A Multimodality Approach to Recalcitrant Warts

A four-step approach to treatment may speed remission of common warts.

**WITH TED ROSEN, MD**

The management of recalcitrant common warts can be frustrating to patients and dermatologists alike. Warts may not respond to common first-line therapies, and sometimes they do not respond to more aggressive interventions, either. Many of the patients that present to the dermatologist have been referred by pediatricians or primary care providers who have had little to no success with standard interventions for common warts. Some questioning and history-taking often reveals that the patient has already received all the usual treatments that the dermatologist would have considered. These recalcitrant warts very often require a multimodality approach that consists of both in-office treatment and follow-up at-home care.

**TABLE 1. THE FLACC TOOL**

In the dermatology clinic, it is not necessary to derive a Face, Legs, Activity, Cry, Consolability (FLACC) score; rather, the clinician should look for any level 2 indicators of pain in the five domains.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Description</th>
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<tbody>
<tr>
<td>Face</td>
<td>0 = No particular expression or smile</td>
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<tr>
<td></td>
<td>1 = Occasional grimace/frown, withdrawn, or disinterested</td>
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<tr>
<td></td>
<td>2 = Frequent/constant quivering chin, clenched jaw</td>
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<tr>
<td>Legs</td>
<td>0 = Normal position or relaxed</td>
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<tr>
<td></td>
<td>1 = Uneasy, restless, tense</td>
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<tr>
<td></td>
<td>2 = Kicking or legs drawn up</td>
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<tr>
<td>Activity</td>
<td>0 = Lying quietly, normal position, moves easily</td>
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<tr>
<td></td>
<td>1 = Squirming, shifting back and forth, tense</td>
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<tr>
<td></td>
<td>2 = Arched, rigid, or jerking</td>
</tr>
<tr>
<td>Cry</td>
<td>0 = No cry</td>
</tr>
<tr>
<td></td>
<td>1 = Moans or whimpers, occasional complaint</td>
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<tr>
<td></td>
<td>2 = Crying steadily, screams or sobs, frequent complaints</td>
</tr>
<tr>
<td>Consolability</td>
<td>0 = Content and relaxed</td>
</tr>
<tr>
<td></td>
<td>1 = Reassured by occasional touching, hugging, or being talked to, distractable</td>
</tr>
<tr>
<td></td>
<td>2 = Difficult to console or comfort</td>
</tr>
</tbody>
</table>
THE FOUR-STEP APPROACH
While every case is unique, a frequently effective approach to treatment of recalcitrant verruca vulgaris involves four steps:

- Paring
- Freeze (cryotherapy)
- Bleomycin
- Tazarotene gel.

The first three steps are performed in the office, while high-concentration tazarotene gel is applied daily for two to three weeks at home.

Paring is generally performed, but it may not be appropriate or necessary in all cases.

Freezing may confer best results when performed somewhat aggressively, up to 20 to 30 seconds. Many dermatologists may feel uncomfortable with such a prolonged freeze, worrying about inducing pain. Clinicians can use a modification of the Face, Legs, Activity, Cry, Consolability (FLACC; see Table 1) Tool to ensure patient tolerability of the freeze. The FLACC Tool was developed to access the experience of pain in non-verbal pediatric patients, but older children, adolescents, and adults all communicate pain with similar non-verbal cues: leg movements, grimaces, and groans.

Usually one long freeze/thaw cycle is suggested, though two cycles may be used.

Bleomycin may be applied immediately after freeze, when the epidermis has been compromised. Scarification is usually the method of delivery: multiple small superficial wounds to the wart surface while it is covered with the bleomycin solution (diluted to 1 unit/ml). These wounds can be made by a blood lancet or by the tip of a larger gauge needle (e.g., 18 or 20 gauge). Even though this results in relatively superficial delivery of the drug, some patients will continue to experience discomfort at the site for many hours. Use of bleomycin may not be tolerated in some younger patients and may not be suitable for use at select times for certain individuals. For example, a student athlete should not receive bleomycin on a plantar wart the day before the state finals.

Occasionally patients—and clinicians—wonder about the role of cantheridin in the topical management of common warts. While efficacy of the agent is reasonably reliable, access can be unpredictable. Also, it is relatively easy to cause blistering, which is not desirable and is likely to cause dissatisfaction and discomfort in patients. For these reasons, the agent may not be an ideal intervention for recalcitrant warts.

Cold sores, or herpes simplex labialis (HSL), affect a significant proportion of the US population. Up to 90 percent of adult Americans test positive for HSV-1 serum antibodies, and 20 to 40 percent of the population is estimated to experience regular episodes of HSL.\(^\text{12}\)

Topical over-the-counter and prescription antiviral medications and oral prescription antiviral medications are widely used to treat HSL, and these are shown to reduce the duration of an HSL episode. Relatively new to the treatment palette is a prescription topical formulation that combines acyclovir 5% and hydrocortisone 1% cream (Xerese, Valeant Dermatology), which dermatologist Mark Kaufmann, MD says is an option to consider, especially heading into cooler months. Any antiviral therapy can be used to shorten a herpetic episode, he says, “but the addition of cortisone makes it so that the time that the patient does have an episode is less miserable.”

Studies show that the combination of antiviral acyclovir plus anti-inflammatory low-potency hydrocortisone reduces discomfort, helps to reduce the size and duration of lesions, and can even prevent the development of ulcerative lesions. Clinicians have long suspected that adjunctive use of corticosteroids would provide symptomatic relief for HSL patients receiving antiviral therapy, but the approach...
had not been studied. “We now have proof,” Dr. Kaufmann says, that the two agents can be used together without interfering with the antiviral effect.

Key to optimal therapy, Dr. Kaufmann says, is to initiate treatment at the very first sign of an herpetic eruption. HSL lesions are initially associated with minor burning, stinging, and/or itching during the prodromal stage. “Patients know the signs,” Dr. Kaufmann observes. “Evidence shows that any antiviral is going to be most effective when it is started as soon as possible following the initial experience of symptoms.”

In the pivotal Phase III trials for acyclovir 5% and hydrocortisone 1% cream, combination therapy was associated with a decrease in the rate of ulcerative lesion formation, healing time for ulcerations, and cumulative lesion area.1 Of 2,437 subjects randomized into the study, 1,443 subjects experienced a recurrence and initiated therapy during the trial period (ACH n=601; acyclovir n=610; vehicle n=232). At enrollment, subjects were randomly assigned to initiate therapy with either acyclovir 5% and hydrocortisone 1% cream (ACH cream), acyclovir 5% in the cream vehicle, or vehicle alone at the first sign of recurrence. Among ACH-treated patients, 42 percent did not develop ulcerative lesions, compared to just 35 percent of those treated with acyclovir alone and 26 percent of those receiving vehicle alone.

Compared with placebo-treated subjects, those treated with ACH cream had a 50 percent reduction in cumulative lesion area and a reduction in healing times. Average healing time for ulcerations in the ACH treatment group was 5.7 days compared to 6.5 days for controls. The average healing time was not statistically different between ACH and acyclovir.

Acyclovir 5% and hydrocortisone 1% cream is approved for use in patients as young as 12 years of age, and an analysis of Phase III trial data confirm that the agent is safe for use by adolescents and well tolerated. Treatment is indicated for five times per day for five days. Treatment has not been associated with development of resistance.2

Dr. Kaufmann notes that while dermatologists wisely are cautious when prescribing topical corticosteroids for use on the face or mucosa, Xerese contains hydrocortisone—a Class 7, low-potency corticosteroid—in the same 1% concentration that is marketed OTC in the US. Used as directed, it is unlikely to pose any risks for corticosteroid-related side effects. Treatment was well-tolerated in studies.

Very rarely is HSL associated with functional or long-term cosmetic impairment. However, outbreaks are typically associated with discomfort and short-term cosmetic impairment, as well as anxiety for some individuals. Combination therapy may address these common patient needs. “In addition to decreasing the amount of time that a patient has an episode, this treatment is shown to reduce the severity of an outbreak,” Dr. Kaufmann observes.


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**TABLE 1. HSL THERAPIES**

**Oral**

- valacyclovir 2g BID; one day
- famciclovir 1500mg (three 500mg tablets) single dose
- acyclovir 400mg five times daily for five days

**Topical**

- **five times/day for five days**
  - acyclovir 5% cream or ointment
  - penciclovir 1% cream
  - acyclovir 5% and hydrocortisone 1% cream
  - N-docosanol 10% cream (OTC)