



Treating cutaneous warts

What are the options?

Key points

- Most people develop cutaneous warts at some time in their life; around 65% of warts regress spontaneously within two years.
- Prevalence of warts is increased in patients with reduced cellular immunity and genetic conditions such as epidermodysplasia verruciformis.
- First-line treatments for cutaneous warts include freezing and home topical therapy with a salicylic acid preparation plus heating, paring and zinc oxide cream.
- When prolonged use of first-line treatments fails or is unsuitable, then treatment options include:
 - chemical therapies such as caustic agents, cantharidin
 - immune system modifiers such as diphencyprone, imiquimod, cimetidine
 - physical therapies such as duct tape occlusion, destructive treatments.

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First-line treatments for cutaneous warts include freezing and home topical therapy with salicylic acid preparations combined with plus heating, paring and zinc oxide cream. If prolonged use of these treatments fails or they are unsuitable then a wide range of chemical, immunological and physical treatment options are available.

Warts are caused by infection with a human papillomavirus (HPV). Most people develop cutaneous warts at some time in their life, with a point prevalence of 20% among Australian school children, slowly declining with increasing age.¹⁻³

Papillomaviruses are closely related to nonenveloped DNA viruses and are highly species-specific. HPVs show considerable diversity; the complete DNA sequence is known for about 120 HPV genotypes, and partial DNA sequences for at least another 80 genotypes.⁴ DNA sequencing reveals a phylogenetic tree where the virus groupings match their biological behaviours. The clinical subtypes of HPV

infection and the commonly associated HPV genotypes are outlined in the Table.⁵

CLINICAL PRESENTATION

The clinical presentation of warts depends on the infecting HPV genotype and the site affected. Common warts (*verruca vulgaris*) occur on the hands, fingers, elbows and knees. These warts occur particularly on the fingers (including periungual or subungual sites) but also on the dorsal area of the hands (Figure 1).

Palmar and plantar warts may be solitary or multiple. On the soles, mosaic warts are more superficial plantar warts that have coalesced into larger plaques, usually on weight-bearing sites (Box 1, Figures 2a to c). Myrmecia (Latin

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for anthill) are thicker endophytic plaques of wart sloping to a central depression. Occasionally, large confluent plaques of plantar warts occur. Palmar and plantar warts are usually painless but can sometimes be surprisingly painful, particularly when on weight-bearing sites.

Plane (flat) warts are more subtle than common warts, presenting usually with numerous, flesh-coloured to slightly red-brown papules or small plaques. They most often occur on the dorsum of the hands or nearby forearms and are also seen on the face and neck (Figure 3).

Rarely seen are epidermoid cysts of weight-bearing areas of the sole. These contain mainly HPV type 60 – one of a number of HPV genotypes that cause warts with inclusion bodies seen on histology.

PATHOGENESIS

Wart infection occurs:

- directly via skin-to-skin contact, either from person to person or through auto-inoculation to adjacent skin
- indirectly via contaminated surfaces and objects such as showers in the home, at swimming pools or gymnasiums.

Infection is promoted by minor abrasions and maceration that allow HPV access to basal keratinocytes. The circular DNA of HPV becomes a replicon in the nuclei of epithelial basal cells, creating a long-term reservoir of viral DNA. The incubation period is up to 20 months for experimental HPV infections, but clinical experience suggests it may be considerably longer in some cases. Approximately 65% of warts regress spontaneously within two years.⁶

Warts can be persistent and have high recurrence rates. Furthermore, treatment may not prevent further HPV transmission (although the risk is low if the warts are not clinically apparent). Possible reasons include:

- the persistence of HPV DNA in normal-appearing skin surrounding the warts, as shown by polymerase chain reaction (PCR)
- the resistance of HPV to heat and desiccation
- the ability of HPV to evade the host's

TABLE 1. CLINICAL SUBTYPES OF HPV INFECTION AND THE COMMONLY ASSOCIATED HPV GENOTYPES

Infection type	HPV genotypes*
Skin	
Common warts (hands, fingers, elbows, knees)	1, 2, 4, 27, 57
Palmar and plantar warts	1, 2, 27, 57
Mosaic warts (soles)	2
Myrmecial warts (soles)	1
Plane (flat) warts	3, 10
Epidermoid cysts of the sole (with inclusion bodies) [†]	4, 57, 60, 63, 65
Butcher's warts (mainly seen in meat or fish workers)	7 (not animal sourced)
Digital squamous cell carcinoma and Bowen's disease	16
Epidermodysplasia verruciformis (EV) [†]	3, 5, 8 (and many others)
EV squamous cell carcinoma [†]	5, 8
Mucosa	
Anogenital warts (condylomata acuminata)	6, 11
Higher-grade intraepithelial neoplasias (cervical warts, penile bowenoid papulosis, erythroplasia of Queyrat)	16
Invasive cancers (cervix, vulval, penile, oral)	16, 18, 31, 45 [‡]
Warty (condylomatous) squamous cell carcinoma	16
Oral warts	6, 11
Heck's disease (oral focal epithelial hyperplasia) [†]	13, 32 (only)
Conjunctival papillomas	6, 11
Nasal inverting papillomas [†]	11, 57
Recurrent respiratory papillomatosis	6, 11

ABBREVIATION: HPV = human papillomavirus.

* Many more HPV genotypes are less often linked to some of these clinical forms.⁵

[†] Occur rarely.

[‡] These four genotypes account for around 80% of cervical cancers.

immune defences through mechanisms that include the absence of a viraemic phase in HPV infection, which minimises the systemic immune response; and low-level expression of viral proteins in the lower layers of the epidermis where antigen-presenting cells are most prevalent. Eventually, protective type-specific immunity does develop.



Figure 1. Moderate-sized common warts (verruca vulgaris) on the finger and subungual area of the thumb.

Some conditions associated with an increased prevalence of warts are shown in Box 2. Warts are much more prevalent in people with reduced cellular immunity. Epidermodysplasia verruciformis is a rare genetic disease that involves infections with HPV genotypes that do not produce warts in normal individuals. The disease is mostly autosomal recessive (caused by

mutations in the *TMC6* or *TMC8* genes, which encode transmembrane proteins involved in zinc transport). Onset is usually in childhood. Clinically, this condition is highly polymorphic with widespread lesions usually resembling plane warts or pityriasis versicolor.

HPV infection is responsible for the vast majority of cases of cervical carcinoma, and HPV vaccination will likely significantly reduce the incidence of this carcinoma in the future.^{7,8} HPV infection is also strongly linked to anogenital squamous cell carcinoma (SCC) and some SCCs of the head and neck. Other HPV-associated conditions prone to transforming to invasive SCC are the higher-grade intraepithelial neoplasias of male or female genital sites (cervical warts, penile bowenoid papulosis and erythroplasia of Queyrat) and inverted papilloma (mostly seen in the nasal cavity).

Only some HPV genotypes are oncogenic, as they encode proteins that

suppress known human tumour suppressor proteins. This mechanism allows proliferation of the viral genome in tissues that routinely ‘turn off’ cell proliferation as the epithelial cells differentiate. Non-oncogenic HPV genotypes lack these proteins. The incidence of HPV-related malignancies is higher in people with a deficiency in cell-mediated immunity or epidermodysplasia verruciformis.⁵

DIFFERENTIAL DIAGNOSES

Corns or calluses

Corns or calluses are the main differential diagnosis but are uncommon in younger people. Repeated focal pressure or friction causes protective thickening of the skin, making that area firmer and more prominent, leading to a vicious cycle. Corns and calluses on the hands are mainly seen in manual workers and on the feet from poor fitting footwear, abnormally shaped feet or bony prominences on weight-bearing sites.

1. CASE: A YOUNG MAN WITH MOSAIC PLANTAR WARTS

Presentation

A 19-year-old man presented with mosaic warts on the left sole and smaller warts elsewhere on his soles, fingers and the dorsum of his hands (Figures 2a to c). He swam regularly and played soccer. He had used a proprietary wart paint daily for a month with no benefit. His GP froze the warts on two occasions two weeks apart. No blisters developed; some of the warts on the dorsum of his hand cleared but most persisted. The patient then used a wart home freezing device three times over three weeks with no benefit.

Treatment

I explained to the patient that warts of this type are often slow to respond to treatment and that he had not used the treatments for long enough to give them a fair trial. We elected to pare and solid freeze the warts, followed by combination home topical therapy. This comprised hot water soaks followed by application of 17% salicylic acid and 17% lactic acid in a collodion base at night and zinc oxide cream during the day, both under occlusion with a dressing tape. The patient did not return for follow up.



Figures 2a to c. Mosaic warts on the left heel and smaller warts elsewhere on the soles in a 19-year-old man.



Figure 3. Multiple plane warts on the dorsum of the hand and fingers.

Corns are more focal with a hard keratinous seed; calluses are broader. Except for the central seed of a corn, paring with a surgical blade shows persistence of the normal skin markings, which are absent in the heart of a wart. Warts often also show black dots from thrombosed capillaries and bleeding from capillaries from more superficially located dermal papillae. These features may be clearer with dermoscopy. Macerated interdigital warts are difficult to distinguish from (soft) interdigital corns.

Neoplasms

Verrucous carcinoma (epithelioma cuniculatum type) is a rare low-grade, well-differentiated SCC on the soles of older adults. The term 'cuniculatum' refers to a rabbit burrow-like appearance with deep furrows. Verrucous carcinomas can gradually penetrate, destroying the subcutis, fascia or bone, and often recur after attempted removal but rarely metastasise. In the past, they were thought to result from HPV infection but stricter histopathological criteria suggest this is an uncommon factor.⁹

Rarely, in situ SCC (Bowen's disease) occurs between multiple toes or as periungual or subungual disease with warty change and/or granulating erosive change. HPV infection is probably a common aetiological factor.^{10,11} This clinical presentation can also signify subungual melanoma, which is often amelanotic. If there is any doubt then biopsy is mandatory.

Psoriasis and tinea

Psoriasis purely of the palms and soles may be a distinct entity to psoriasis vulgaris, but the latter may include palms and soles as well as other sites. The plaques are well demarcated, red and scaly and vary from involving small, localised areas to confluent over most of the palms or soles. They can be thick and fissured. Sterile pustules may be present. Tinea should also be considered.

Hypertrophic lichen planus

Hypertrophic lichen planus most often occurs on the legs and dorsal area of the feet. The thickened scaly plaques have a livid hue and are usually itchy; the thickening results from repeated scratching.

Rare disorders

Punctate palmoplantar keratodermas include a number of rare inherited disorders, punctate porokeratosis and arsenical keratoses. The dorsal surfaces are usually spared.

Tuberculosis verrucosa cutis is rare in Australia but should be considered in immigrants from endemic areas. It occurs in individuals who have been previously infected with *Mycobacterium tuberculosis* after exogenous inoculation with this bacterium at sites prone to trauma. The lesion begins as a small, subtly inflamed wart-like papule, which gradually enlarges to a firm red-brown verrucous plaque.

TREATMENT OF WARTS

There are few specific antiviral therapies to treat HPV infection. Most therapies aim:

- to physically remove visible warts
- to be cytotoxic to infected cells or
- to induce an immune response against the wart.

As warts are benign and self-limiting, patients – especially children – may not require treatment, and therapy likely to induce permanent scarring should be avoided. There is no evidence that aggressive removal of warts results in a better long-term outcome nor that temporary interruption of therapy is a problem.

2. CONDITIONS ASSOCIATED WITH AN INCREASED PREVALENCE OF WARTS⁵

- HIV infection
- Organ transplantation
- Some haematological malignancies (e.g. chronic lymphocytic leukaemia and Hodgkin's disease)
- Idiopathic CD4 lymphopenia
- Some rare genetic immunodeficiency syndromes (e.g. common variable immunodeficiency, severe combined immunodeficiencies, ataxia-telangiectasia, Fanconi's anaemia, Wiskott-Aldrich syndrome, DOCK-8 deficiency, WHIM syndrome, WILD syndrome)
- Epidermodysplasia verruciformis

The treatment recommendations below are based on personal experience and evidence from clinical trials. Using the strict criteria of evidence-based medicine, a recent Cochrane review concluded that of the treatment options for warts, only topical salicylic acid preparations are superior to placebo.⁹ Another similar review concluded that 'significantly higher remission rates may be expected only with cryotherapy and salicylic acid used in combination'.¹⁰ These conclusions are difficult to assess as there are few properly controlled, adequately sized trials to compare the range of available treatments. Despite this, many less adequately controlled trials report high response rates to the investigated treatments.

Treatment selection

Therapies may be divided into home therapies and those administered by a clinician. Combinations of therapies are often used. Some treatments are more suitable for anogenital warts than for plantar warts and vice versa. This article concentrates on therapies likely to be used by general practitioners, podiatrists and dermatologists for cutaneous warts. Treatment

3. SOME TREATMENT OPTIONS FOR CUTANEOUS WARTS

First-line treatments

- Cryotherapy (e.g. liquid nitrogen)
- Home topical therapy
 - heat (microwavable seed bags or hot water)
 - salicylic acid preparations
 - zinc oxide cream

Other treatments*

- Chemical therapies: cantharidin, caustic agents, formic acid, bleomycin, 5-fluorouracil, oral retinoids, adapalene, cidofovir
- Immune system modifiers: sensitising agents (e.g. diphencyprone), imiquimod, cimetidine, therapeutic vaccination, intralesional vaccines or antigens
- Physical therapies: home freezing with dimethyl ether plus propane, duct tape occlusion, destructive treatments such as surgery, electrosurgery, laser
- Others: photodynamic therapy, folk remedies

* Options when warts do not respond to prolonged use of first-line treatments or when first-line treatments are unsuitable.

options for cutaneous warts are summarised in Box 3.

Important factors in deciding which modalities to use for a specific patient are:

- likely effectiveness
- cost of the product or of repeated visits to the practitioner
- which treatments have been tried previously and their adequacy (e.g. appropriateness for site, compliance, number of attempts and duration of treatment)
- likely compliance and issues that affect this (e.g. pain, particularly for children or people who are constantly on their feet, practicality and time constraints)
- side effects.

Advice to patients

It is important to explain to patients that all available wart treatments are slow to work and unreliable (prone to failure) and that warts are prone to recur after apparently successful treatment. No single treatment is much more effective than others. A rule of thumb is that the success rate for any individual treatment modality is approximately 70% after three months or longer of treatment. If a treatment appears to have had a partial effect by three months and is tolerated then I encourage patients to continue with that treatment for a few more months before abandoning it.

Preventive measures, such as wearing thongs when showering and not picking at warts, are also important (the latter may spread the HPV infection or allow peringual warts to develop).

AN APPROACH TO TREATMENT

After discussion of the treatment options with the patient, a useful approach is as follows. The use of this approach in a patient with mosaic warts is outlined in Box 1.¹¹⁻¹³

Freezing

Solid freezing should be offered because a single freeze occasionally clears warts. Thick warts may be pared with a blade. With liquid nitrogen (boiling point -196°C), the freeze time needs to be long enough to induce blisters but not cause deep necrosis. Application is equally effective with cryosprays or thick cotton tip applicators but the latter often requires longer application times to achieve the same level of freezing.

Freezing is painful and most young children will not tolerate it. Topical local anaesthetics are not effective enough for the freeze times required. Various methods of distraction may allow braver children to tolerate it. I explain that freezing does not kill HPV but rather destroys the skin harbouring it, so hopefully exposes the virus to allow immune recognition. However, warts often re-appear in the healing skin.

I also instruct patients or their carers to snip off the roof of the resulting blister to

reduce viral load and to apply povidone iodine ointment daily to the healing skin. Healing usually takes a week or two so the treatment is less suitable for physically active people.

If the warts do not clear or recur after a single freeze then the next main options are repeated cryotherapy or home topical therapy. Cryotherapy is usually repeated every two to three weeks until the warts clear, which may require many treatments. It is common for children not to be prepared to return for multiple treatments – a point that I emphasise to parents insisting on aggressive treatment. Studies have investigated more frequent freezing, with marginally improved results.

Clinicians should be aware that melanocytes are more sensitive to cryotherapy, so hypopigmentation (temporary or long-term) is a risk in darker skinned people. This is less of an issue on the feet than on the hands. Freezing is prone to lead to a ‘donut’ of recurrent warts around the freeze site.

A home freezing device that uses dimethyl ether and propane is claimed to be effective for treating warts. In my experience, this treatment often fails. A study found the achieved minimum temperature of 0°C at 40 seconds (compared with -20°C at 20 seconds for liquid nitrogen) was probably insufficient for therapeutic effect.¹⁴ In addition, patients probably often do not adequately follow the instructions because of pain.

Home topical therapy

Home topical therapy is a good alternative or adjuvant to freezing. It is cheap, convenient and minimally painful. I recommend that patients combine daily application of a compounded or proprietary salicylic acid preparation with physical treatments such as heating and paring of the wart and application of zinc oxide cream. Details of this strategy are shown in Box 4.

Products often claim to remove warts rapidly. I explain to patients that many months of treatment are required before the treatment should be abandoned as ineffective.

4. A HOME THERAPY STRATEGY FOR CUTANEOUS WARTS

1. Heat the warts for 15 to 30 minutes every evening

This is reported to be an effective stand alone modality. Heating can be achieved with microwavable flax-seed hot bags or by soaking the feet or hands in a baking dish or bowl of water at a temperature that is almost uncomfortable.

2. Dry the feet or hands and apply a wart paint under dressing tape overnight

I recommend 40% salicylic acid compounded in white soft paraffin as a cheap keratolytic wart paint (made up by the pharmacist on prescription). Over-the-counter proprietary alternatives are available with a similar formulation (17% salicylic acid and 17% lactic acid in a collodion base; including Dermatech, Duofilm Liquid and Wart Clear Solution). Collodion dries to form a rubbery film. Collodion also contains colophony, a common cause of allergic contact dermatitis (as seen with some brands of fabric adhesive tape). Another proprietary option (Wart-Off Paint) contains 20% salicylic acid, 12% lactic acid and 10% podophyllum resin in an ether-ethanol base.

Any of these paints should be applied moderately generously each night to each wart, and then occluded overnight with dressing tape (e.g. Micropore), which is removed the next morning.

3. Remove the soft surface of the warts each morning with a pumice stone or nail file and apply 36% zinc oxide cream generously, also under dressing tape

If daytime topical treatment is undesirable, such as for cosmetic or time reasons, then oral zinc sulphate is an alternative (10 mg/kg to a maximum dose of 600 mg daily for two months). There are trials suggesting that either form of zinc has efficacy.

If the warts become too sore then the night-time treatment is temporarily stopped and re-started once the discomfort settles, initially applied every second day and then daily if tolerated. The morning treatment is bland so is continued.

If the warts appear to clear then the treatment is stopped but if the warts recur it is recommenced. If time is limited then the heating step can be omitted.

OTHER TREATMENT OPTIONS

If the warts fail to respond to prolonged use of the above treatments or there are issues with the treatments then a range of options exist.

Chemical therapies

Caustic agents. Repeat applications of caustic agents are reported to be effective. These include monochloroacetic acid or trichloroacetic acid, 35 to 80% in water or 80% phenol, each applied weekly with a salicylic acid preparation on the other days. The acids cause immediate quite painful stinging that lasts for a prolonged time so are less suitable for children. They also cause temporary frosting of the skin, which is prone to later pigment change. Another option is 10% silver nitrate in water, applied every second day for months.

Glutaraldehyde. Glutaraldehyde is a bacteriocidal and virucidal antiseptic. A 10% glutaraldehyde solution in a water-ethanol base is available as a wart treatment (Diswart). It is prone to causing allergic contact dermatitis so I do not recommend its use for warts. Treated skin hardens and turns a brown colour.

Cantharidin. Cantharidin is available from some dermatologists and some hospital dermatology outpatient clinics. It is a vesicle-forming terpenoid found in 'blister beetles'. It activates serine proteases that destroy epidermal desmosomal proteins, so the healing blisters do not scar.

The application of cantharidin is not painful. Blisters develop after hours to two days, usually with no or manageable pain, and heal within a week. Cantharidin is particularly useful in children who often

do not associate any later pain with the treatment and so are usually prepared to return for repeat therapy.

Preparations include 0.7% cantharidin in a film-forming base and 1% cantharidin plus 20% salicylic acid and 2% podophyllum in a collodion base. They are not available from most pharmacies. Cantharidin is only for office use: a thin smear is applied to each wart and allowed to dry. Occlusion is not required but if used increases the intensity of the blister. Some recommend washing cantharidin off a few hours after application but removal is difficult and is not needed. Cantharidin is applied every one to two weeks until new warts stop appearing; usually many applications are needed. Zinc oxide cream can be applied on the days cantharidin is not applied.

Bleomycin. This chemotherapy agent is injected into each wart. It binds DNA causing single-strand breaks. It is used only for recalcitrant warts and is made up in syringes by hospital pharmacies so is available only through dermatology outpatient clinics. Protocols vary, but typically bleomycin sulphate 0.25 to 1 mg/mL is injected up to three times to a maximum total dose of 4 mg. The injections are very painful so prior local anaesthetic is used. The area may remain painful for a week or so after treatment. The warts develop haemorrhagic necrosis by two to three weeks, which can be removed by paring. Reported cure rates vary from 14 to 99%. Systemic toxicity does not occur with this method but it is not suitable in pregnant women. Local complications include nail loss or dystrophy for periungual injections, Raynaud's phenomenon in treated digits and local urticaria.

Methods harnessing the immune system

Diphencyprone (DCP). Also known as diphencyclopropanone, DCP is used for more treatment-resistant multiple warts and can be very effective. It is available from compounding pharmacies. Most patients develop a delayed hypersensitivity reaction (allergic contact dermatitis) to DCP and this immune attack is probably responsible

for clearing warts. Squaric acid dibutyl ester is an alternative sensitising agent. Because these chemicals are used only for wart therapy, the allergy is of limited consequence.

The clinician applies 2% DCP to a small area of normal skin to induce sensitisation (dermatitis at the site) within 10 days. The patient then applies 0.1% DCP and 15% salicylic acid in white soft paraffin to the warts, initially a small amount every third day. The treated area must be carefully taped to ensure the DCP does not contaminate other sites as it will cause contact dermatitis wherever it touches the skin. If no reaction occurs by a week after DCP application then the frequency of application is slowly increased to each night, and then the amount applied is gradually increased, aiming to achieve a low to moderately active persistent local dermatitis.

Some patients need to apply DCP only every few days to maintain the dermatitis. Occasionally the concentration of the DCP must be increased to 0.2% to achieve the

required reaction. It can also be used as a liquid, usually in acetone at a lower concentration (0.01 to 0.05%) and can be applied from daily to weekly to maintain the required moderate level of dermatitis. Some patients become exquisitely allergic to DCP and develop more severe local reactions or widespread urticarial or eczematous reactions. A marked reduction in DCP concentration will sometimes allow continued treatment in these situations. I also prescribe a potent topical corticosteroid so it is available to treat a too strong local reaction. DCP usually takes months (sometimes six to 12) to clear warts.

Imiquimod. Imiquimod activates the innate immune system via toll-like receptor 7, causing mild to substantial inflammation. Available as sachets of 5% imiquimod cream, it is expensive, not covered by the PBS for this indication and is mainly used to treat genital warts, basal cell carcinomas and solar keratoses. It has poor penetration through keratin so is unlikely to work on areas with thick skin such as the palms and soles.

Penetration may be enhanced by repeated paring of the warts, cryotherapy, occlusion and/or concurrent use of salicylic acid. An ideal treatment regimen has not been developed.

Oral cimetidine. Oral cimetidine (30 to 40 mg/kg daily in two divided doses to a maximum of 2400 mg daily for three to four months) stimulates production of some cytokines. Initial uncontrolled studies suggested efficacy, but two double-blind, placebo-controlled studies failed to confirm efficacy for recalcitrant common warts.^{15,16}

Therapeutic vaccination. The commonly used HPV vaccine is effective against and specific to HPV types 6, 11, 16 and 18 and is effective in preventing most anogenital warts. The therapeutic use of HPV vaccines for already present anogenital and mucosal warts has not been reported as yet. Similarly, there are no trials on the therapeutic use of these vaccines for cutaneous warts, but one group has reported clearance of recalcitrant cutaneous warts in six patients.^{17,18} Despite

the vaccine being active against HPV genotypes not usually found in cutaneous warts, it may have an effect in some patients via epitopes shared by cutaneous and anogenital HPV genotypes. The ability of HPV vaccines to prevent the development of common cutaneous warts has not been investigated. Vaccine development is ongoing, raising the prospect of therapeutic vaccines against cutaneous warts.

Physical therapies

Duct tape. This occlusive plastic industrial adhesive tape is applied over the warts and left on for four to six days. The wart is then debrided with a blade or pumice stone and the duct tape reapplied in the same way. Early studies of its use for two months showed complete clearance rates in 60 to 85% of patients treated. However, later placebo-controlled studies found poor response rates.^{19,20}

Destructive treatments. Destructive treatments such as excisional surgery, electro-surgery and carbon dioxide laser treatment are likely to cause scarring and should not be used for plantar warts on pressure-bearing sites as the firm scars become a nidus for equally troublesome and difficult to treat calluses or corns. These treatments can be used for recalcitrant warts on non-weight-bearing sites. However, permanent scarring is still an issue and warts not uncommonly recur, presumably as there may be wart virus in surrounding clinically normal skin. Excisional surgery is not practical for large or numerous warts. Carbon dioxide laser treatment is expensive. The smoke plume from electro-surgery and carbon dioxide laser treatment may carry infective virus so has a small risk of causing airway warts in the people in the room.

Less common treatments

Other treatments have been reported as successful in small series. They are used infrequently.

5-fluorouracil cream (5%). This is a chemotherapy agent used mainly to treat solar keratosis. Significant wart clearance rates have been shown in a number of trials

of 5-fluorouracil used either alone with tape occlusion or mixed with 10% salicylic acid cream.^{21,22}

Oral retinoids (acitretin or isotretinoin). These can help debulk warts by reducing epidermal proliferation. The infection usually persists, so relapse is likely on stopping treatment. Oral retinoids can be helpful in patients with extensive hyperkeratotic warts and immunosuppressed patients and to enhance the effectiveness of other treatments.^{23,24}

Cidofovir. The antiviral agent cidofovir is a purine nucleotide analogue that can be extremely effective for plantar, anogenital, oral and laryngeal warts, even in patients with immunodeficiency.²⁵⁻²⁷ It can be administered by systemic infusion (5 mg/kg once weekly), intralesional injection (2.5 mg/mL) or as a 1% gel or cream (available through compounding pharmacies). Side effects of systemic cidofovir include nephrotoxicity and bone marrow suppression, but topical treatment of skin lesions is usually well tolerated. Cidofovir is expensive and so is infrequently used.

Adapalene. Adapalene 0.1% gel is a vitamin A analogue used mainly as acne therapy.

85% formic acid solution. This is punctured into warts every second day up to 12 times.

Folk remedies. On the basis of scanty published literature and anecdotal reports, repeated direct applications of banana peel, milk weed thistle latex and fig tree latex have been recommended for the treatment of warts.^{28,29}

Photodynamic therapy. This therapy involves a topical photosensitiser and a light source or pulsed-dye laser and is mainly used to treat vascular lesions.³⁰⁻³² These techniques have cleared a significant number of warts in small series. They are available from some dermatologists in private practice.

Intralesional injection. Injection of various vaccines or antigens into the largest wart can be successful. Antigens used include *Candida albicans*, *Trichophyton* spp., *Propionibacterium acnes* and mumps, measles and rubella vaccine or antiserum.

CONCLUSION

Warts are an unpleasant and embarrassing viral infection experienced by most people. On the more serious side, some genotypes have oncogenic potential, and a small number of patients with deficiencies in cell-mediated immunity can suffer overwhelming numbers or very large warts. Warts can be frustrating to treat and our enthusiasm to treat can be tempered by the fact that the majority resolve spontaneously in a few years. The many available treatments make treatment choice confusing, and their unreliability and potential side effects frustrating. There is a lack of large well-controlled trials to best guide treatment. The development of HPV vaccines against anogenital warts is exciting but these vaccines are considered to have a very limited role in controlling cutaneous warts. **MT**

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A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

COMPETING INTERESTS: None.

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