, Michelle.

Michelle: It was indeed.

Blake: With that, we'll wrap up this episode. We hope that this episode doesn't pale in comparison to the others. We hope you'll join us next time for our episode on disorders of hyperpigmentation.

Aaron: Thank you, Michelle, for sharing your time and expertise with us today.

Michelle: Thanks, Aaron, thanks, Blake, loved catching up with you both.

Blake: We'd also like to thank Jo Coughlin and Peter Monaghan at the Skin Health Institute.

Aaron: We hope you've enjoyed this episode of *Spot Diagnosis*. Remember, these podcasts are not meant to replace medical advice. If you have a skin condition that requires attention, we strongly

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encourage you to see your medical practitioner. This podcast was recorded using Zoom in the context of stage four restrictions in the coronavirus pandemic in Melbourne.

Blake: Listeners who want more information on the subject, a transcript of this episode and links to other resources can be found on our website, spotdiagnosis.org.au that's spotdiagnosis.org.au.

Aaron: Please share *Spot Diagnosis* with your friends and colleagues. Rate and review us, let us know what you think. We'd really appreciate your feedback and any suggestions.

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