TRANSCRIPT

S1.E3. Psoriasis (Part 2)

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Dr. Tom Kovi: Hello and welcome to *SpotDiagnosis*. I am Dr. Tom Kovi.

A/Prof. Alvin Chong: I'm Associate Professor Alvin Chong. We are your hosts.

Tom: We have with us, A/Prof Peter Foley. This is part two of our podcast episode on psoriasis. In this part, we will talk all about the management of psoriasis. Now, there's been an explosion of new therapies for psoriasis. That's what we'll be focusing on today, in addition to the conventional therapies such as topicals and phototherapy. Professor Foley, how would you go about choosing therapy for psoriasis patients?

A/Prof. Peter Foley: The choice of treatment in psoriasis is based on many factors, particularly subjective and objective disease severity. But it's also important to take into consideration comorbidities that the patient may have, patient preference, the therapeutic efficacy and the safety and tolerability of the agents that we might consider. Generally speaking, mild disease, which is probably three quarters of patients with psoriasis, can be controlled with topical therapies alone. That's something that doesn't need specialist attention. It's something general practitioners can manage, topical therapies and making sure any comorbidities are dealt with. However, with more moderate to severe disease, the topical therapies alone are probably not going to be sufficient, so we will add in phototherapy or a systemic therapy. Any attempt to treat extensive disease with topicals alone really is going to add to frustration for both the patient and the clinician, and it's going to result in failure of therapy, and it's a cost that no one needs to bear.

It's important to take the subjective impact, as well as the objective disease when classifying severity. For example, involvement of the face or involvement of genital disease can often be severe, even though the extent of disease is quite limited.

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Alvin: Peter, before we jump into pharmacotherapy, can you talk to us a little bit about lifestyle modification for psoriasis? Does it actually work?

Peter: Lifestyle modification can help. We know cigarette smoking makes psoriasis more likely to occur, but also more difficult to treat. Cessation of smoking is important upfront. We know that alcohol consumption tends to correlate with psoriasis severity, so encouraging alcohol moderation is important. The impact of diet is controversial. There's some low-quality evidence to suggest that Mediterranean diet might be helpful, but isn't necessarily so. Probably what's more important from a dietary point of view is aiming for and maintaining ideal body weight.

Tom: Okay, let's talk about topical therapy. What are some of the topical treatment options on the market?

Peter: It's important when treating psoriasis that the therapies we use aren't irritant. It's trying to make sure we're not irritating and aggravating the condition because psoriasis often exhibits the Koebner phenomenon with extension into areas of trauma or injury. It's adding things such as emollients, making sure the skin is well moisturised. We most frequently prescribe topical corticosteroids. We also tend to use vitamin D analogs. In an off label manner, we use calcineurin inhibitors.

Tom: Do you have any tips for using topical corticosteroids?

Peter: Corticosteroids are generally well tolerated and can be used very safely. However, it's important to use the appropriate strength for the body area that's being treated. We tend to use mild steroids on the face and in the flexures, or we use non-steroids such as the calcineurin inhibitors, tacrolimus, which needs to be compounded by pharmacists or pimecrolimus. We use more potent topical steroids on areas such as the elbows or knees. What's really important is that patients don't continue to use the topical corticosteroids once they've dealt with the thickness and scaliness and there's just mild redness left or patients using the steroids as a preventative treatment because that's when they'll run into problems with skin atrophy, telangiectasia, purpura, and striae.

Tom: There are a few different kinds of steroid cream, which one do you recommend for the scalp?

Peter: Scalps tend to require something that's easy to apply. A bit different if there's a bald scalp, you can use whatever formulation you like. But people that have hair on their scalp, we tend to use lotions such as mometasone or methylprednisolone. We also have a clobetasol shampoo that we can use, and there is a combination product of betamethasone dipropionate and vitamin D analog calcipotriol in a gel form that can be applied to the scalp. We less frequently now tend to use formulations that contain tar or dithranol because of the mess that they tend to make, the staining and the smell, and they're also more difficult because they are usually in a cream base, which is hard to apply to the scalp.

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Tom: How frequent would you apply these creams?

Peter: If I was asking a patient to use something like mometasone lotion, I get them to apply after showering, so once a day. If they're using clobetasol shampoo, then it's applied for 15 to 30 minutes before showering, initially on a daily basis, but decreasing the frequency as time moves on. The same with the combination calcipotriol and betamethasone overnight, applied initially on a daily basis, but then decreasing frequency and used as required.

Tom: What about the vitamin D analog? What can you tell us about those?

Peter: Whereas most of the therapies we have with psoriasis are really targeting the immune system, and that includes topical corticosteroids, the vitamin D analogs are primarily working to encourage the overactive skin cells to mature in a more orderly manner and not proliferate so rapidly. Of note, recently calcipotriol as a monotherapy has been withdrawn from the Australian Market.

Tom: I understand that recently there's been a new formulation as a foam with the combination therapy of vitamin D analog and steroid, can you tell us, why is that a good thing?

Peter: The combination of vitamin D analog and corticosteroid is available in gel formulation ideally suited to the scalp or hair bearing areas, ointment, which is what we typically use for plaques and, more recently, a foam formulation. The foam formulation has volatile elements that as they evaporate, create a supersaturated solution that drives in both the corticosteroid and the calcipotriol, which results in a more potent therapy.

Tom: Very interesting. Just in terms of practicality, can you comment on the cost for our patients of these topical formulations?

Peter: The combination product vitamin D analog and corticosteroid in all three formulations are available on the Pharmaceutical Benefits Scheme, so they are the cost of a standard prescription.

Tom: How quickly would you expect to see the improvement on their skin after using these topical formulations?

Peter: Whilst, some patients may notice improvement within the first few days, generally speaking, we'd encourage people to use their topicals for at least a few weeks before determining whether or not the treatment was effective.

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Tom: Just lastly on topicals, I know that tar has been used for treating psoriasis for over 2000 years. What's the role of tar nowadays in psoriasis?

Peter: Tar has been around for millennia for treating psoriasis. It's slower in its onset of action than corticosteroids but can induce a more prolonged remission if people respond to the tar. Unfortunately, it's messy, it's smelly, it stains, so most patients do not accept tar as a preparation to be used on their skin.

Tom: Our tip number one, topical vitamin D analog and corticosteroid topical treatment can be effective for limited area of psoriasis.

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Alvin: Peter, the next line after topical treatments is phototherapy. Can you tell us a bit about how phototherapy is used for psoriasis?

Peter: Many people with psoriasis are aware that their psoriasis tends to get better in summer. They've made that observation themselves. That's because ultraviolet radiation, particularly UVB has anti-inflammatory as well as anti-proliferative effects. Nowadays, we tend to use a form of phototherapy called Narrowband UVB. It's narrowband in the sense that it is only several wavelengths of UVB that seems to be the most beneficial in terms of effects on psoriasis whilst minimising the potentially carcinogenic effects of ultraviolet light.

Alvin: Are there any particular patients you would recommend phototherapy for?

Peter: Because, in the main, people receiving phototherapy have large areas of skin exposed to the ultraviolet radiation, we tend to reserve it for people with at least 5% body surface area involved, particularly once topical therapies as monotherapy become impractical. It's a useful therapy in pregnant women because there are no adverse effects apart from the potential for getting sunburn. But it's important to realize that UVB depletes folic acid, so folate supplementation is important.

Alvin: What can a patient expect with phototherapy? What do they have to do? Can you tell us?

Peter: For phototherapy to be effective, the patient with psoriasis needs to attend a center with a phototherapy booth at least twice and ideally three times per week. When the patient comes in, they undress to expose the areas of skin that need to be treated. We generally get them to wear protective goggles so they're not staring at the UV lights and keep their underwear on. -They're standing in a cabinet surrounded by vertical UV emitting fluorescent tubes. The tubes are six feet long, and they emit UVB. The patients are only in the machine for a few minutes as these machines now can really emit quite high doses of UV in a short period of time.

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Alvin: Peter, how effective is phototherapy?

Peter: The results from psoriasis are a little bit unpredictable but most patients do very well with Narrowband UVB. They need to have at least five to ten treatments before they can see that it's starting to work. In general, a course of therapy is between 15 to 25 or even 30 treatments but it's not a cure. The person with psoriasis still has that underlying genetic immunological driver and eventually, the psoriasis will recur.

Alvin: Generally, how much does phototherapy cost for the patient?

Peter: The majority of centers with UVB as an option charge the Medicare rebates so there's no out of pocket expenses for most patients.

Tom: Ultraviolet radiation causes skin cancer?

Peter: Ultraviolet radiation, particularly ultraviolet B, is the main driver of skin cancer, both melanoma, and non-melanoma skin cancer. By using Narrowband UVB though, we're really using what's most effective, targeting in the immune system whilst trying to minimize that carcinogenic or mutagenic potential of the ultraviolet light. It's why we use it as a course of therapy and get people to protect the most sensitive areas so they keep their underwear on, and unless there is psoriasis on the face, we get the person to cover their face as well. To date, the evidence is there's a very little increased risk of developing skin cancer with Narrowband UVB.

Alvin: I know that there are some European countries that send their bad psoriatic patients to the Dead Sea for a period of UV/Dead Sea treatment. It's thought to be very cost-effective and very efficient. What do you think of that, Peter?

Peter: Certainly, anecdotally I have had patients who have been to the Dead Sea and they do seem to respond quite well whether it's because of the relaxed atmosphere, whether it's due to the altitude being below sea level, whether it's due to the amount of ultraviolet light that is present at the site, whether it's the salinity of the Dead Sea itself is open to debate. When people have tried to mimic the salt concentrations and do it in baths and UVB away from the Dead Sea, it doesn't seem to make any difference. But certainly patients will frequently return from the Dead Sea with stories demonstrating how well their skin has improved.

Tom: Our tip number two: phototherapy can be effective as a second-line therapy for widespread psoriasis.

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Tom: Let's move on to the systemic therapy for psoriasis. What are the options for systemic therapy?

Peter: Broadly speaking, we can classify the treatments for psoriasis as traditional agents and the biological therapies. The traditional agents are usually taken orally and would include methotrexate, which can also be given subcutaneously, acitretin and cyclosporine. The biological therapies of which there are now a range of options, are usually administered subcutaneously.

Tom: When should a patient be referred to a dermatologist?

Peter: I think it's appropriate to refer any patient to a dermatologist when either the patient or the treating doctor feels that disease control is not adequate, and is beyond what the general practitioner is comfortable prescribing.

Tom: Let's start first with methotrexate. What can you tell us about it?

Peter: Methotrexate is the most commonly prescribed systemic agent for psoriasis by dermatologists. It's most commonly given orally but can be administered subcutaneously, particularly if patients have issue with gastrointestinal upset. It's taken once a week, and it's really important to emphasise that it's weekly, not daily. It is effective in around about 40% of patients. When we talk about effective, we talk about a 75% reduction in the psoriasis area and severity index after 12 to 16 weeks of therapy. That's about 40% of people will do that well. It's usually taken in combination with folic acid to try and particularly protect the bone marrow but also try and reduce gastrointestinal side effects.

Tom: What do we have to worry about in terms of side effects when patients are taking methotrexate and how do you monitor them?

Peter: Generally speaking, methotrexate is very well tolerated. The two side effects we're particularly concerned about or interested in detecting early is bone marrow suppression so regular full blood examinations required. It's usually only an issue if the patient inadvertently takes the medication daily. We're also concerned about potential hepatotoxicity. We monitor the liver quite frequently for patients on methotrexate. It's more of a concern if the patient is overweight, has diabetes, has dyslipidaemia or is a heavy drinker. Other more nuisance side effects rather than sinister side effects would include nausea or gastrointestinal upset, fatigue, alopecia and occasionally mouth ulcers. It's important to realise that methotrexate, as it works on the immune system, may predispose patients to infections.

Tom: Tip number three: low dose methotrexate is generally safe to use. Make sure that they're on a weekly dose, not a daily dose, and that they're also taking folic acid to minimise the side effects.

If a patient has widespread psoriasis or joint involvement, then methotrexate is actually a pretty good option to treat both diseases.

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Tom: How about cyclosporine? What's good about it?

Peter: The advantage of cyclosporine is its really rapid onset of action. We often use it as a crisis buster for patients with acute severe flares of disease, where we need to bring them under control very rapidly. We often use it for erythrodermic or in-patients. Unfortunately, because of its potential toxicity, the generally accepted view is it should not be used for more than two years cumulatively, in people with skin disease.

Tom: When you mentioned that there are some side effects that we need to be aware of, what are the particular side effects that you're talking about?

Peter: Over time, we are particularly concerned about nephrotoxicity and hypertension. Hypertension can come on quite quickly, but we know that over time, it tends to become more pronounced. There's also issues with nausea, and commonly gum hypertrophy, hypertrichosis and also, there can be some neurological toxicity so tremor or paraesthesia, can be seen. As it is a more immunosuppressive therapy than most of the other treatments for psoriasis, there's also concerns with long term use with infection and malignancy.

Tom: Now we've talked about both methotrexate and cyclosporine. When do we use acitretin?

Peter: Acitretin, unlike methotrexate and cyclosporine, does not work on the immune system or has very little impact on the immune system. It's mainly used to try and encourage the skin cells to slow down, so to multiply less rapidly and to mature better. We don't have the immunosuppression concerns that we do with the other agents.

Unfortunately, acitretin is much slower in its onset of action and fewer people tend to respond to therapy. It can be used in combination with ultraviolet light, so phototherapy plus acitretin is an effective treatment. It really gives the phototherapy a bit of a boost. Unfortunately, with higher doses of acitretin, patients tend to not tolerate the mucocutaneous side effects. Acitretin is probably one of the leading agents in the treatment of pustular psoriasis.

Tom: Apart from the side effects in terms of the dry mucous membranes, are there any other downsides?

Peter: Acitretin is a teratogen and it tends to be metabolized in a reverse direction and is maintained in the body. For females of childbearing age, it should not be used. The other issues are nuisance - dry lips, dry nose, dryness of the skin, and we do need to keep an eye on the patient's lipids.

Alvin: Peter, one of the great advances in the treatment of inflammatory diseases, in our age, is the rise of biologic therapy. Psoriasis is one of these diseases that has had a lot of benefit from these biologic treatments. What should a generalist know about using biologics in psoriasis?

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Peter: Whilst we often talk about the biological therapies as being new treatments for psoriasis, it is important to remember the first biologic for psoriasis was PBS listed in 2006, and they have been used in a clinical trial setting for two decades now. Whilst they are relatively new, we have become quite familiar with them over time. I don't think a general practitioner needs to know all the details of how we choose which biological therapy we are going to use on an individual patient, but it's important to know what the drug is targeting. So what's the mode of action? How frequently the patient needs to have their injections or, in the case of infliximab, their infusions? What are the safety issues and what needs to be monitored and what tolerability needs to be discussed with the patient? The role of the general practitioner is to help us in monitoring the patient.

Alvin: How effective are these biologic treatments?

Peter: There are several subclasses of biological therapies for psoriasis, some target human necrosis factor-alpha, some target interleukin 17, and some target interleukin 23, either by itself or in combination with interleukin 12. These therapies, particularly the newer agents, we are expecting upwards of 60% or 70% of people achieving at least a 90% reduction in their skin scores. Really quite dramatic improvement in the objective severity of the disease, and that's reflected in the quality of life measures that we use.

Alvin: Yes, these treatments are absolutely amazing. I remember starting patients who have had lifelong psoriasis on biologics and, for the first time, you could actually see the color of their skin without the disease. Let's talk a little bit about how our patients are getting these therapies. What would they actually need to do to get biologic treatment nowadays?

Peter: As with all new agents for any disease state, the biological therapies are expensive. It seems if you have a new agent, it needs to be expensive. As a consequence, there are restrictions in terms of access to therapy. Patients need to have moderate to severe disease, and that can either be on the face, palms, or soles or widespread psoriasis. We use a measure called the Psoriasis Area and Severity Index, and patients need to have a PASI score of greater than 15 after a minimum of six weeks of therapy of at least two of our traditional agents, acitretin, methotrexate, cyclosporine or phototherapy or contraindications to therapy or developed toxicity from these agents.

In addition to the restrictions on access to therapies, many patients and even doctors are not aware that these new agents are available. I think it's important that we educate both the medical profession and the public that we do have new therapies, but they are reserved for people with objectively severe disease who don't respond to conventional therapies.

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Alvin: What are the side effects that biologic treatments can give?

Peter: Most of the time, the biological therapies are very well tolerated, and both the long term and short term safety shows no greater impact than currently available oral or topical therapies. For most people, there are no side effects. Patients may experience injection site reactions because they are injecting a protein into their skin that just means redness and swelling and sometimes itch or pain around the site of the injection. The medications are working on the immune system, so patients may be more prone to infection or they may find it harder to shake infections. We screen patients for chronic infections prior to commencement of therapy. We screen everyone for tuberculosis and, ideally, the patient should be screened for hepatitis B and C. We encourage everyone on a biological therapy to have an annual influenza vaccine and we would encourage people to be vaccinated to hepatitis B and have five-yearly pneumococcal vaccine.

Alvin: What about the malignancy risk, Peter?

Peter: So far, and this is after more than a decade for the earlier agents, the only signal relating to malignancy seems to be related to a slight increased risk of non-melanoma skin cancer. There were initial concerns about possibly increasing risk in lymphoproliferative disease, however, that doesn't seem to be borne out and some of these agents have been used in millions of patients.

Alvin: Obviously, vaccinations are pretty important if anyone is going to be immunosuppressed. What vaccines can you not give these patients if they're on a biological treatment?

Peter: If a patient is on a biological therapy, then any live or live-attenuated vaccine is contraindicated. It is particularly relevant to patients who want to have yellow fever to head off to more exotic destinations, but also varicella, measles, mumps, and rubella.

The killed vaccines such as tetanus, meningococcus, hepatitis and then annual influenza vaccine is not a concern and they are to be encouraged.

Tom: Tip number four, there are now very effective biological therapies for patients with severe treatment-resistant psoriasis. Consider referral to a specialist care to access these medications.

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Here is the end of our two-part podcast on psoriasis where we talked about what is psoriasis, the epidemiology, the clinical features, the comorbidities, and how we manage psoriasis both in a GP setting and in a dermatologist's setting. We would like to thank Professor Foley very much for his time to talk to us about psoriasis. We would like to also acknowledge our production team, Peter Monaghan and Joanne Coughlin for podcast support.

Alvin: We would like to thank Dr. Sunny Singh for helping us reviewing the content. I'm Alvin Chong, and with me is—

Tom: Dr. Tom Kovi.

Alvin: We hope you've enjoyed listening to this series of *Spot Diagnosis*. We hope you have enjoyed this podcast. 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.

Tom: For those who would like to access something further information on this subject, we have placed a transcript, together with some further education and information resources for you on our website. I also want to do a shout out for the GP education events that we run at the Skin Health Institute. Just go to spotdiagnosis.org.au.

Alvin: Please share *Spot Diagnosis* with your friends and colleagues. Rate and review us. Let us know what you think. We would really appreciate your feedback and any suggestions. Thank you for listening.

More information, and other dermatology education resources, can be found on our website at

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