Treatment options for managing non-genital warts

Shaheen Haque Hussain BSc, MRCP and **Jane Sterling** PhD, FRCP

Warts are common but often treatment is not indicated. If it is required there are many treatments available targeting different aspects of wart virus infection, but there is currently a paucity of high quality evidence to support the use of most. Here we look at the various options.


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Warts are very common human papillomavirus infections of the epidermis, affecting up to 30 per cent of children and young adults. In most cases, the diagnosis is clear, and home remedies are used before medical advice is sought.

Cutaneous warts can often be left untreated as they are likely to clear spontaneously and frequently do not interfere with function. However, many regard them as unsightly and this alone prompts a search for treatment. If warts are numerous (see Figure 1), cosmetically visible, prolonged in duration or painful due to bulk or cracking (see Figure 2) treatment may understandably be pursued more vigorously.

Childhood warts have a greater chance of spontaneous clearance than those in adults. Duration of several years in adults is not unusual, while in children, most warts have cleared within two years. In addition, all treatments have higher cure rates in children compared with adults.

Treatment of warts can be challenging and finding an easy and effective remedy, free of side-effects, is still to be achieved. Several recent reviews of wart treatments do give us a picture of what to expect when embarking on a course of treatment and what to explain to the patient, indicated in the following important steps in treating warts:[1–5]

- exclude immune compromise if warts are unusually severe
- manage expectations
- consider which possible home treatments would best suit the patient
- persist with treatment
- consider second-line treatments.

It is firstly important to consider if the warts are unusual. If extensive, large or over five years (10 years in an adult) in duration, then the possibility of immune compromise should be considered (see Figure 3). If the patient has no other unusual infection history, no risk factors for immunosuppression, a normal full blood count and lymphocyte subsets, this is unlikely. The contribution of the patient's immune response

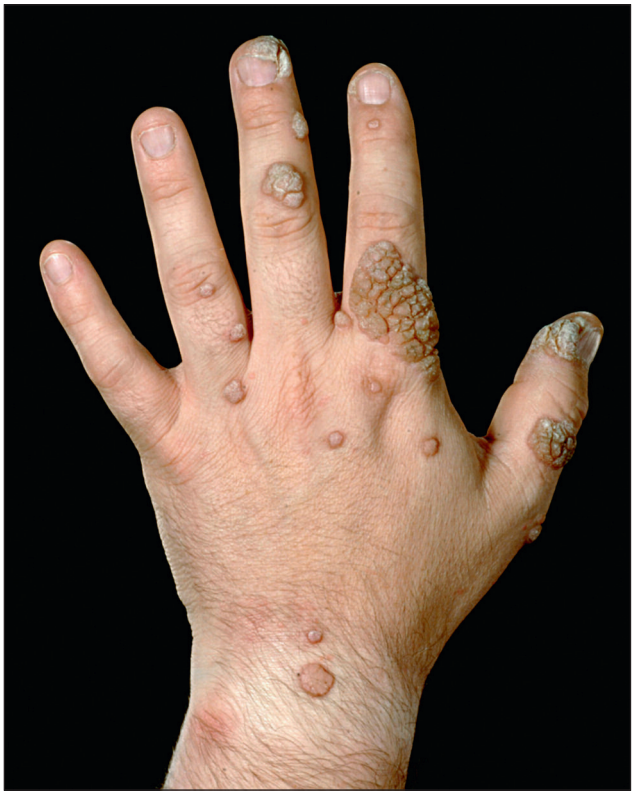

Figure 1. Numerous warts may prompt more vigorous treatment

to the physical methods of treatment is central to clearance and cure. The most successful wart treatments probably have no more than a 50–70 per cent chance of success within three months, with cure rates of placebo treatment averaging 25 per cent. Treatment may be prolonged, so patients need to be aware that there is no easy answer. Most treatments can be self-applied, but education in how to use, how often, when and for how long, is important to ensure adherence.

A possible treatment algorithm for warts in immune competent individuals is shown in Figure 4. Treatments can be broadly divided into destructive, virucidal, antiproliferative and immunological, with varying mechanisms of action (see Table 1). Only salicylic acid, glutaraldehyde, formaldehyde, silver nitrate stick and cryotherapy are recognised in the UK as licenced treatments for cutaneous warts, but many other treatments can be effective and are in common use. Most treatments will work better if the wart is regularly debulked by rubbing down with an emery board, foot file or gentle paring with a corn remover. This also helps to reduce discomfort due to pressure of the wart.

First-line/home remedies

Salicylic acid

Salicylic acid (SA) is available in several over-the-counter (OTC) products containing 10–26 per cent SA in a collodion or acrylate base or up to 50 per cent in an ointment (see Table 2), and is also available as specially manufactured cream or ointment preparations. The mechanism of action involves gradual softening and peeling of the surface keratinous layers (keratolysis) plus induction of mild inflammation. Treatment needs to be regular (daily) and sustained (two to three months) to be effective. In most studies, clearance rates at three months are about 15–50 per cent. Combination therapies of SA with cryotherapy, 5-fluorouracil (5-FU), podophyllotoxin, cantharidin, laser and imiquimod have all been reported to improve efficacy, but studies are small or anecdotal.

Glutaraldehyde and formaldehyde

Glutaraldehyde and formaldehyde, both available OTC, kill the virus as it leaves the surface of the skin, so should act to prevent spread. They also have a drying and hardening effect on the skin and can make rubbing down easier. Both can stimulate an allergic contact dermatitis in susceptible people. Glutaraldehyde 10 per cent is available in an aqueous/spirit base (Glutarol) and is applied daily. Formaldehyde is available as a 0.75 per cent gel (Veracur) and can be used three times a week as a soak for plantar warts (3–4 per cent formaldehyde in water as a special). The unaffected skin of the toes and dorsum of the foot should be protected by paraffin ointment before immersing the sole in the solution for approximately 20 minutes.

Occlusotherapy

The use of duct tape as a treatment for warts was heralded as an effective and pain-free therapy in 2002, but has not been duplicated in subsequent placebo-controlled trials. Occlusion reduces proliferation and softens the keratin layer due to maceration, so can help with some aspects of wart management. There is limited evidence to suggest that occlusion in addition to topical therapies improves cure rates, perhaps due to improved penetration of the applied substance.[6]

Vitamin D analogues

Vitamin D analogues licensed for use in psoriasis act by reducing epidermal proliferation and thus can be expected to

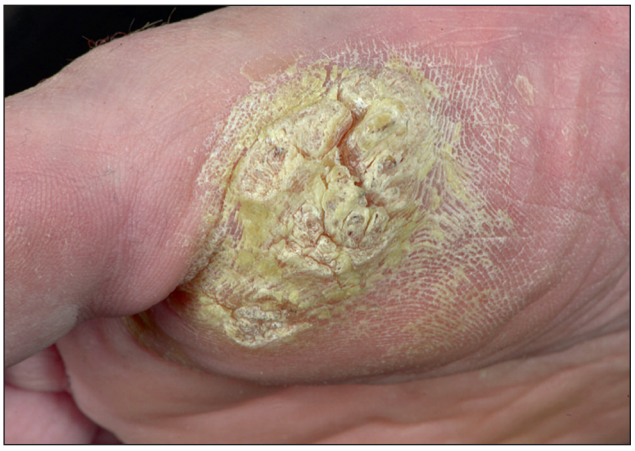

Figure 2. Troublesome warts on sole; some warts can be painful due to bulk or cracking

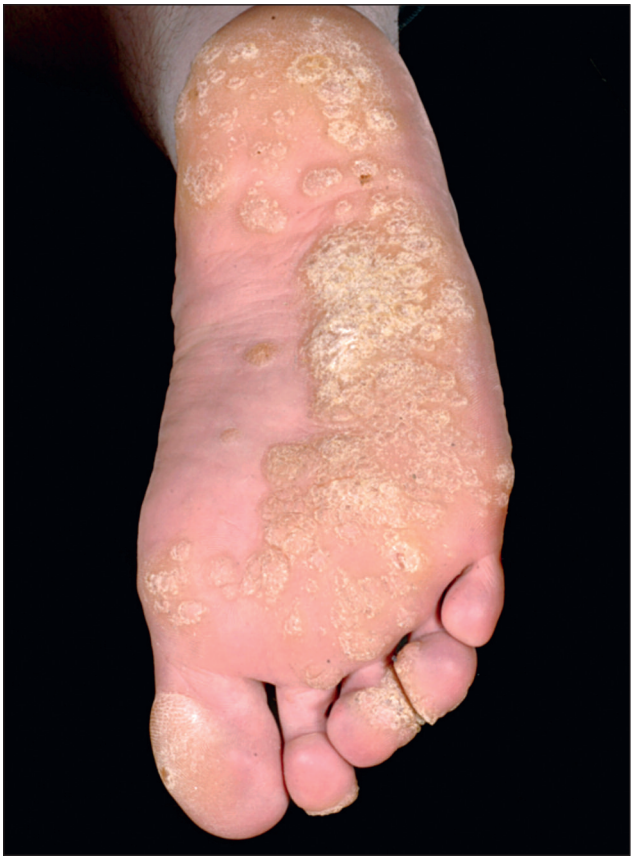

Figure 3. Widespread warts on sole; immune compromise should be considered in the case of extensive warts

have an effect in warts. Preparations available in the UK are not licensed for use in warts, but maxacalcitol, applied at least once daily for three to six months induced wart clearance in 59 per cent of treated warts in studies from Japan.

Podophyllotoxin

Podophyllotoxin (0.5 or 0.15 per cent) is licensed for the treatment of anogenital warts. It penetrates poorly into keratinised warts, but this can be improved with paring and occlusion. There are no placebo-controlled studies on its use in cutaneous warts.

Retinoids

Topical retinoids, licensed for use in psoriasis and acne, can have a useful effect on flat warts in children, clearing up to 70 per cent of lesions within three months.[7] Oral retinoids, such as acitretin, reduce epidermal proliferation and so debulk warts. Although not a routine treatment due to adverse side-effects, they may be considered as short-term therapy in combination with other topical treatments.

Chemotherapeutic drugs

Chemotherapeutic drugs, applied topically or intralesionally, can induce wart clearance. A 5 per cent cream of 5-FU is

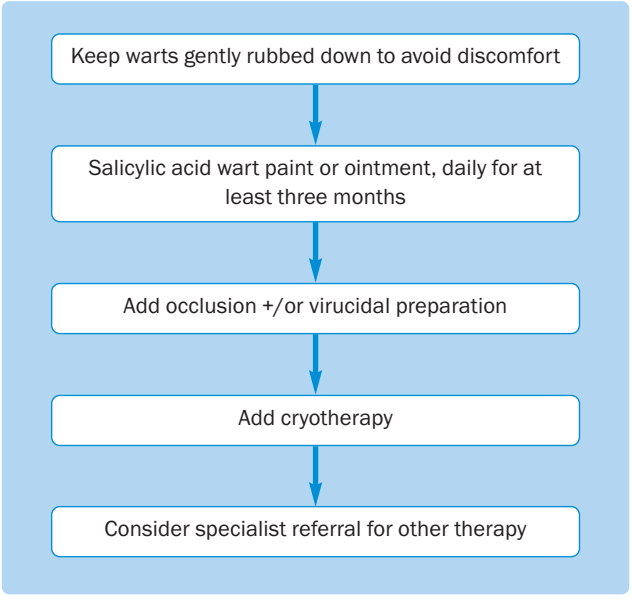

Figure 4. Algorithm for treatment of cutaneous warts

licensed for treatment of actinic keratosis (AK), Bowen's disease and superficial basal cell carcinoma (sBCC). It has been used as treatment for cutaneous warts with clearance rates of 50–95 per cent in small studies. The combination of 5-FU 0.5 per cent with SA 10 per cent has been available on the continent for much longer and has been reported to clear 63 per cent of cutaneous warts.[8]

Imiquimod is licensed for treatment of anogenital warts, sBCC, Bowen's disease (as 5 per cent cream) and AKs (as 3.75 per cent cream). Anecdotal and small study reports of daily or twice-daily 5 per cent application suggest that it may be useful either alone or as an adjunct to other treatments for warts.

Second-line

Cryotherapy

Dimethyl ether with propane is available OTC, but liquid nitrogen cryotherapy is colder, acts faster and produces a more aggressive freeze, with greater tissue damage.[9,10] Cryotherapy produces best effects when administered every two to three weeks and with enough tissue damage to be classed as 'aggressive'. Average cure rates of 50 per cent make it equivalent to SA.

However, treatment needs to be repeated regularly, and children in particular may find the treatment too painful. If there is no improvement after three months or a total of five freezes, then this may not be a suitable treatment.[11] Overzealous freezing can occasionally damage underlying nerves, tendons or the nail bed, and on the lower legs may lead to ulceration resulting from slow healing. Hypopigmentation can occur after freezing of dark skin.

Sustained application of heat at 44°C can also stimulate wart clearance, but methods for heat application are not readily available.

Destructive	Damages or destroys the virus-infected epidermis
Virucidal	Kills the virus as it leaves the skin surface
Antiproliferative	Reduces or stops cell division, leading to less bulk of wart
Immunological	Stimulates the body's immune response (may include any treatment that produces inflammation)

Table 1. Mechanism of action for wart treatments

Surgery

Surgical removal of warts is best avoided at sites of pressure, such as the soles, as the resulting scar may be equally uncomfortable and reinfection of the healing scar is a possibility as surgery does not always remove all virus-infected tissue. It can, however, be a very effective treatment for filiform warts in the beard area or for isolated warts on the limbs.

Laser can be used to destroy virus-infected tissue. The pulsed dye laser is used most commonly but this and other lasers are only available in specialised units.

Photo-dynamic therapy

Photo-dynamic therapy (PDT) is a destructive treatment available in some secondary care units. Aminolevulenic acid (ALA), applied to warts as a 16 per cent cream (Metvix), is activated by light of a specific wavelength, triggering chemical damage and tissue destruction of ALA-absorbed wart cells.

Treatment is painful during the light irradiation. It is more specific than cryotherapy or laser treatment, but depends on good absorption of the applied ALA and then adequate penetration of the light. Success rates are higher for thin or plane warts, but there are reported clearance rates of 80–90 per cent.

Treatment	Strength	Base	Preparation
Salicylic acid	11% 12% 16.7% 26% 50%	colloidon colloidon colloidon polyacrylate colloidon paraffin ointment	Cuplex Salatac Bazuka Salactol Duofilm Occlusal Bazuka Extra Strength Verrugon
Formaldehyde	0.75%	gel	Veracur
Glutaraldehyde	10%	IMS and water	Glutarol
Silver nitrate	40% 95%	pencil applicator	Avoca

Table 2. Strength and properties of formulations available OTC that patients can use to self-treat warts

Phenol and silver nitrate

These caustics are another method of producing epidermal destruction. Care must be used to avoid damaging the surrounding skin. Reported clearance rates, however, are good. Phenol is not licensed for warts and only available as a special preparation.

Topical immunotherapy

Topical immunotherapy agents induce an allergic contact dermatitis, and when applied regularly to warts can result in over 80 per cent clearance. In the UK, diphencyprone (diphenylcyclopropanone) is used most frequently. It is an unlicensed medication and must be used with care and applied every one to four weeks under specialised supervision.[12,13]

Numerous other treatments have been used in small numbers of patients or in small trials and may be used in specialised units or for patients with extremely troublesome warts, but are not currently recommended outside these situations. These include topical cidofovir, intralesional immunotherapy, intralesional bleomycin, chemotherapy limb perfusion and oral retinoids.

Other therapies

Other treatments that so far have a poor evidence base include herbal remedies, homeopathic therapies, hypnotherapy, acupuncture, oral or topical zinc preparations.

Conclusion

Skin warts are caused by a chronic infection with human papillomavirus. If spontaneous clearance is delayed or if the warts are troublesome, topical treatment with a salicylic acid preparation used regularly for a few months can induce resolution. If this fails, a number of other therapies with varying degrees of discomfort, patient and practitioner commitment, cure rate and cost can help to induce immune response and should be considered.

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Declaration of interests

None to declare.

Drs Haque Hussain and Sterling are consultant dermatologists, Department of Dermatology, Addenbrooke's Hospital, Cambridge