TRANSCRIPT

S2:E10 – Viral warts

Dr Blake Mumford: "*Take one of the large, black snails. Rub it over the wart, and then hang it on a thorn. This must be done nine nights consecutively, at the end of which time the wart will completely disappear. For, as the snail exposed to such cruel treatment, will gradually wither away, so it is believed that the wart, being impregnated with its matter, will slowly do the same.*

Welcome to 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, and I'm joined again today by Dr Aaron Robinson.

Aaron is a consultant dermatologist at the Skin Health Institute, and also an adjunct senior lecturer with the University of Melbourne working in public and private practice.

Dr Aaron Robinson: Thanks, Blake. As some of you will have worked out already, the topic of today's podcast is viral warts. The opening quote describes one of the many completely ineffective historical remedies for viral warts.

Our guest speaker today is Dr. Mark Darling. Mark is a Consultant Dermatologist at the Skin Health Institute, specializing in male genital skin disease. He also has a public appointment at the Melbourne sexual health clinic and works in private practice. Mark, welcome to the *Spot Diagnosis*.

Dr. Mark Darling: Thank you for inviting me.

Blake: Mark, to get us started, can you share with our listeners a fun, obscure dermatological fact that they might not know?

Mark: Well, my fun fact is not actually about viral warts themselves, but about one of the treatments. So one of my favorite therapies for warts is cantharidin solution, and cantharidin is an extract from an actual beetle called Cantharis vesicatoria, which is also known as the Blister Beetle.
And these beetles produce a secretion which causes irritation and blister formation when in contact with the human skin. And we use the extract from the crushed up beetles to apply to the warts, causing them to blister. So our treatment is quite literally beetle juice.

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

Blake: I wonder what the manufacturing process looks like for cantharidin solution? Thanks very much, Mark. Over the millennia, many fanciful folk theories have emerged about the cause of viral warts, and how to get rid of them. The theories were wonderfully creative, and some of them are associated with the darkest parts of our history.

Viral warts were one of the many skin lesions identified as witch's, or devil's marks, and used as evidence during witch trials in the 14th to 16th century. We now know that viral warts are caused by the human papilloma virus, or HPV. For the purposes of learning and discussion about management, it is important to divide viral warts into two different subtypes. Anogenital viral warts, and non-anogenital cutaneous warts.

So Mark, why is it important for our listeners to realize the difference between anogenital viral warts and non-anogenital cutaneous warts?

Mark: Human papilloma virus, or HPV, is an extremely common virus that can affect both the skin and the mucous membranes. This can lead to a variety of different clinical manifestations depending on where it affects the body, although most HPV infections are transient and may not cause any symptoms.

So there's in the region of 200 distinct HPV subtypes, some of which are responsible for causing specific forms of warts. For example, type 6 and 11 are most commonly associated with low-risk anogential warts, and subtypes 3 and 10 are associated with plane warts found on Keratinized skin.

Most people will be familiar with warts being common in children and this is often when our first exposures to HPV occur given our immature immune systems at an early age. The effects will frequently stimulate warts on the skin. We often notice these on the hands and feet for example. Anogential warts usually occur in sexually active adults. They spread through close physical contact and they are responsive to different forms of treatment compared to the common non-anogential warts.

They can be challenging to treat, and frequently associated with a lot of stigma that can affect individuals and relationships with others. And HPV can also infect other sites, such as the oral mucosa and the larynx.

Blake: Mark, can you tell us, how exactly does HPV result in viral warts?

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

Mark: Infection of HPV occurs through breaks in the skin, or mucosa. It then hides in the basal layers of the epidermis, evading the immune system and infects the keratinocytes above it, causing them to proliferate and cause the hyperkeratotic lesions we know as warts.

Infected keratinocytes also constantly shed new virus particles, and the time of acquisition of infection is very difficult to ascertain as they can have a long and variable incubation period, sometimes weeks, months, or even a year.
Infected keratinocytes also constantly shed new virus particles, and the time of acquisition of infection is very difficult to ascertain as they can have a long and variable incubation period, sometimes weeks, months, or even a year.

Blake: There's lots of different terms used to describe the clinical manifestations of viral warts. Verruca vulgaris, plane warts, plantar warts, condyloma acuminata, what do these terms actually mean?

Mark: So, verruca vulgaris is a term used to describe common warts, and these are usually thickened papules, or small lumps, with a papillomatous surface. And these are often warts you see in childhood, and frequently occur on fingers, toes, and sometimes around your nails.

Plantar warts are warts which occur on the feet, and these are often called verrucas. They can be very persistent and sometimes painful, and when clusters of warts start to coalesce on the feet, we call these mosaic warts.

Plane warts is a term we use to describe flat warts, and these are usually found in the face, back of the hands, and the lower legs. Condyloma acuminata is the name given to anogenital warts, which means people who have HPV infection affecting the anus, perineum, external genitals or sometimes the internal genital tract.

Aaron: Mark, how common are viral warts? And why do people get them?

Mark: Well, first I think it's helpful to distinguish between infection of human papilloma viruses, which we all get at some point in our lives, and viral warts. So being exposed to various strains of HPV throughout childhood and adulthood is normal, and usually our immune systems, and indeed the barrier function of our skin and mucous membranes, is enough to prevent a wart from occurring.

Some of us, however, will then go on to develop viral warts. These can be large enough to be easily visible, but many warts however will go unnoticed, for example they may be so small that they're not clinically apparent, or occur at sites that are challenging to examine, for example the genitals.

This makes it very hard to estimate how common they are, and indeed why some people are more troubled by warts than others.

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

Blake: It's time for the first **skin tip** of the episode.

Infection with human papilloma virus does not always result in visible warts, but the absence of a wart does not mean that that person is not contagious.

Aaron: Mark, are there particular groups of people who are more prone to getting viral warts?

Mark: Yes, definitely. The most prone group to developing warts are children, and this is primarily because of their relatively naïve immune system, which will not have developed any resistance to different strains of HPV. The other group who are particularly prone to warts are those who are immunosuppressed, for example organ transplant recipients or patients on immunosuppressive therapies, and also patients who have an immune deficiency, for example HIV.

People with certain skin conditions may be also more prone to warts, particularly conditions affecting the barrier function of their skin, for example atopic dermatitis. Certain occupations can also leave people more susceptible to warts, for example occupations where maceration or microtrauma of the hands facilitates inoculation of the virus through the skin, such as meat and fish workers, or people in trades who work with their hands throughout the day.

There are also situations where individuals may have a high exposure to HPV viruses, including health care professionals. People with high numbers of sexual contacts, including sex workers, would also be at increased risk.

Blake: For the purposes of this podcast we're going to first talk about anogenital warts, and then we'll talk about non-anogenital cutaneous warts, or common warts as they're also known.

Mark, can you describe for our listeners what do anogenital warts look like?

Mark: Firstly, as a reminder, most people with genital HPV infections are asymptomatic and don't have warts visible to the naked eye, and when they do occur they're usually pink or flesh colored, or sometimes brown, and they're small papules a few millimeters in diameter.

They are usually multiple, and often have a filiform surface, but can be flat or pedunculated and can coalesce to form plaques. Occasionally, they may become very protuberant, and really begin to develop a cauliflower-like appearance.

They're found on all parts of the penis, vagina, perineum, pubic area and around the anus. They usually don't cause discomfort, although they can coalesce quite rapidly in some cases.

Aaron: So Mark, how are anogenital warts transmitted?

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

Mark: HPV is the most common sexually transmitted infection in the world and it occurs through close skin-to-skin contact during sexual activity.

Blake: What is your approach to a patient who you've just diagnosed as having anogenital warts?

Mark: I like to highlight to patients that warts are benign, but it's important to be aware that HPV strains often coexist, and the presence of one strain may indicate risk for infection for a more high risk or oncogenic strain. For example HPV types 18 and 16, which account for approximately 80% of cervical cancers.

Women, or any person with a cervix, should therefore undergo regular cervical screening, as per usual.

Blake: It's time for another **skin tip**. It's important to remember that sexually transmitted infections hunt in packs. Testing for other sexually transmitted infections should be performed if a diagnosis of anogenital warts has been made.

Aaron: Anogenital wart treatments are divided into those that the patient can self-apply at home, and clinician-applied treatments. Can you please take us through the self-applied treatment options first?

Mark: There's two main types of topical treatment that can be applied at home. No one treatment is superior to other. The first one is Podophyllotoxin, sometimes known as Wartec or Condyline paint and this is a cream or solution that's applied to the warts. It acts as an antimitotic agent, stopping cells from replicating. It can cause a localised irritant reaction, and it can be tricky to apply to some areas that are difficult to visualise, for example around the vulva, which can become quite irritated. It doesn't penetrate the keratin layer well, so it's not good for sites other than mucosal surfaces.

And secondly, imiquimod cream, or also known as Aldara, is the other commonly used topical therapy, and this activates immune cells to help get rid of the localized infection and it can also cause localised irritation and more rarely can cause systemic or flu-like symptoms.

Both of these treatments need to be applied regularly and you have to follow the instructions, and it can take a number of weeks for them to start to work.

Aaron: And what about the clinician applied treatment options?

Mark: So cryotherapy is an excellent way to treat warts. Liquid nitrogen is applied directly to the wart, and it's done for a few seconds with either a cryogun or a cotton wool tip, and it causes cell death and can also stimulate an immune response. It will often take a few treatments to work,

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

usually spaced between three to four weeks apart. It can be uncomfortable both during the freeze and also in the healing phase.

Ablative lasers can be used if available, but these can be expensive, and sometimes other caustic agents are sometimes tried such as trichloroacetic acid. For lesions that are isolated to the keratinised skin, for example the shaft of the penis or suprapubic area, cantharidin can also be used, however it has to be used by quite experienced practitioners.

Blake: Clinician applied treatments definitely sound cooler, cryoguns, ablative lasers, and caustic acids. Is there a place for surgery in the management of anogenital warts?

Mark: Well, curetting, or scraping off pedunculated or very thick warts can be helpful, and rarely for very recalcitrant warts, or large warts, excision or debulking is indicated, but this is rarely a first line option.

Aaron: So Mark, what are some of the red flags that you'd watch for in patients with anogenital warts?

Mark: The main concerns are in patients that have warts that are unresponsive to treatment, individuals who are immunosuppressed, and those who the warts are behaving in an abnormal way, such as abnormal growth or spread.

The possibility of coexisting high-risk HPV subtypes that are oncogenic should be considered. If you suspect the genital lesion may be malignant, referral to a specialist is recommended. Biopsies are usually performed to exclude types of intraepidermal carcinoma, the early stages of cancerous transformation, such as penile, vulval, or anal intraepidermal neoplasia, and immunosuppressed patients are at particular risk of these conditions.

Widespread warts may also be a marker of a potentially undiagnosed immunosuppressed state, for example HIV. Anogenital warts are also uncommon in children, and when this occurs a careful history is important to obtain, and the possibility of sexual abuse should be considered. But it's important to note that anogenital warts in children can occur out of this context through autoinoculation.

Blake: It's time for our third **skin tip**. The development of new, widespread severe viral warts can be a clue to an underlying immunosuppressed state, such as HIV, hematological malignancy, or an undiagnosed genetic disorder.

Let's talk about an Australian success story, the human papilloma virus vaccine. Australian-based researchers Ian Fraser and Jian Zhao were instrumental in the development of this vaccine in the

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

1990s and Australia was one of the first countries to roll out a fully government-funded population-based HPV vaccination program.

Mark, can you tell our listeners about the impact that this program has had in Australia?

Mark: The HPV vaccination has been rolled out nationally since 2007, initially for girls and extended to boys in 2013. Uptake of vaccinations in school-aged children in Australia has been amongst the highest worldwide.

Initially, the vaccination was available as a quadrivalent vaccination. This provided protection against HPV 6 and 11, which are responsible for most genital warts, and also HPV 16, and 18, which are high-risk HPV subtypes associated with oncogenic effects, most notably cervical cancer.

Nonavalent vaccination, which targets nine strains of HPV, replaced the original vaccination in 2018 and this covers additional strains of high-risk HPV types. The impact of these vaccinations is already being seen and incidence of high-grade cervical abnormalities in vaccine-eligible age cohorts of women are well documented by the cervical screening registers nationally.

Reduced incidence rates of anogenital warts in Australia are some of the greatest globally to date. Over time we expect to continue to observe a downward trend in these rates of cervical dysplasia but also penile, anal, and vulval cancers.

Blake: We've covered anogenital warts now. We're now going to move to the cutaneous or common warts. Mark, how do you diagnose the more common garden variety cutaneous wart?

Mark: Warts are usually diagnosed clinically and have characteristic features which makes visual diagnosis relatively easy, but sometimes you have to look very closely with a dermatoscope or magnifier to clinch a diagnosis.

Dermatoscopes are very helpful as warts usually have quite characteristic features when we look very closely. For example, we have quite a lobular structure, we can often see black dots in the center which represent thrombosed capillaries.

When we look at plantar warts closely, we can commonly see distortion or interruption of the normal skin lines and markings, which is helpful, and also depending on the site, they often have a papilliform or a rough surface.

Swabs of blood tests are not helpful in diagnosing warts. Very rarely, a biopsy may be required to reach the diagnosis, and this is often performed to exclude the possibility of an alternative diagnosis histologically, particularly if there's concern regarding dysplasia.

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

Blake: We briefly mentioned autoinoculation already, but what are some of the common areas that you might see this phenomenon?

Mark: As mentioned, autoinoculation is where the warts or HPV virus is spread by the host from one area of the body to another.A good example is people who habitually bite their fingers. They spread the warts by traumatising the skin around the fingernails, causing periungual warts, which can be painful and difficult to treat.

They might even often autoinoculate onto the lips if they're very unlucky. Shaving with razors or other types of hair removal can spread warts across the skin, for example, in the face or in the bikini area.

Other types of microtrauma, such as picking and scratching, particularly in children can spread the warts from the fingers to other parts of the body including the genitals. Repeated microtrauma on the hands or the knees, particularly in certain occupations such as tradesmen can also spread the warts across a larger surface area, creating more extensive or very thick warts.

Aaron: Are there any other lesions that can resemble warts that you need to watch out for or any danger signs that people should be aware of?

Mark: Yes, so other infections can sometimes resemble viral warts, particularly molluscum contagiosum which are common in children can be very widespread. Some infections can also mimic viral warts, for example, syphilis infection, which can very very rarely cause a form of genital wart.

A number of benign skin growths, particularly seborrheic keratoses, which are extremely common, can have a very, very warty surface and there are some inflammatory conditions that can look like warts, for example, lichen planus or lichen nitidus.

The other lesions that can resemble viral warts are dysplastic lesions. These include low-grade lesions like actinic keratoses, small patches of Bowen's disease, or keratoacanthomas. Importantly, squamous cell carcinomas can take on a very warty-like appearance and if there's any concern regarding this type of diagnosis, a biopsy or excision is almost always indicated.

Blake: And the sort of signs you'd look out for in that situation would be continued growth and perhaps ulceration, is that right?

Mark: Yes.

Blake: Okay, so for the management of cutaneous warts, we'll go through a couple of commonly encountered scenarios, and I'll get you both to comment on how you might deal with them. First

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

up, sometimes a particularly stubborn plantar wart can develop in an adult. What is your preferred treatment approach for this? And Aaron, let's start with you.

Aaron: Plantar warts can be challenging and very frustrating for the patient and the clinician and often require multiple treatments. Cryotherapy, ideally with paring is often used initially, and many of our patients have had multiple treatments with this by the time they get referred to a Dermatologist.

Pairing and treatment with cantharidin is often used by Dermatologists in combination with salicylic acid, which when painted on the wart causes a blister to form underneath the wart. This can result in resolution although often over multiple treatments.

Other treatments that can be employed include topical DCP, which is diphenylcyclopropenone. This triggers a contact hypersensitivity reaction to stimulate inflammation directly at the wart once patients have been sensitised.

In more refractory cases, direct injection of the chemotherapy drug bleomycin into the wart can be considered. Lasers have also been used by some dermatologists with varying effectiveness.

Mark: I agree with Aaron's suggestions. The only other thing I might add is for very keratotic and symptomatic warts, a podiatrist can also be helpful just for maintaining comfort by de-bulking.

Blake: And just for the medical students who might be listening, pairing of a wart is the careful debriding of the hyperkeratotic tissue on the top of the wart in order to reach the HPV-infected tissue at the base so that it can be treated directly. Is that right?

Aaron: That's correct, Blake.

Blake: What can you use to do that?

Aaron: Usually that can be performed just very carefully with a scalpel, in experienced hands.

Blake: How about a child with multiple viral warts? Let's start with Mark first this time.

Mark: Sadly cryotherapy in children is usually quite a traumatic experience. If warts are very extensive, it may not be a good first-line option. As Aaron mentioned, DCP can be a very effective treatment. In children with multiple warts, this can be a good choice as it's a topical treatment that can be applied at home by parents.

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

It's applied in a very dilute preparation every few days in accordance with maintaining the desired response. And it can take a number of weeks to work, and parents need to be given very clear instructions of how to apply the topical agents.

It can be remarkably effective, but it can also trigger a secondary eczematous response, which might need to be managed accordingly.

Blake: And Aaron, what about you?

Aaron: For children with multiple viral warts, I quite like using cantharidin in this situation because it doesn't hurt to apply, and it's usually very well tolerated by the children and their parents. It does however need to be applied in the clinic.

Blake: And let's move on to our next scenario. How do you manage periungual warts, which can be a bit of a problem for nail biters, Aaron?

Aaron: As with all warts, it's important first to counsel the patient about the factors that may be contributing to the spread or autoinoculation of their warts, and in this case, try to reduce the trauma to the area.

Periungual warts can also be difficult to treat, but can be treated with similar methods as for plantar warts. Cryotherapy can be very painful in the area around the fingertips. So topical treatments such as cantharidin or DCP are often preferable.

In some cases, therapy with systemic retinoids, such as acitretin may also be helpful to reduce the growth or the thickness of the warts.

Blake: Our final scenario. What about those plain warts, the more flat variety. What do you do about those? Mark, you first?

Mark: So plain warts can be particularly numerous and they're common on the back of the hands and on the face. I like to use topical retinoids, such as tretinoin. They are often, however, relatively asymptomatic and may not require any specific treatment at all, and they often self-resolve over time.

Blake: Aaron, anything to add?

Aaron: I agree with Mark that topical tretinoin can be quite helpful in this situation, particularly when they're on the face, as tretinoin is tolerated very well in this area.

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR

Blake: All right. Thanks very much, guys. With that we might bring this episode to a close. We hope you enjoyed it, warts and all.

Aaron: Thanks, Blake, and thank you Mark for your time and for sharing your expertise with us today.

Mark: Thank you for having me.

Blake: We also like to thank Jo Coughlin 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 in Melbourne using Zoom in the time of stage four lockdown during the coronavirus pandemic.

Blake: For 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.

Alvin: For Australian GPs listening, you can receive RACGP CPD Activity points for listening to *Spot Diagnosis,* further information is available on our website at 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.

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

www.skinhealthinstitute.org.au/podcasts

ABN: 58 895 584 259
Registered Charity A 12501

Level 1
80 Drummond Street,
VICTORIA 3053 AUSTR