



TRANSCRIPT

S2.E9 Hyperpigmentation

Dr Blake Mumford: 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'm Dr Blake Mumford, Education and Research Fellow at the Institute. My co-host, again, today is Dr Aaron Robinson. Aaron 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. In our last episode, we covered skin disorders which cause hypopigmentation and depigmentation. In this episode, we'll be flipping it around and talking about skin disorders which cause hyperpigmentation. And we're joined again by 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 is also a senior consultant at the Royal Children's Hospital and has published extensively in journals and dermatology textbooks in this field and lectured locally and internationally. Recently, Michelle was awarded the International League of Dermatology's, Young Dermatologist's Achievement Award in 2019 in recognition of her contribution to dermatology globally, and for her work with underserved communities.

Michelle, thanks for allowing us to put you on the spot again.

Dr Michelle Rodrigues: Thanks so much, Aaron. It's really nice to be back.

Blake: Michelle, it's two episodes in a row now, but do you have another fun obscure dermatological fact for our listeners?

Michelle: Well, the famous actor, Morgan Freeman actually has really small spots on his cheeks. I don't know if you've ever noticed them, but they're called dermatosis papulosa nigra which is a really common, benign skin growth that occurs in patients with skin of colour.

Blake: There you go. You'll never see Morgan Freeman in the same way again. Disorders of pigmentation can have a profound impact on the mental health of patients. In certain cultures, darker skin, particularly when it affects the face can have a significant social impact. For example, in a landmark study, it was found that 65% of melasma patients were dissatisfied by their hyperpigmentation all or most of the time. More than half reported embarrassment and frustration, and 40% experienced an impact on their interpersonal relationships.

Michelle, before we get started, could you give our listeners a bit of a quick recap of what gives the skin its pigment and how it is produced?

Michelle: Melanocytes are small cells that make melanin, or pigment, that's the pigment, or melanin, and that actually gives skin its colour. But the number of melanocytes is actually consistent amongst different racial groups. It's the melanosomes that store and transport the pigment that actually have the subtle differences within skin colours. So, it's the size, density, and distribution of the melanin within the melanosomes that actually gives skin its colour. So, those that have lighter skin generally have small clustered groups, those that have darker skin generally have larger individually dispersed and dense groups throughout epidermis.

Interestingly, one of the main protective effects of melanin is to prevent skin cancer and help protect us from UV irradiation.

Aaron: If getting a tan is the body's way of adapting to UV exposure, does having a tan provide protection from skin cancer? And is a tan healthy?

Michelle: Well, there's never such a thing as a healthy tan, but it's interesting to note how different cultural groups actually feel about darker skin. Those in the Western world will see a tan as being a sign of health and prosperity. But those from maybe Asia or Africa to name a few, have deeply ingrained social and cultural beliefs that darker skin types are possibly less attractive, possibly more likely to be associated with lower socioeconomic backgrounds. So, I think that's a really interesting perspective to know about.

Of course, the cumulative of ultraviolet light radiation increases the risk of basal and squamous cell carcinomas. Blistering and peeling sunburns on the contrary increase the risk of developing melanomas. I think it's important for us to acknowledge that, while some sunlight is important for the synthesis of vitamin D, the amount of sun that's required to get optimal vitamin D levels is actually quite low. And in general, it's not enough to actually generate a tan anyway.

Blake: All right. That's interesting. Michelle, can you explain the difference between a solar lentigo and ephelides? These are two sort of common pigmented lesions that you might see in the clinic.

Michelle: Sure. Solar lentigines are a hyperpigmented macules that are pretty round or oval in shape. And they're common in sun exposed areas of the skin like the face, the backs of the hands. They're induced by natural or artificial sources of ultraviolet radiation, and the incidence increases with age. And in general, they don't really fade as much as, say, ephelides or a freckle would. As I've just mentioned, ephelids, or ephelides, is actually just a fancy name for a freckle. And in contrary to solar lentigines, they're actually an inherited characteristic. They're light brown or tan spots on the skin.

Of course, freckles are more common in those with fair-skinned, Celtic skin types, people with skin phototype one. That's people that have red hair will often have freckles. Melanocytes produce more pigment than usual within these lesions and they're pretty prominent in summer.

Aaron: Michelle, I imagine that melasma would be a common issue you deal with your patients. What is melasma and which patients are at risk?

Michelle: Melasma is a really important one, and I'm glad that we're raising this. Because I think we see literally hundreds of patients with melasma every month at Chroma Dermatology. And it's a really chronic and relapsing condition of hyperpigmentation, and I think it's important that we don't just dismiss it as being merely cosmetic. And the reason I say this is it can really adversely affect a patient's quality of life. And it's been well-documented in research globally. What's interesting is that it actually affects all groups across all ethnic groups in a very similar way.

However, the people that are more likely to be affected are patients that are female, patients who've, potentially have lots of outdoor exposure, those with darker skin types. So, it presents commonly as light brown patches on the skin, and it can be seen on areas like the forehead, malar region, even the upper lip and the chin.

Blake: Why does this happen, Michelle?

Michelle: Those that are sort of involved in melasma research are really still trying to work this out, because it's an incredibly complex and multifactorial condition. We used to think that this was predominantly hormonal. Women would get it. If you were on the oral contraceptive pill, you might get it. And it was even called 'hormonal pigmentation'. But the reality is that patients can get it when they've had none of these exposures or none of these risk factors, and even men can get it on occasion. At this stage, we think it's due to a combination of both genetic predisposition, ultraviolet light, visible light, and heat exposure, as well as hormonal and vascular influences. It's really quite complex.

Blake: Our listeners may have heard the term, chloasma before. What does this term mean?

Michelle: Chloasma is exactly the same as melasma. So, it's just another word to describe exactly the same condition.

Blake: Is one term preferred?

Michelle: I kind of like using the word melasma because it's more inclusive in the literature, and there's certainly more documented on it. I think the word 'chloasma' is gradually being faded out really with time. I much prefer the term 'melasma'.

Blake: I see what you did there Michelle

Blake: Do you ever need to biopsy to confirm the diagnosis or are there any other helpful tests?

Michelle: Well, melasma is usually a clinical diagnosis but rarely, a skin biopsy is needed to differentiate it from other conditions. The main one being exogenous ochronosis, which is a condition that's caused often by application of topical agents, that tend to darken the skin, over time. And it's an undesirable side effect of these topical agents. Things in particular that can cause this is, you know, high doses, prolonged use of hydroquinone, resorcinol and other heavy metals.

Aaron: What are some of the management options for patients with melasma?

Michelle: I think the most important thing is photoprotection, and it's absolutely critical to make sure that the patients are wearing sunscreen, that they're wearing it every day, that they choose sunscreen that they're likely to commit to using in the long-term. Visible light protection is also very important, so it's important to discuss that with the patients. In terms of topical therapy, there's such an abundance of topicals at the moment, both prescribed and over-the-counter. The gold standard is still hydroquinone and it can be purchased over the counter in a concentration of 2%.

Higher concentrations can be obtained with the prescription, but it really shouldn't be used for more than a few months at a time. Because prolonged use can cause skin irritation, allergy, and that dreaded ochronosis that we talked about before. In addition to this, there are potentially skin-directed therapies like certain chemical peels, laser and energy-based devices that have been reported for melasma. But what I will say, an important factor is that laser and device therapies can actually irreversibly worsen this condition.

And I think that those of us that specialise in melasma will often see these tragic cases of worsening of melasma over time with multiple different laser and energy devices, radiofrequency devices. So, I think that they really need to be avoided. And despite Chroma Dermatology seeing a significant number of patients with melasma, and despite us having quite difficult cases, often referred by other Dermatologists, I would say that the use of energy-based devices is literally less than 2% of the patients that we see.

There's also finally, systemic, tranexamic acid reported, but there is a risk of arterio-venous thromboembolism. And this risk has been heightened or increased as a result of the COVID pandemic. So, I think it's certainly best for patients to discuss this directly with their dermatologist. And I think at this time, dermatologists will be quite cautious with this going forward. And I think the other thing to tell the patients in the management is that this is chronic and relapsing. So, anyone who thinks that they can kind of remove this with a cream or a lotion or potion, really needs to think again and be educated on the realistic outcomes from treatment.

Blake: Michelle, you're referring to the increased, hypercoagulable state that COVID-19 infection can cause when you're talking about the risk of tranexamic acid, is that right?

Michelle: That is right, there's been multiple reports of increased arterial and venous thromboembolism, so DVT, PE, stroke, in particularly young, healthy, and otherwise normal, functioning, adolescents, sometimes. So, this has been quite scary. And I think, adding to it a treatment that could possibly increase this risk is something that we should probably all be avoiding right now.

Aaron: Thanks, Michelle. What's the natural history of melasma? And does it ever self-resolve?

Michelle: Well, for some patients, interestingly and this is a small proportion they'll say they got their melasma potentially during pregnancy, and now it's all settled. But the vast, vast majority of

patients will describe chronic relapsing lifelong conditions, unfortunately, and it doesn't seem to get better necessarily after menopause.

Blake: There are a few medications which are known to cause issues with hyperpigmentation. Some of our listeners may know these already, so I'll make this a bit of a quiz again. Can you guess three medications which cause hyperpigmentation before the timer is up?

Michelle: In that time, you may have thought about many medications that can induce pigmentation. But the three main ones that come to mind are amiodarone which can cause a bluish tinge on the skin. Minocycline which can cause a blue gray pigmentation predominantly on sun exposed sites of the skin, and the same with cumulative exposure over many years or decades. And finally, hydroxychloroquine and this can cause a brown muddy pigmentation, predominantly on the anterior shins and within scars.

Blake: Acanthosis nigricans, as the name suggests, is a disorder which causes hyperpigmentation. What is it exactly?

Michelle: Thank you so much for bringing this up, Blake, because acanthosis nigricans is an increasingly common condition that I'm seeing at Chroma Dermatology. And the reason is because it causes velvety hyperpigmented plaques, mainly in the flexural areas like the neck and the axilla, but it's really important to recognise and it was first described in 1975, as many of the listeners probably know, you know, in a pretty landmark study that showed that there were important cutaneous signs of insulin resistance. It's also seen in obese individuals, patients that have polycystic ovarian syndrome, and, you know, even other hormonal conditions, such as acromegaly or Cushing's.

Very, very rarely, acanthosis nigricans can be seen in an extensive form and it can even involve mucosal surfaces. But this is a really, really rare subtype, and it's seen in those patients that actually have malignancies.

Aaron: So, Michelle, how do you approach treatment? And does treating the underlying disease help in acanthosis nigricans?

Michelle: I think holistic care is really the key, and involving the general practitioner if possible, to really help educate the patient on the importance of diet, exercise, nutrition planning, all those things that are critical to improving insulin resistance overall. And I will often explain to the patients that lifestyle factors really are the key. Nothing that we do topically or in any other fashion, is ever going to get rid of this completely, that the biggest and most important factor is those lifestyle things that need to be addressed. So hopefully, the general practitioner is happy to work with the dermatologist to assist in that and from the dermatologist and starting something like a topical keratolytic, like a retinoid to try to flatten and lighten the affected areas is a good option. But without treatment, things will often progress. And I think if a patient is unwilling or unable, for whatever reason to really engage in a good diet, exercise, and nutrition plan, it's going to be pretty difficult to manage.

Blake: I'm sure our listeners are probably wondering what the acanthosis part means as well. Michelle, what does that mean?

Michelle: That's really interesting. So, acanthosis is a term that we use to describe thickening of the epidermis. And that's certainly what we see and what we feel when we touch the areas that are affected by acanthosis nigricans. You can feel that it's raised and velvety and a very fitting name.

Aaron: Michelle, just briefly, could you tell us about some of the congenital disorders which cause hyperpigmentation?

Michelle: There are a really vast array of congenital disorders that present with hyperpigmentation. Some of them actually have systemic associations, like incontinentia pigmenti, and LEOPARD syndrome, for example, that may involve other body systems. And so, it really is important to know that any child who's born with any form of hyperpigmentation really should be referred to a Dermatologist for further evaluation. And when these children get to us, depending on what things look like, we may need to refer to a multidisciplinary team.

If it's as simple as a café-au-lait macule or a congenital melanocytic naevus it might be something that we can manage on our own. But in many cases, I'm taking these patients to the Royal Children's Hospital with me at that clinic to be evaluated by pediatricians and other relevant specialists.

There are also other things that cause more localised congenital hyperpigmentation. An example of these include things like Mongolian spots; this is commonly seen in those with skin of colour. It has a slate brown or bluish tinge plaque, it's often seen in the sacral or lumbar region of infants. And it's due to failed migration of melanocytes from the neural crest across to the basal layer of the epidermis and the second one is naevus of Ota. I know this is one of your favorite diagnoses, Blake, which is a dermal melanocytic hamartoma, and it's common in those with Asian ancestry, usually distributed along with first and second branches of the trigeminal nerve, and it generally looks pretty blue-gray. It may actually involve the sclera of the eyes, so it's important to have a look there as well.

You know, there are so many other interesting pigmentary disorders that, you know, we see and treat at Chroma and Royal Children's, but I guess we'd need another episode to discuss them all.

In summary, definitely important for patients with congenital hyperpigmentation to be referred so that systemic associations can be considered and evaluated further if needed.

Blake: Naevus of Ota sounds like it might be something out of Star Wars. And with that, we'll bring our episode to a close. We hope this episode has brought some colour to your day. Thanks for joining us for this episode.

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

Michelle: Thanks so much, guys. I've had a really, really fun time with you.

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

Blake: For listeners who want more information on this 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.

Alvin: For Australian GPs listening, you can receive RACGP CPD Activity points for listening to *Spot Diagnosis*, we are also running workshops for GP's. Further information is available on our website at spotdiagnosis.org.au.

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