Dermatologically Tested Podcast

16. Dr Thivi Maruthappu on being a skin detective

Matt Gass 0:15

Welcome to another episode of Dermatologically Tested, the podcast of the British Association of Dermatologists. Today we are talking to a bit of a skin detective, as our expert specialises in spotting the clues on the skin of underlying diseases, particularly genetic disease,

Harriet Dalwood 0:29

I have no idea what to expect with this topic and I'm really excited to find out more to be honest.

Matt Gass 0:35

Genetic disease is not something that I'm really knowledgeable about. So yeah, obviously, there is a genetic component to a lot of skin disease, but you know, I think this should be really fascinating and I think we'll be sort of straying outside of skin disease at points here, because, as I said, this is sort of about spotting the signs of conditions which aren't necessarily skin related.

Harriet Dalwood 0:40

Yeah, absolutely

Matt Gass 0:57

But have aspects on the skin. So, without any further ado, we'll welcome our guest today, Dr. Thivi Maruthappu, consultant dermatologist with a special interest in the skin and systemic disease. Welcome, Thivi.

Dr Thivi Maruthappu 1:11

Thanks, Matt. lovely to be here. Hi, Harriet.

Harriet Dalwood 1:14

Hi, Thivi. Yes, lovely for you to join us. We can't wait to get stuck in and I guess I'll get cracking with the first question. Your interest is in skin and systemic disease as Matt just said, and can you just explain a little bit about what this actually means?

Dr Thivi Maruthappu 1:29

Yes, sure. So, one thing that really fascinates me is how the skin can tell us so much about what else is going on inside our body, and I really became interested in this when I was a medical student. When you're a student, the first thing they tell you, when you examine a patient is have a look at your patient, look at their skin on their hands, look at their nails, look for any changes in the nails that might indicate that they have something else going on. Then you have a look at the skin of their face, and the mouth and their lips. Every single organ system that we studied, there was something in the skin that we needed to look for and it really made me think, wow, the skin is not just protecting us from the environment, it is a clue, it is our guide, and it is really telling us so much about our internal health. That really was so fascinating to me. When I started doing dermatology, the conditions that I was really drawn to were those that had internal features. I specialise in psoriasis, and one of the areas that I specialise in is psoriasis and joint disease, so psoriasis and psoriatic arthritis, and sometimes the first clue that you have arthritis is just a few nail changes of psoriasis in your nail and to me, that's amazing that you can pick up so much just from looking at the skin.

Matt Gass 2:44

Yeah, I mean, I think that's a really interesting perspective to come from and it's not something that I've necessarily considered before, I think this is going to be really interesting. So, you talk about these, I suppose they are clues that the skin gives you, maybe from skin disease, maybe from something else. How helpful is this, particularly for medical professionals to understand this? Also, I suppose there is an element for the general public as well, in terms of educating them about this sort of feature.

Dr Thivi Maruthappu 3:12

Yeah, so that's a really great question. I think it's incredibly important that healthcare professionals are vigilant for skin signs of something else going on, so if we take acne, for example, acne is so common, but if you have additional clues with acne, if someone is noticing that they have hair loss, as well, if their periods are slightly irregular, well, maybe that person doesn't only have acne, maybe they've got polycystic ovarian syndrome, does that need further investigation? Is that going to affect their periods and how they go on to conceive?

These are just the first clues, and a patient may come to you with just the skin symptom but it's asking those extra questions that's going to help you to work out if there is something else going on. I had a patient last week actually, who came to see me with acne and when I asked a few more questions, it turns out they had boils in their armpits and their groin and they had been too embarrassed to tell anyone, and that with acne is the first clue that someone also has hidradenitis suppurativa, which is a chronic inflammatory condition which leads to boils, often in folds and the creases of the skin. That definitely needed further treatment and actually treating the acne and the hidradenitis together. Looking after both elements of their skin condition was really important for that patient and also for their long-term health care as well. Looking at the big picture in your patient, and the same goes in our psoriasis clinic, so when we look at patients who have psoriasis we're always looking to see, have they got arthritis as well because we have so many treatments for

psoriasis, we can start with creams, we can use light therapy, sometimes tablets or injection treatments but if this patient also has an arthritis and that arthritis is severe, causing distress of the joints, now that is irreversible, and we need to be really aggressive with our treatments. We wouldn't just be thinking creams, we would be thinking, right, this patient may need to go on a tablet, or even an injection treatment.

That's when the skin is really giving us clues to more that's going on and there are many different skin signs of internal disease. It's something we learn a lot about, as I mentioned, in medical school, but also for our exams, when we are training to become qualified doctors and hire professionals specialising in certain fields, common questions that come up are, what are skin signs of certain underlying cancers that can be hidden? Sometimes your skin is the only clue that you might have cancer going on and that can present as different specific rashes in combination with symptoms, for example, weight loss, or for example, a lump, but there are clues there, and just asking those few extra questions relevant to that skin condition can help us to work out what else might be going on.

Matt Gass 6:04

Yeah, I mean, that's really interesting. So, I suppose it's a combination of perhaps diagnosing something that wouldn't otherwise be diagnosed or catching something early or catching something that somebody doesn't want to talk about.

Dr Thivi Maruthappu 6:15

Yes, exactly.

Matt Gass 6:16

I mean, I thought the example of the patient who had something more serious that they didn't feel able to talk about was really interesting and challenging, and obviously, we'd say to all patients, don't be shy with your doctors,

Dr Thivi Maruthappu 6:28

Yes.

Matt Gass 6:28

Your doctor has seen it all before, but at the same time, we know that it's not necessarily as straightforward as that.

Dr Thivi Maruthappu 6:35

Absolutely.

Matt Gass 6:36

And it's easy to say that from where I'm sat.

Harriet Dalwood 6:38

I mean you touched upon, obviously, the skin being a sign or a clue that something might not be quite right, and I know that you obviously have a have a keen interest also in nutrition. So, nutrition is something you're particularly interested in, how can our hair and skin be an early warning sign that there might be something off with a nutrition deficit, or something?

Dr Thivi Maruthappu 7:02

So, one of the most common reasons for hair loss, particularly in women, is low iron levels. If someone's coming to you with hair loss, and hair loss can be devastating, people can have clumps of hair falling out in the shower, and that can be absolutely demoralising, it can affect people's confidence so much. If I've got someone coming to me with hair loss, then part of the workup for that is asking them about their diet, whether they're vegetarian, vegan, are they taking any supplements? What are their periods like? if they've got heavy periods, they may be losing a lot of iron every month, and then going on to perform, after examining the patient, relevant blood tests to look for underlying causes.

Iron deficiency causing hair loss is so easy to treat and so rewarding because, you know, if someone's been struggling with hair loss, and it's something simple, like a low iron level, and supplementing that can be extremely important. But again, coming back to, is this a clue of something else going on? Why is their period so heavy? Why are they losing so much blood? If that's the case, then is that something that needs further investigation? That may be something they need to see their doctor about. Have they got fibroids? Is there something else going on? So again, it's using that as a jump board to go and look at something else that might be happening.

Matt Gass 8:19

Fantastic. Yeah, I mean, that's really interesting. There are all these sorts of strands that seem to come together.

Dr Thivi Maruthappu 8:28

Yeah, being a detective, isn't it?

Harriet Dalwood 8:30

I mean, it really is like, truly, looking at all the clues and all the information.

Dr Thivi Maruthappu 8:37

I love that you can work something out from looking at the skin, for example, inflammatory bowel disease can present with skin rashes, and we, as the skin specialist can be the only person to pick it up, and then we have to go on and refer to specialists and that can be incredibly life changing. Something like celiac disease, which so many of your listeners commonly read about and are concerned about, can present with a skin rash, a really itchy rash on the elbows and the knees called dermatitis herpetiformis. Once the patient is identified with celiac disease, if they go on a gluten-free diet, that's the most effective treatment for that rash. So again, that's another really nice clue that something else is going on.

Matt Gass 9:25

Yeah, well, I mean, we saw this a lot during the pandemic, possibly one of the recent examples of this is COVID-19, the various skin rashes that play a part, and I can't remember the stats off the top of my head, but I remember studies showing that in cases with otherwise very few symptoms, skin rashes, were often the only obvious symptom.

Dr Thivi Maruthappu 9:49

Yes.

Matt Gass 9:50

And so yeah, really relevant,

Dr Thivi Maruthappu 9:52

Really relevant and fascinating because the number of different rashes linked to COVID is huge, so we really had to learn a whole new vocabulary for COVID rashes. COVID toes, I mean, that is now in the public vernacular, that was in the Daily Mail, and particularly in children, that might be the only clue that they had a COVID-19 infection.

Matt Gass 10:15

Yeah.

Dr Thivi Maruthappu 10:15

And I've had patients coming to clinic who've had COVID, and they have had severe hair shedding after COVID. Telogen effluvium, which is a shedding of your hair after an incredibly stressful event, sometimes we see it after someone's had a baby, or they've had surgery, but we saw it a great deal after COVID. And I've seen some really bizarre nail changes as well due to COVID that I've never seen before in my career.

Matt Gass 10:41

Well, exactly. Yeah, I was about to say, yes, because with COVID, it's the whole dermatology sort of gamut. It's the hair, the nails, and the skin that, you know, we've seen changes in, and we get a huge number of inquiries from people asking if we can confirm whether or not they've had COVID, based on changes they've had, obviously, that's not something that we can do, but it shows you.

Harriet Dalwood 11:04

Just how prevalent it is.

Matt Gass 11:05

Yeah, and how, I think more and more people are becoming aware of it. Obviously, it's not just COVID, that does this, there's all sorts of things. In fact, that brings me on to an area that you've been particularly interested in, which is the link between your genes and skin disease, but also how there can be this link between the effects that your genes have on your skin, and the effects that your genes have internally. Obviously, that's really fascinating, but quite complex, so perhaps you could explain it broad terms, firstly, what the link is between our genes and skin disease, and then we can go on to tackle the other things.

Dr Thivi Maruthappu 11:40

It's a big umbrella, really your genes and your skin. So, what I was studying during my PhD is mistakes in the gene and what happens when we have these little mistakes or mutations in the gene. How does that show up in our skin? Does that show up anywhere else? I was really lucky to be working in a lab where this was a really vibrant area for research. My PhD supervisor actually identified a gene which gives you thick skin on your hands and feet but also causes deafness.

Why would a gene that causes thick skin on your hands and feet also caused deafness? Well, again, these genes that perform these important roles in the skin, how the cells are connected to one another, are expressed in other areas of the body, they have other roles. That really is the subject of the work that I did in my PhD, the other roles of genes that are important in our skin, and what they do. And one of the genes that I studied was fascinating; we made some really important discoveries on the heart, and the link between the heart and the skin.

Harriet Dalwood 12:50

It would be good to know what the challenges are when treating the genetic disease, which affects the skin, but it would also be great to delve a little bit further into the connections that you did find between the heart and the skin as well.

Dr Thivi Maruthappu 13:03

Yeah, sure. So, when it comes to treating genetic skin disease, really, it is so varied. You can have very mild genetic skin disease with almost no symptoms or signs, sometimes people don't even know that they have it. Or you can have extremely severe genetic skin diseases that start from birth and early childhood, for example, Epidermolysis Bullosa, which is caused by a number of different genes, but the one that we commonly associate with mutations in keratin genes.

Keratins are one of the most abundant proteins in the skin. So, they're clearly important for how our skin cells function and when these genes don't work properly, when there's a mistake in those genes, what happens in these children is that they develop widespread blistering rashes all over the skin, and that can be incredibly difficult to manage. Because at the moment, we can't go back and fix that gene, we are managing the side effects, the downstream effects of that mutation; we're not able to really target the cause of it. So that's why it can be really challenging to treat genetic skin diseases. But it's important to say genetic skin disease is a huge umbrella and there can be enormous variations as well, in the severity of the skin condition.

Matt Gass 14:18

Yeah, I think that's a really important thing to say, because when you think about genetic disease, you think about the more extreme end immediately because that's the sort of more talked about area of genetic disease. But I think that's an interesting point to make, and definitely worth emphasising and I think it's good to just talk about the challenges in treating genetic disease, and presumably, there are challenges as well with getting diagnoses with genetic disease in general, which perhaps we'll come on to this in more detail, but perhaps why it's important to be aware of other signs.

Dr Thivi Maruthappu 14:55

Yes, definitely because the clues can be really difficult to put together, and again, it's kind of like being a detective putting all the different pieces of the puzzle together and working out that actually, this is a fault in a gene that's underlying this condition and inherited fault in the gene. Family history can be really important, so in some of the patients that I studied, asking about a family history and knowing the family tree was really important in picking up who might be carrying that gene.

Harriet Dalwood 15:25

So Thivi, you were a lead author on a paper which investigated the visible dermatological signs of a very rare heart condition. It would be great if you could tell us a little bit more about that, and what you found out in that research paper?

Dr Thivi Maruthappu 15:37

Sure. Yeah, of course. So, in this research paper, we studied quite a rare heart condition called arrhythmogenic cardiomyopathy, which is an inherited disorder of the heart muscle. It's one of those conditions that is so difficult to pick up, because the clues that you have it are so subtle. Sometimes, people can have some palpitations or feel out of breath but it's it can be incredibly

dangerous, because people can have heart attacks very suddenly and it is also a common cause of sudden cardiac death. Arrhythmogenic cardiomyopathy is something we think about when we think about athletes who dropped down suddenly in the middle of a match. That's often what is the underlying cause, they had almost no symptoms before that, and a really normal heart scan, but suddenly, they dropped down during a period of very heavy physical activity or exertion, and so it's something that cardiologists are very vigilant about. The problem is that although it can run in families, there can be very few symptoms that somebody is carrying the disease, so the genes aren't always straightforward and so finding out that somebody has it, picking up the diagnosis is something that the cardiologists do based on a number of different symptoms. We looked at a group of patients who had arrhythmogenic cardiomyopathy, and we worked off a very rare form of arrhythmogenic cardiomyopathy, which is inherited.

You have to carry both forms of an abnormal gene to get it and it typically presents in children actually, very early in life, with thickened skin. That's the first sign, thickened skin on the palms and the soles, along with very curly or very frizzy hair and then these young children go on to develop cardiomyopathy, which can be fatal. These inherited forms are called carvajal disease or naxos disease, and again, these are extremely rare. We took what we learned in the rare form of the disease, and we thought, why don't we look at the common form of the disease, and see if patients have the symptoms and the signs, do they have hair problems? Do they have skin problems? The rare form of the disease is caused by mutations in either one of two genes. One is called desmoplakin, and the other one is plakoglobin, and both of these genes are really important glue, so they stick ourselves together, they stick our skin cells together, and they stick our heart cells together.

So, when they're not working properly, the heart cells can't communicate with each other as effectively and so the conduction of electrical current, electrical impulse, through the heart isn't equal. That is why these patients can develop irregular heart rhythms, and when their skin cells aren't stuck together properly, you think of the places on your skin that undergo the highest stress every day, your feet and your hands, you're walking every day, your whole body weight is going through your feet, you're using your hands multiple times a day, so when your skin is subjected to stress, it responds, because it's not glued together properly, by thickening. So that's how your hands and your feet respond, and we think that you get this curly frizzy hair, because the glue that sticks your hair follicle together, goes at an angle instead of standing up straight. And when it's angled, you get curly hair, and when it's stand up straight, you get straight hair. So that's what we think was going on in the children.

Then we started to look at adults who we knew had the mutations but not inherited in the same way, inherited in a dominant way so they had one abnormal gene. We worked with the heart hospital, who were originally based over at UCL, and then moved to join us at Barts. We looked at all of their patients who carried this gene, and I used to go over to the clinic and I would pick up my patients in the waiting area, examine their hair and examine their skin and see if we could see any features, and to be honest, then I was a bit annoyed with my supervisor because it was on a Sunday, I thought oh, you're getting me out of bed on a Sunday to go and have a look at these patients. Oh, my goodness, I mean, what a waste of my time, this isn't what I signed up for. When I got there, I got the shock of my life, these patients were lined up in the waiting area with curly hair, and I was just looking at them, like, how is this not already published? How can we don't know about this already? That's crazy. So, they were all lined up waiting to have their heart scans. So, I started talking to them all one by one. I just couldn't believe listening to their stories. It was just so interesting, these families had a history going back several generations, in fact, of people in their family who had died

suddenly and that was the only reason that they had been picked up as having Arrhythmogenic cardiomyopathy. So, one of my patients, their sister had died aged 20, playing squash, she died suddenly. After that, the whole family had to be investigated for cardiomyopathy and these patients would send me pictures of their relatives from all over, you know, all over the world deceased relatives so that I could look at their hair because they obviously didn't have pictures of the hands and feet, but the curly hair became such a signature for so many of the patients who had the abnormal gene. In fact, one of them said, oh, we know who carries the gene, because we know they have the curly hair, so they had actually noticed it themselves. So that became a really fascinating project. This was this kind of side project on my PhD, but it ended up taking a lot more of my time, because it just ended up being so interesting and I just personally felt like it was so important that we had clues for these patients and their families. When you hear these stories over and over again, any additional clues that you can have to pick up the diagnosis is going to make a difference. So, it was really rewarding, actually, it was a great project to work on.

Matt Gass 21:47

Yeah, I mean, it sounds amazing. I mean, really, really interesting, and really important. Like you say, I mean, the patients themselves had recognised this, but the clues had never been picked up sufficiently to get published. I mean, that's really, really interesting. I suppose I just wanted to understand a little bit better, what sort of tests are normally done to find this? Because the obvious examples that people will be aware of is when it happens to a sports person, and, you know, I think a lot of people are always amazed that,

Dr Thivi Maruthappu 22:17

Yes.

Matt Gass 22:18

That, you know, in such a professional arena that these sorts of things aren't caught, presumably, it's quite subtle and quite difficult to diagnose.

Dr Thivi Maruthappu 22:26

Absolutely. So, the sports players particularly undergo rigorous screening to see if they have any cardiac abnormalities, and they will undergo yearly screening as well, it is incredibly aggressive because they're so vigilant about it. But the fact is that the condition can occur as it's sudden cardiac death, it's a sudden condition, and the heart can look structurally completely normal before the episode. With arrhythmogenic cardiomyopathy, the way that it's diagnosed, there are taskforce criteria, the ARVC taskforce criteria, they use a whole different load of criteria to make the diagnosis because the features are so subtle, and they're constantly reviewing the taskforce criteria. Patients would undergo baseline tests, each would start off with an ECG 24-hour heart monitoring, Echo, cardiac MRI, that's what my patients were waiting for when I went to see them, they were all waiting to have their yearly cardiac MRI testing, and also more interventional procedures as well. Yeah, they undergo these rigorous tests on a very regular basis, but it is difficult to diagnose the

condition and the symptoms can appear later in life as well, which is why the screening for family members is extended over a period of time.

Harriet Dalwood 23:46

Yeah, I was fascinated to know, if people with ACM, were born with the curly hair, or does it develop later? Or can it just be a mix? Are they sometimes born with curly hair, and then does it sometimes develop later for other people?

Dr Thivi Maruthappu 23:58

So, the curly hair they are born with, in all the patients we studied, the curly hair seems to be there from when they're little. So, there was one of the patients had a two-year-old, and they have very curly hair. And they are like, oh well, you know, she's probably got the gene, which hasn't been tested yet. But even if you have the curly hair, it doesn't necessarily tell you if you're going to have severe cardiomyopathy, or very mild or almost no cardiomyopathy. So, it doesn't necessarily tell you that you will go on to develop a fatal heart condition, certainly not. It's just a clue that you may be carrying the gene, and then how that gene goes on to be expressed or function in that person is dependent on a whole load of other factors.

Matt Gass 24:42

Yeah, so I mean, presumably, the curly hair, it's just another tool in the toolbox for medical professionals. It's not sort of...obviously there's a lot of curly haired people out there, so, you know, yeah, they can't be testing everybody that turns up with curls, but it's just a really useful clue, I suppose if there's other things going on.

Dr Thivi Maruthappu 25:02

And the other side was obviously the skin on the hands and feet. So one of our patients is a podiatrist, she goes, oh, yeah, well, I have weird feet, I know that, I've always had weird feet. A lot of them used to say, I'm always having to scrape off this thick layer of extra skin, I get these really thick bands on my feet, I just thought I had ugly feet. So it wasn't...I wouldn't say it's a really hard and fast sign. Lots of people have those sorts of changes if they do a lot of sport, for example. We have some lovely photographs in the paper of some really characteristic changes in the skin of the feet in some of our patients. And again, that's the stress, that's the area of your body that's going to show stress because you're putting your body weight through your feet. And if your skin cells can't stick together as well as they should do, then that's the response that they have, they thicken to compensate.

Matt Gass 25:54

I know that this has just been one area where you've looked at the genetic clues that play out on our skin and hair. Perhaps you could talk about some of the other research that you've done, because I mean, I find this fascinating going in I know a little bit about genetic skin disease, but obviously, this is genetic disease, you know, outside of dermatology, there's just this dermatological link that you and your colleagues have identified. So yeah, I'd love to hear a little bit more about some of the other research you've been doing.

Dr Thivi Maruthappu 26:23

Yeah, sure. So, we also studied, during my PhD, we also studied a rare condition again, inherited, called tylosin, with esophageal cancer and what this condition is, is tylosin, which is a thickening of the skin, again as the hands and feet, but it's strongly linked to developing a soft cell cancer. So, 95% of patients will develop carcinoma of the oesophagus, usually before the age of 65. And again, this is something that is really inherited in families. So, there are a few clusters of these families. One up in Liverpool, another one, I think over in the Netherlands, another one in the States. There are these families that have been studied in great detail, their genes have been examined, and actually my PhD supervisors' team was one who identified the gene that underlie this condition.

So why on earth does thicken skin on the hands or feet give you an oesophageal cancer? How are these two things linked? Again, it's a really bizarre link, isn't it if you think about it, but actually these patients, they don't just have thickened skin on the hands of feet, they have it in their mouth as well. They develop these thick white patches in their mouth and in their oesophagus. And we think again, it is this overactive stress response. So, the gene that underlies dialysis with oesophageal cancer is called iRhom2. iRhom2 regulates a lot of different inflammatory cytokines, so, a lot of different messengers, and we also show that it regulates keratin, and a particular keratin called keratin 16, which is responsible for wound healing. It's the keratin that you need, if you cut yourself that's the keratin that goes up to help bring that wound back together, along with lots of other different factors. So, iRhom2 seems to be really important in regulating wound healing. And what we think in tylosin; this is wound healing gone wrong, this is wound healing gone out of control.

So, the food that you're eating, chewing, and swallowing is causing injuries to the oesophagus. And when those injuries don't heal properly, and they're exaggerated, this exaggerated wound healing, eventually, this goes awry, and you end up developing a cancer in the oesophagus. And so that was working out the links between the skin and the oesophagus; it was really fascinating part of this research. But what is common between this project, but also the previous project, is that we are able to biopsy the skin so much more easily than we can heart tissue, or orsophagus tissue, of course, yeah, so that's, that's where the skin comes into handy. It's easy to take a sample of the skin, study those cells under the microscope and see what's going on with them and see if we can relate these findings back to say, for the example, the oesophagus or the heart. And that's what the cardiologist found so fascinating. Oh, my goodness, it's so hard for us to get heart biopsy but you guys can just come in and take a skin biopsy.

This is really handy. So, we were seeing changes in the skin that were similar to the changes in the heart. With the second project, we would see similar changes in the skin that we would see in the oesophagus as well. And so, we were learning from the skin and bringing what our findings from the skin back to be helpful in a disease that was much more important and significant than what was going on to the skin. So really helping our colleagues by studying the skin and we can take those

findings of a rare disease and we can help to use them to study more common diseases and diseases that, for example, oesophageal cancer that isn't inherited. That was the next part of the project that was happening after I left is can we use the findings that we found in this rare disease, can we use them to learn more about more common forms of oesophageal cancer, or more common forms of heart disease as well?

Harriet Dalwood 30:15

The links and everything. It is like a detective movie, almost a very, very fascinating, and very exciting. Like you said, it could then be used to hopefully diagnose things that are maybe more common in the future. Very fascinating stuff.

Dr Thivi Maruthappu 30:29

I'm glad you think so. Thanks, Harriet.

Matt Gass 30:31

So we've talked a lot about genetic conditions today. And they can be hard to identify and hard to treat. But are there any, any recent developments, or upcoming developments for people with genetic skin disease, which you think are particularly exciting?

Dr Thivi Maruthappu 30:44

Yeah, so definitely. So recently, the Nobel prize was awarded to a couple of scientists who developed a technology called CRISPR-Cas9, and CRISPR-Cas9 is gene editing. It is incredibly clever technology that we nicked off bacteria, so they do this already. So we borrowed what these clever bacteria were using and we can use that to edit human DNA, and if we think of the DNA, like being our instruction manual, and a mutation as being a mistake, or a typo in our instruction manual, so CRISPR-Cas9 is so clever, it can come in, find that mutation, cut it out, and replace it with normal DNA, and you think, right, okay, we are so far off being able to use this in humans, but actually, my mind was completely blown when I read an article recently in the New England Journal of Medicine, where CRISPR-Cas9 was used in humans to treat a rare condition, a type of amyloidosis, and it was effective. So, there are many groups across the world looking at using this gene editing technology to correct mutations in the skin.

The skin is the perfect place to test this because we can take a sample of skin, we can monitor for improvements, it is easy to observe. We really are, you know, should be at the forefront of this sort of technology, and we have diseases that really need this. So, I mentioned at the beginning, Epidermolysis Bullosa, particularly the recessive dystrophic subtype, that in gene editing for these rare diseases is being investigated. In the long term, we really hope that these will provide an effective treatment for patients with genetic conditions where at the moment, we are not able to offer them really targeted treatments.

Matt Gass 32:42

I mean, that's fascinating. I mean, the idea of a tailored treatment that can fix such an underlying condition is incredible. So much of dermatology is about management of conditions.

Dr Thivi Maruthappu 32:54

Absolutely.

Matt Gass 32:55

And managing symptoms and there's many, many chronic conditions which have a genetic element. What an exciting area of research, and yeah, I look forward to seeing that as it develops, and hopefully more and more exciting research papers come out of it around dermatology and, and other areas.

Dr Thivi Maruthappu 33:13

Yeah, that would be amazing. Definitely.

Matt Gass 33:16

Fantastic. Well, thank you so much, Thivi, for joining us today. I mean, this was really interesting and just could have been a really challenging episode, I think in terms of a really complex topic, but I thought you explained it all so brilliantly, and absolutely loved it. So thank you.

Dr Thivi Maruthappu 33:31

Thanks, Matt. Thanks, Harriet. Thank you both. Thanks so much for having me.

Matt Gass 33:36

Well, thank you very much. Dr. Thivi Maruthappu. What a fantastic guest. I think we managed to say fascinating, or synonym of fascinating about 50 times during that podcast episode, but I think that's because we were both learning so much.

Harriet Dalwood 33:50

Yeah, absolutely. I mean, I felt like I learned so much on a subject that I really did know next to nothing about really.

Matt Gass 33:58

I'd like to say it was from a low bar from my point of view.

Harriet Dalwood 34:01

Same here. Absolutely same here. As for the next episode. I hope you will join us because we'll be talking all about cosmetic procedures, specifically non-surgical cosmetic procedures such as botox and filler, so it should be a truly fascinating one, you might say, and we hope that you join us in two weeks' time.