Condylomata acuminata (genital or venereal warts) pose a significant health concern, especially amongst young adults. Considered to be one of the most common forms of sexually transmitted infections (STIs), external genital warts (EGWs) are caused by infection with the human papillomavirus (HPV), the same virus that causes the majority of cervical cancers. Relatively recent therapeutic advances include a topical immunomodulatory agent and a prophylactic vaccine, which have significantly broadened the options for management. Herein, a review of conventional and newer therapies will be discussed.

**Introduction**

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**Background**

**HPV Facts**

Over 100 HPV types have been described, 40 of which infect the anogenital tract; the most common of these are HPV types 6, 11, 16, and 18. HPV 6 and 11 are low risk for causing cancer, but they cause 90% of genital warts. HPV 16 and 18 are considered to be high risk types and contribute to 70% of cervical cancers.

**HPV Pathogenesis**

The principal route of genital infection is through sexual contact. The virus is believed to enter through micro-abrasions in the epithelium. Transmission to newborns by way of passage through the infected birth canal can also occur. The infection rate between sexual partners is approximately 60%. The incubation period for EGWs can range from weeks to years before clinical lesions are detectable. Consequently, unless sexual contact has been limited to a single partner, it is not advisable for patients to attempt to identify the source.

**Risk Factors**

It is estimated that 550,000 Canadians are affected by HPV annually. The rate of infection appears to accelerate following the onset of sexual activity and decrease with increasing age. Prevalence is highest amongst individuals under 25 years of age. The risk level is based on a combination of factors including age, lifestyle, immunocompetency, and other variables, such as:

- becoming sexually active at an early age;
- engaging in unprotected sex;
- previous infection with another form of STI;
- sexual promiscuity of partners;
- lifetime number of sexual partners;
- immune status.

Male circumcision may reduce the incidence of HPV infection according to a recent study by Tobian, et al. Also, because HPV can be present anywhere along the anogenital tract, the use of condoms may only provide partial protection.
In most cases, direct visual inspection can identify the growths on the genital mucosa. Anogenital warts are generally asymptomatic, but can cause pruritus, bleeding, mild burning, and present as:

- lesions that appear primarily on surface areas of the vulva, penis, and perianal skin.
- small, discrete, sessile, flat or raised papules/nodules.
- large exophytic masses.
- a singular papule or multiple verrucous clusters.
- lesions that range in colour from whitish, pink, and flesh-coloured to reddish brown.
- a multifocal distribution that generally correlates with regions sustaining the greatest degree of friction during sexual activity.
- The lesion prevalence in women may be attributable to larger surface areas of mucosal skin.

For hard-to-see warts, a 3%-5% acetic acid solution (i.e., white vinegar) can be applied to the suspect lesion (Figure 1). After a few minutes, the condylomata should appear as whitened patches on the mucosa. Positive changes are not diagnostic for HPV, as these results can also be produced by lichen planus, yeast infections, and other skin disorders.

A biopsy may be considered if:

- diagnostic uncertainty exists.
- lesions are unresponsive to conventional treatments.
- lesions worsen during therapy.
- the patient is immunodeficient.
- the warts are pigmented, indurated, fixed, bleeding, or ulcerated.
- A Pap test can help to establish the presence of a cervical lesion.

Diagnosing Features

Prior to making a confirmed diagnosis, it is necessary for clinicians to obtain medical and sexual histories from patients, if they are not already known. Examination of the mouth and throat, pelvic region, entire genital tract, and thighs may reveal nodules that are indicative of, but not limited to, infection with HPV. Screening for other STIs may also be considered, especially in high-risk individuals.

- The primary treatment objectives are to eliminate visible warts and limit the psychological distress caused by EGWs. In about 10%-30% of patients, EGWs are usually self-limited in immunocompetent individuals and typically resolve within 12-24 months if left untreated; however, lesions may also remain unchanged, or proliferate in size and number.
- The spectrum of available treatments includes self-applied and provider-administered therapies.

Figure 1. Algorithm for treatment of suspect lesions

Treatment
## Treatment (continued)

<table>
<thead>
<tr>
<th>Method</th>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antiproliferative Therapies</strong></td>
<td></td>
<td></td>
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<tr>
<td>Podophyllum resin 10%-25%</td>
<td>• Physician-administered</td>
<td></td>
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<tr>
<td></td>
<td>• Removal of warts by destruction of infected tissue</td>
<td></td>
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<tr>
<td></td>
<td>• Potential for systemic toxicity</td>
<td></td>
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<tr>
<td>Podophyllotoxin 0.5% solution or gel</td>
<td>• Can be applied by the patient</td>
<td></td>
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<tr>
<td></td>
<td>• Low cost, low toxicity</td>
<td></td>
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<tr>
<td></td>
<td>• It does not contain any mutagenic substances, unlike those found in podophyllum resin</td>
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<tr>
<td><strong>Immunomodulatory Therapy</strong></td>
<td></td>
<td></td>
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<tr>
<td>Imiquimod 5% cream</td>
<td>• Self-administration may improve patient adherence</td>
<td></td>
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<tr>
<td></td>
<td>• Enhances the cytotoxic immune reaction, which is usually seen as an inflammatory response</td>
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<tr>
<td></td>
<td>• Apply directly to the affected skin 3 times/week for up to 16 weeks; frequency of application can be reduced if there is concern over the degree of inflammation</td>
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<tr>
<td></td>
<td>• Has a low rate of recurrence due to reduction of the viral load</td>
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<tr>
<td></td>
<td>• Effective for treating multiple warts covering larger areas, as well as subclinical lesions</td>
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<tr>
<td></td>
<td>• Side-effects are mild to moderate and include local erythema and erosion at the site of application</td>
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<td></td>
<td>• Has a higher drug cost than podophyllotoxin</td>
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</tr>
<tr>
<td><strong>Destruction/Excision Therapies</strong></td>
<td></td>
<td></td>
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<tr>
<td>Topical trichloracetic acid 85% (TCA)</td>
<td>• Causes cellular destruction by chemical cautery</td>
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<tr>
<td></td>
<td>• Most effective when treating small, moist lesions</td>
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<tr>
<td></td>
<td>• Damage to surrounding tissue can be minimized by protection with petroleum jelly</td>
<td></td>
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<tr>
<td></td>
<td>• If TCA is applied to nonaffected tissue, instruct patients to wash the area with liquid soap or baking soda</td>
<td></td>
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<tr>
<td></td>
<td>• Can cause pain and ulceration</td>
<td></td>
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<tr>
<td>Local cryotherapy</td>
<td>• Most common destructive mode</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Involves freezing with liquid nitrogen</td>
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<tr>
<td></td>
<td>• Offers ease of use with no systemic effects</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Can cause pain and ulceration</td>
<td></td>
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<tr>
<td></td>
<td>• Safe for use during pregnancy</td>
<td></td>
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<tr>
<td>Electrodesiccation</td>
<td>• Warts are burned off with a low-voltage electrical current</td>
<td></td>
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<tr>
<td>Excision by scissors, curette, or scalpel</td>
<td>• Provides definitive clearance of abnormal tissue</td>
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<tr>
<td></td>
<td>• Particularly suitable for larger exophytic warts</td>
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<tr>
<td></td>
<td>• Local anesthesia is required</td>
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<tr>
<td>Ablative laser</td>
<td>• Use of CO₂ laser therapy is usually reserved for extensive and/or treatment-resistant warts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• May require a long time for recovery and is expensive</td>
<td></td>
</tr>
<tr>
<td><strong>Combination Therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination therapy can provide a better result over monotherapy</td>
<td>• Cryotherapy combined with imiquimod appears to be very commonly used</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Initial therapy with imiquimod may reduce wart size and improve surgical outcomes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Initial treatment with imiquimod followed by excision of residual lesions may provide long-term clearance of EGWs, especially if prior monotherapy was insufficient</td>
<td></td>
</tr>
<tr>
<td>Excision/destruction + imiquimod</td>
<td>• Due to cidofovir’s broad antiviral activity, it has been used successfully as a topical gel for refractory patients</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Treatment options for genital warts

The therapeutic horizon may include a topical formulation whose active constituent is a defined mixture of catechins extracted from green tea with demonstrated efficacy and safety for EGWs. This herbal prescription drug gained US FDA approval in 2006 for the treatment of external genital and perianal warts caused by certain strains of HPV.
The most widely used treatment modalities can be broadly categorized as antiproliferative, immunodulatory, destruction/excision, and combination therapies (Table 1).

The majority of therapeutic options provide symptomatic relief rather than treat the disease itself. The one exception is a topical immune response modifier (i.e., imiquimod), which exerts a field effect that can target both clinical and subclinical manifestations of HPV.

Therapeutic decisions should be guided by wart type, location, number, sex, patient preferences, physician experience, and unique circumstances (e.g., young age, immunosuppression, and pregnancy).

For vaginal mucosal warts, treatment options include cryotherapy and topical TCA 80%-90% (physician-applied).

Given the wide range of patient and treatment variables, there is a lack of conclusive evidence confirming the superiority of any one modality, or combination thereof, over another.

The majority of patients require a course of therapy rather than a single treatment.

Depending on the therapeutic modality used, a suggested wait time of 1-3 weeks is recommended before retreatment, in order to allow for adequate healing of treated lesions to occur.

It is important to iterate to patients that available treatments can induce wart-free periods, but none provide complete clearance of HPV infections.

**A Prophylactic Approach**

In 2006, Health Canada approved a quadrivalent HPV vaccine that acts against HPV types 6, 11, 16, and 18.

- It is indicated for use in females 9-26 years of age and is given as a 0.5mL injection intramuscularly in 3 doses at 0, 2, and 6 months.
- The quadrivalent vaccine is 97% effective in preventing vaginal and vulval intraepithelial neoplasia, and is 99% effective in preventing genital warts caused by HPV types 6 and 11.
- There is no evidence suggesting that therapeutic benefits may be derived from the immunization vaccine if patients are already infected with vaccine HPV types.
- Recent studies suggest that the quadrivalent vaccine may also provide cross-protection against HPV strains that are not contained in the vaccine, but are closely related. However, the durability of immunity and the significance of these findings remain to be established.

Studies investigating this vaccine in males are underway.

**Conclusion**

- For the initial treatment of genital warts, many patients prefer self-applied therapies.
- Because monotherapy is often insufficient, combination therapy may be more advantageous.
- Throughout the course of treatment, patients must be monitored for response rate and side-effects.
- An inadequate response to treatment necessitates a transition to other therapies or modification of the existing approach.
- According to the Canadian Consensus Guidelines on HPV, due to its favourable efficacy, safety, and tolerability profiles, as well as the lowest recurrence rate, imiquimod represents an effective strategy for the management of genital warts, and should be considered prior to initiating more invasive options, such as destructive/excision or laser therapies.

The increasing incidence of HPV infections is of mounting concern and the most prevalent clinical manifestation of this communicable disease is genital warts. Upon confirmation of diagnosis, patient-specific treatment that is accompanied by education on limiting the risk of transmission and HPV-associated diseases, as well as recommendations for regular screening, are warranted. Although disease morbidity can be mild, the emotional distress of having genital warts can result in severe psychological impacts; hence, successful management is essential.

**References**

Moisturizers: An Essential Component in Eczema Management

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2 Faculty of Medicine, University of Toronto, Toronto, ON, Canada
3 University Health Network (Western Division), Toronto, ON, Canada

Background

Atopic dermatitis (AD) or eczema is a chronic, relapsing form of skin inflammation that is attributable to multiple pathogenic, genetic, and environmental factors, as well as a dysfunctional epidermal barrier. Immune responses involved in AD culminate in dry skin, pruritus, and IgE mediated sensitization to food and environmental allergens.1 An improved understanding of crucial skin barrier defenses and the inflammatory cascade that drives disease activities has led clinicians to reassess conventional approaches to treatment and recognize emollients for their therapeutic potential. Accordingly, emollient-based moisturizers and cleansers have been established as essential adjuvants for successful AD management.

The Role of Moisturizers in Optimal AD Management

A persistent feature of AD is dry skin that is caused by a combination of intrinsic disease mechanisms and hyperreactivity to exogenous factors. Some treatments for AD can further exacerbate xerosis, itching, and irritation. Such external insults on an already impaired skin barrier drive the dry skin cycle and leave skin vulnerable to microbial infections. For these reasons, maintaining hydration and restoring epidermal barrier defenses provide the rationale for moisturization therapy.

What are moisturizers?

- Moisturizers are composed of a combination of key ingredients that are categorized as emollients, humectants, and occlusives, which work synergistically to enhance hydration and barrier function.
- A randomized controlled study showed that well-designed formulations incorporating these constituents can improve the epidermal barrier function and increase skin hydration levels; however, the effects are determined by individual product composition.5,7

How do moisturizers work?

- The mechanism of action of emollients may be elucidated as a role substitution by lipid ingredients, which take on the functions of naturally occurring lipids that are either absent or impaired in eczematous skin.
- Treatment of the skin with moisturizers can repair the skin barrier, increase water content, reduce transepidermal water loss (TEWL), and restore the lipid barriers’ ability to attract, retain, and redistribute water.
- The maximum effects are derived from prophylactic and frequent use.
- Moisturizers maintain hydration in the skin by slowing TEWL. In doing so, they help dry and/or aging skin to improve its structural integrity, appearance, and tactile properties.
- By covering tiny fissures in the skin and providing an occlusive protective film over the stratum corneum (SC), moisturizers restore the epidermal barrier, and reduce the penetrability of allergens and irritants.

Moisturizers demonstrate adjuvant properties

- Regimented moisturization has become standard adjunctive AD therapy by serving as a foundation to support pharmacologic measures, reducing the need for topical corticosteroids and calcineurin inhibitors, and mitigating the side-effects from medications.
- During flares, OTC combination preparations containing a moisturizer with a topical corticosteroid (e.g., clobetasone and hydrocortisone) are helpful to control inflammation and restore the skin barrier.
**Emollients**

- Emollients are mainly lipids and oils that hydrate and improve the appearance of the skin by contributing to softness, smoothness, and improved flexibility.
- The lubricity of some moisturizers can influence consumer satisfaction and product preference.
- The SC of AD patients have significantly reduced levels of ceramides (lipid molecules), which are important components of skin structure.
- The topical replacement of lipids serves to ‘fill the cracks’ between clusters of desquamating corneocytes.

**Humectants**

- Humectants attract and retain hydration in the skin by enhancing water absorption from the dermis into the epidermis or absorbing water from the external environment.
- Many humectants also have emollient-like properties.\(^7\)
- The most effective humectant is the trihydroxylated molecule, glycerin, which is also commonly referred to as glycerol.
- Glycerin is the most widely used humectant.

- A double-blind study comparing glycerin with urea showed that although both compounds were equally effective in treating xerosis, glycerin caused significantly less adverse skin reactions.\(^8\)
- Urea is another commonly used humectant that is effective against TEWL.
- Avoid the use of urea-containing moisturizers in young children due to potential irritation.

**Occlusives**

- Occlusives reduce TEWL by creating a hydrophobic barrier over the skin and contributing to the matrix between corneocytes.
- Efficacy is enhanced when occlusives are applied to slightly dampened skin.
- Their main limitations include odour, potential allergenicity, and a ‘greasy’ feel.
- Petroleum jelly (petrolatum), in a minimum concentration of 5%, is the most effective occlusive, followed by lanolin, mineral oil, and silicones.
- Silicone-based derivatives (e.g., dimethicone) are oil-free alternatives that are noncomedogenic, nonirritating, nonsensitizing, and more cosmetically acceptable.

The following adapted guidelines for the use of moisturizers in AD, developed by the National Institute for Health and Clinical Excellence,\(^9\) serve as practical advice for patients and their doctors.

- Physicians should be prepared to offer patients a choice of unperfumed emollients:
  - suited to the patients’ needs and preferences.
  - for everyday moisturizing, as well as emollient-enriched washing and bathing formulations.
- Moisturizers should be:
  - used more often and in larger amounts than other treatments.
  - used even when AD is clear.
- **Recommendations for Use**
  - used while using other treatments.
  - offered as a single or combination product (offer alternatives if one formulation causes irritation or does not gain patient acceptance).
  - easy to apply throughout the day.
  - Recommend leave-on moisturizers in large quantities.
  - Instruct patients or their parents on sufficient and proper application.
  - When multiple topical products are used concurrently, instruct patients to apply them one at a time, allowing for several minutes to pass in-between applications.
  - Consider increasing the use of emollients if patients report difficulties in controlling itch.

The regular use of mild cleansers is an important aspect of optimal AD management. Not only is cleansing an essential part of basic hygiene, but it also removes dirt, sweat, bacteria, and exfoliated cells, which prepares the skin to receive topical medications and improves drug absorption.

- AD lesions are commonly colonized with *S. aureus*. Routine cleansing can enhance antimicrobial activity against *S. aureus* and decrease the chances of infection.
- Care must be taken to minimize any further weakening of the SC barrier during cleansing. The use of improper techniques and unsuitable cleansing agents on the face or body can initiate flares or exacerbate AD.
- **Mild Skin Cleansers**
  - The use of anionic detergents (i.e., soaps) can alter the pH of skin, resulting in increased sensitivity to irritants and conditions that can promote bacterial proliferation.\(^10\)
  - While removing excess sebum, cleansers can also inadvertently damage intercellular lipids, which can lead to further impairment of the barrier function and cause dry skin.
  - Cleansers that are suitable for eczematous skin are generally based on mild synthetic surfactants that cause minimal barrier disturbances.
  - Non-ionic surface-acting agents (e.g., silicone and polysorbate) are less likely to cause irritation and are pH-compatible with the skin.
Silicone surfactants, such as dimethicone, are effective at eliminating surface debris without completely stripping away protective oils. Emollients contained in cleansers can minimize barrier damage by emulsifying dirt and oil for easy removal, while at the same time replacing lipids that are lost during the washing process.11

Using the 4 Rs of AD Management

The best practice management of AD must include patient education. Physicians are encouraged to provide verbal and written information on AD and selected treatments, as well as practical demonstrations of proper administration. These instructional measures should be reinforced during each consultation in order to promote treatment adherence and improve outcomes. Remembering the 4 Rs can simplify the multi-layered approach for management.

Recognize

- Recognize and diagnose the condition promptly so that treatment can be initiated.
- AD patients have a predisposition for developing other atopic conditions, such as asthma and allergic rhinitis.1
- Encourage patients to maintain a diary to track foods eaten, flares, and the use of medications, moisturizers and cleansers, which can help guide therapeutic decision-making.

Remove

- Avoidance is a central AD management strategy. Identify and eliminate relevant triggers (e.g., irritants, aeroallergens, and foods) and seek ways to reduce stress.
- Mild cleanser use can help to remove surface dirt, irritants, and microbes.
- Consider allergy testing to identify triggers.

Restore

- The regimented use of emollients can partially repair and restore the skin barrier and reduce infections and allergic reactivity.
- Body washes that are formulated with nonirritating surfactants, emollients, and humectants can replenish barrier lipids during cleansing to minimize TEWL. Lukewarm baths (5-10 minutes in duration) are recommended over showers.
- Creams and ointments are more effective for eczematous skin. Apply moisturizers 3-5 minutes after bathing.

Regulate

- When flares occur, interrupt and regulate inflammatory responses with immediate treatment in order to break the itch-scratch cycle and limit AD severity.
- Therapeutic strategies include topical corticosteroids, topical calcineurin inhibitors, antimicrobials, and oral antihistamines, as well as routine skin care.
- In patients exhibiting an inadequate response to therapy, assess treatment adherence, side-effects, and review moisturizer and cleanser use during each clinic visit.

Conclusion

Due to the chronicity of AD, as well as multiple factors contributing to its etiology, successful management requires a multipronged approach that includes lifestyle modifications, adaptations to skin care practices, and medical intervention. Although topical corticosteroids are firmly established as the cornerstone therapy, long-term and overuse are associated with skin atrophy and adverse systemic effects. The combination of moisturizers with topical steroids can have a significant steroid-sparing effect, especially in children with mild-to-moderate AD. A therapeutic approach that incorporates patient education and emollient therapy can complement pharmacologic measures to extend periods of remission and significantly lessen the disease burden.

References

To get more information, Canadian medical professionals and consumers can access all of our sites from www.SkinCareGuide.ca or go directly to:

**Patient sites:**
- AcneGuide.ca
- BotoxFacts.ca
- ColdSores.ca
- DermatologyCare.ca
- EczemaGuide.ca
- FungalGuide.ca
- HerpesGuide.ca
- Lice.ca
- MildCleanser.ca
- MohsSurgery.ca
- PsoriasisGuide.ca
- PsoriaticArthritisGuide.ca
- RosaceaGuide.ca
- SkinCancerGuide.ca
- Sweating.ca
- UnwantedFacialHair.ca

**Medical professional sites:**
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- SkinTherapyLetter.ca
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