Treatment of Molluscum Contagiosum in Adult, Pediatric, and Immunodeficient Populations

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Background: Molluscum contagiosum is a viral infection of the skin that is widely considered to be a self-resolving disease that can be treated with benign neglect. However, the clinical reality is that the disease can vary widely by anatomic site and by recalcitrance to treatment and remains a significant cause of morbidity worldwide.

Objective: The purpose of this review was to compile an updated resource for clinicians that addresses the management of the broad spectrum of molluscum cases that may be encountered.

Methods: A comprehensive PubMed search was performed to identify publications on the treatment of molluscum infection, including presentations that may be rare or difficult.

Results: The specific clinical scenario of molluscum must be considered when selecting the optimal therapy because certain treatments can be more effective for specific patient subpopulations.

Conclusion: Further attention must be directed toward standardizing treatment for molluscum infection based on patient age and immune status.

MOLLUSCUM CONTAGIOSUM is a cutaneous and mucocutaneous viral infection that is commonly observed in school-aged children, sexually active adolescents, and immunocompromised individuals of all ages. The infection is caused by the molluscum contagiosum virus (MCV), a large double-stranded deoxyribonucleic acid (DNA) virus from the Poxviridae family. The MCV genome is covalently linked at both ends and encodes several gene products that are involved in both viral life cycle and host immune evasion.1-3 In otherwise healthy patients, MCV infection presents as a small cluster (11–20) of skin-colored papules that are 3 to 5 mm in diameter.4 Molluscum papules are clinically differentiated from lesions formed by other cutaneous diseases by the presence of a central umbilication. However, this defining feature may be difficult to empirically observe in a variety of clinical scenarios and, instead, may bear an appearance similar to an acneiform eruption. Generally, the papules are benign and asymptomatic, although erythema and itchiness at the site of infection are reported in a subset of patients.

Molluscum is transmitted through skin-to-skin contact with the infected site, through contaminated fomites—such as bath towels and clothing—and through vertical transmission during labor. The virus can also be autoinoculated, spreading from the initial site of infection to other sites on the body.5 In 30% of patients, acute eczema develops around the papules approximately a month after onset of infection.6 Eczema is associated with an increased risk of autoinoculation because patients are more likely to scratch the eczematosus region, thereby spreading the viral particles to other sites of the body. The acute eczema usually subsides spontaneously with the eradication of the molluscum lesions. A further clinical association between molluscum and eczema was elucidated by an Australian study, which found that 62% of children with molluscum contagiosum reported a history of eczema and thus concluded that preexisting eczema likely predisposes children to the infection.5

Papules can appear on all cutaneous and mucocutaneous sites of the body, including the genitalia, as well as the perianal, orbital, and oral mucosa. Molluscum of the genitalia and perianal regions can be either autoinoculated or sexually transmitted. Autoinoculation to the genitalia can usually be distinguished by identifying lesions on
multiple regions of the body; in contrast, most cases of sexually transmitted molluscum are localized exclusively to the genital area. In addition to infecting the genitalia, molluscum can occasionally spread to the oral mucosa—potentially from the genitalia during oral sex—as well as to the conjunctiva and cornea.7,8 The latter scenario may result in chronic conjunctivitis, keratoconjunctivitis, or superficial punctate keratitis, which complicates treatment of lesions in the orbital region.

Although data are limited, several studies have estimated the worldwide prevalence of the infection to be 5.0 to 7.5%.9–11 The prevalence is increased in immunocompromised populations (5.0–18%) and has been reported to be as high as 30% in patients with advanced acquired immune deficiency syndrome (AIDS).10

In healthy patients, cutaneous molluscum contagiosum is a self-limiting disease that often spontaneously resolves in 6 to 9 months, usually without scarring. Current therapy for healthy individuals merely accelerates the clearance process and can be associated with unwanted side effects, such as scarring, erythema, and discomfort. As a result, although permutations of therapeutic strategy may be implemented based on each patient’s unique case, many clinicians simply choose to employ benign neglect for the treatment of molluscum. However, benign neglect is usually effective only in healthy individuals, who are eventually able to mount a successful cell-mediated immune response and overcome the virus’s pathomechanisms. Quality of life is a factor to consider when deciding whether or not to treat a pediatric patient as he or she may suffer chastisement from peers at school if the lesions are visible. Not treating pediatric infections also carries the risk of the disease spreading to classmates, and this consideration may favor the option of treatment over benign neglect.

Currently, there is no Food and Drug Administration (FDA)-approved therapy for molluscum contagiosum. There is not one widely accepted standard of care, which is especially problematic for immunodeficient patients, who often suffer from severe, persistent molluscum. Molluscum infection in the immunodeficient population can become physically and psychologically debilitating, with hundreds of lesions developing on the body. Unfortunately, little is known about the efficacy of various therapies for the immunodeficient population. A plethora of case reports—each describing successful treatment of various singular immunodeficient patients—have been published, but to our knowledge, there is no readily available resource for the compilation and comprehensive consensus of these findings. Finally, although molluscum infection on the genitalia is commonly observed clinically—usually as a result of autoinoculation of conventional molluscum infection—genital lesions can be accompanied by additional issues and problems that the clinician must consider when treating these cases. For example, although conventional molluscum can be managed with benign neglect, sexually transmitted molluscum is important to treat not only for the benefit of the patient but also to prevent spread to sexual partners. Taken together, molluscum presents differently based on the patient population and necessitates specific treatments for each of the myriad presentations. Here we review key findings and insightful clinical observations that have been published on the management of the gamut of molluscum contagiosum infections.

Clinical Management

Molluscum in Immunodeficient Patients

In healthy individuals, molluscum contagiosum is often a self-limiting infection that generally clears completely within several months. On average, 11 to 20 papules appear on the body during the course of infection but spontaneously resolve within 2 months.4 However, in an immunodeficient host, MCV can cause severe, persistent infection with hundreds of lesions that tend to be recalcitrant to treatment. Extensive infection is indicative of an advanced immunodeficient state.

Treatments that lead to wound formation, such as curettage and cryotherapy, can be effective in immunodeficient patients with mild infection. However, overall, such strategies are not optimal in immunocompromised patients for two chief reasons. First, open wounds elevate the risk of additional cutaneous infection, which commonly include candidiasis, human papillomavirus–associated warts, and staphylococcal pyoderma.12 Second, in severe cases, the infection may be so widespread on the body that treating individual lesions may not be practical without risking continual autoinoculation. Several therapies, most of which are immunomodulators, have been described in the literature to be successful for treating molluscum in immunodeficient patients. These treatments include 5% imiquimod cream, interferon-α (IFN-α) injections, and cidofovir.

The most well-described therapeutic agent, topical imiquimod, is available on the market as 5%, 3.75%, and 2.5% creams. It is thought to activate both innate and
adaptive immunity through Toll-like receptor 7 (TLR7), which is involved in pathogen recognition and the release of several immunostimulatory cytokines. A study published in 2000 found 5% imiquimod (applied three times weekly for up to 16 weeks) to be effective in completely eradicating lesions in four of four adults with advanced but stable human immunodeficiency virus type 1 (HIV-1) disease. Interestingly, subjects with HIV-1 had a better overall response to therapy than both their immunocompetent counterparts and the healthy children who participated in the study. Additionally, successful resolution using imiquimod three times per week has been reported in a woman with Sjogren syndrome, a renal transplant patient with multiple giant molluscum, and several other HIV-positive patients with severe molluscum. Imiquimod therapy often results in nonspecific inflammation and dermatitis, especially in skin folds or in areas that have been traumatized due to scratching. Less common side effects include headaches, back pain, muscle aches, tiredness, flu-like symptoms, swollen lymph nodes, diarrhea, and fungal infections.

**IFN-α** is a glycoprotein cytokine that is endogenously produced in response to viral infection and produces many proteins that are involved in inhibiting viral replication. The recombinant form was initially used in dermatology mostly for the treatment of recalcitrant condyloma acuminata until a study, published over a decade ago, described the successful resolution of severe molluscum in 11 patients and 50% reduction in 18 patients (of a total of 30 subjects) after intralesional injection of 1 megaunit of IFN-α weekly for 4 weeks. Since then, several articles have reported its efficacy in treating lesions in patients with other immunodeficiency disorders using various dose frequencies. After the incomplete success of the initial report, the next study in 1999 employed subcutaneous injections and increased dose frequency to 3 megaunits of IFN-α three times a week for 6 months and then, afterwards, weekly injections for 3 months. This treatment strategy successfully achieved 95% clearance of molluscum in two siblings suffering from putative combined immunodeficiency. A 9-year-old with hyperimmunoglobulin E syndrome also underwent the same therapy schedule as the siblings. This resulted in complete clearance of his recurring molluscum lesions, which were previously unresponsive to phenol, trichloroacetic acid, cryosurgery, and imiquimod therapy. Most recently, pegylated IFN-α was shown to completely resolve disseminated giant molluscum after 16 months of treatment in a 31-year-old woman with idiopathic CD4+ lymphocytopenia. However, the regimen could not be increased from 50 μg per week subcutaneously because the patient’s total leukocyte count dropped to as low as 2,900/μL. In patients with low leukocyte levels, it may be prudent to conduct regular white blood cell counts when administering IFN-α treatment so that the regimen can be adjusted accordingly.

Cidofovir, a nucleotide analogue of deoxycytidine monophosphate, has been popularly used to treat cytomegalovirus (CMV) retinitis in AIDS patients. Readily available in the intravenous form, cidofovir prevents viral transcription and replication by inhibiting viral DNA polymerase. Not surprisingly, cidofovir is also effective at inhibiting viral replication in a number of other DNA viruses, including MCV. This discovery was made haphazardly by Meadows and colleagues when an HIV-positive patient was shown to completely resolve disseminated molluscum after being treated with intravenous cidofovir for treatment-resistant CMV retinitis. The man’s molluscum was previously unresponsive to cantharidin, cryotherapy, curettage, IFN-α, and several other first-line treatments. In the same study, another HIV-positive patient also with concurrent CMV retinitis and molluscum contagiosum on the face was successfully treated with intravenous cidofovir at a dosage of 5 mg/kg once a week for 2 weeks, followed by 5 mg/kg once every 2 weeks. This regimen was slightly higher than used for the first patient, whose lesions responded to a dosage of 2 mg/kg once weekly for 2 weeks and then a maintenance therapy of 2 mg/kg every 2 weeks. However, systemic cidofovir is known to be nephrotoxic, so topical cidofovir has been explored as a potential therapeutic agent for immunodeficient patients but has thus far yielded promising but inconclusive results. A third HIV-positive patient in the Meadows and colleagues study achieved successful resolution of recalcitrant molluscum infection on his face using 3% cidofovir cream daily for 5 days a week. The lesions, which originally covered 95% of his face, were completely cleared within 1 month without any sequelae. Moderate inflammation appeared during the second week of therapy but spontaneously resolved 2 weeks later. Similarly, complete resolution of a severe case of molluscum on the face of another HIV patient was recently achieved in one author’s investigational center after 2 months of topical cidofovir compounded into a 2% ointment (unpublished report). Currently, the topical form is not readily available on the market and must be compounded as a 1 to 3% cream (Dermovan, Galderma Laboratory, Fort Worth, TX).

**Molluscum in Pediatric Patients**

Viral infections, such as the human papillomavirus and HIV, can be vertically transmitted from mother to infant if
proper measures are not taken. Although only a handful of congenital cases are reported in the literature, it is believed that MCV can be transmissible during labor as well. Given that MCV has an estimated incubation period of 14 days to 6 months, molluscum lesions may not be visible on the infant at birth and thus could explain the dearth of cases reported in the literature. This observation has led to the hypothesis that most infantile patients presenting with molluscum likely contracted the infection through vertical transmission. A literature review yielded seven reported cases of congenital molluscum. Interestingly, in nearly all reported cases, molluscum lesions appeared in a halo-like ring around the scalp, which is likely associated with the increased cervical pressure placed on this region of the scalp during labor and delivery. Additionally, several of the infants also presented with molluscum lesions on other sites of the body. One 2012 case report identified a linear track of molluscum lesions in the coccygeal region with additional lesions presenting on the back and upper arm in a 1-year-old infant. It is possible to confirm the mode of transmission through viral genotyping, but to date, no studies have examined the genotype of congenital molluscum lesions. As in the case of sexually transmitted molluscum, the main therapy for congenital molluscum lesions is direct destructive measures with curettage or cryotherapy. Alternatively, the lesions have also been successfully resolved with the topical agent 0.7% cantharidin. Although cantharidin is used by many physicians in the United States as an off-label treatment for molluscum, the compound is not currently approved by the FDA and therefore is often acquired from Canada.

Noncongenital molluscum infections in children are responsible for myriad pediatrician and dermatologist visits each year. A common treatment used for these infections is topical cantharidin. Although topical cantharidin is often used to treat pediatric molluscum infections, its potency might not be as evident in this patient population as originally believed. A double-blind randomized clinical trial evaluated the treatment of 29 children ages 5 to 10 years with topical cantharidin. The performance of cantharidin was observed to be similar to that of the placebo. However, the authors conceded that their definition of “clearance” may have been stricter than similar trials, which may have impacted the results. Regardless of this study’s findings, a survey of 95 clinicians indicated a 92% satisfaction rate with cantharidin’s efficacy in treating molluscum, possibly indicating a disparity between objective and subjective satisfaction with the therapy.

Additional therapies for pediatric molluscum include topical imiquimod, curettage, cryotherapy, retinoids, cimetidine, salicylic acid, duct tape, Candida antigen, potassium hydroxide (KOH), and cidofovir. Hanna and colleagues conducted a randomized controlled trial comparing the efficacies of curettage, cantharidin, imiquimod, and a combination of salicylic acid and lactic acid. The study included 124 pediatric patients equally sorted into four groups. For the curettage group, 80.6% required only one visit, 16.1% required two visits, and 3.2% required three visits for treatment of their molluscum. Comparatively, the percentages were 36.7%, 43.3%, and 20.0% for cantharidin; 55.2%, 41.4%, and 3.4% for imiquimod; and 53.6%, 46.4%, and 0% for salicylic and glycolic acid. Thus, curettage was reported as the most potent treatment, along with having the lowest incidence of side effects.

Imiquimod 5% cream has received attention as a pragmatic treatment option for pediatric molluscum infection because the cream can be applied at home, decreasing the burden of parental responsibility of follow-up visits. In a study comparing the effects of imiquimod 5% cream versus cryotherapy for molluscum contagiosum, cryotherapy was performed with liquid nitrogen for two 10- to 20-second cycles on a group of 37 patients at an initial visit and 1 week later if needed, whereas the other group of 37 patients received imiquimod cream five times weekly for up to 16 weeks. Although the investigators observed a more rapid clearance of the infection in the cryotherapy group at 6 weeks, there was no statistical difference between the two groups after a 12-week period, with both groups demonstrating approximately 100% clearance. At a follow-up conducted 6 months after the study, the imiquimod group exhibited a superior cosmetic outcome, with only 2 patients displaying residual hypopigmentation, versus 15 patients with pigmented changes and 8 patients with scarring or atrophy in the cryotherapy group. There were no cases of relapse in the imiquimod group, although there were 3 patients in the cryotherapy group whose infections relapsed at 6 months. An additional study conducted in India evaluated the safety and efficacy of imiquimod 5% cream versus 10% KOH solution, applied 3 days per week, in patients between the ages of 1 and 40. The mean lesion count decreased from 22.39 to 10.75 in the imiquimod group (18 patients) and from 20.79 to 4.31 in the KOH group (19 patients) at the end of 12 weeks. Complete clearance of the infection was observed in 8 (44%) of the imiquimod patients and 8 (42.1%) of the KOH patients. The researchers concluded that both topical methods were effective in treating molluscum, although KOH had a faster onset of action but was also associated with a greater incidence of side effects.
Turkish study examined the application of 10% KOH aqueous solution in 40 pediatric patients with molluscum. Parents were instructed to apply the solution twice a day to all lesions and continue until the lesions showed signs of inflammation or superficial ulceration. Complete clearance was achieved in 37 (92.5%) patients after a mean period of 4 weeks. Local side effects were experienced by 12 children (32.4%), but it was concluded that KOH was a safe, effective, and inexpensive treatment for molluscum in children.36

A study published in 2011 indicated that immunotherapy in the form of intralesional Candida antigen injection may serve as a promising treatment for pediatric molluscum infections. The study participants were administered no more than 0.3 mL of Candida antigen intralesionally at 4-week intervals until clearance of the infection was achieved. The treatment effected complete clearance in 55.2% of the 29 pediatric patients and partial clearance in 37.9%, with a treatment total response of 93%. The only reported side effects were pain and discomfort at the time of injection.37

A final potential oral therapy for pediatric molluscum is the H2-receptor antagonist cimetidine. When administered to 13 children at a dose of 40 mg/kg/d, complete clearance of the lesions was seen in 10 of the patients.38 Although these results seem promising, cimetidine may be effective only in atopic patients.39

Molluscum in Adults

Molluscum infections are most common in children ages 1 to 10, but adult infections also occur.40 Sexually active patients are more susceptible to molluscum infections in specific anatomic regions, mainly the genital area. Molluscum contagiosum commonly infects the genitalia either through autoinoculation of conventional molluscum from other sites of the body or through sexual transmission of the genital lesions on another individual. Regardless of the infection source, genital infection must be attentively managed.

A recently published 20-year longitudinal study indicated that although the rates of other sexually transmitted infections (STIs) in the authors’ community hospital have remained relatively stable over the past two decades, there has been a threefold increase in the number of cases of molluscum infection in the genital and perianal regions.41 A subsequent study found molluscum to be the second most prevalent nonulcerative STI after genital warts. This relative increase is thought to be a result of the persistent and recurrent nature of viral infections.42 One Dutch study reported that sexually transmitted molluscum infections accounted for 1 to 3% of all reported cases of STIs and estimated the worldwide prevalence of sexually transmitted molluscum to be between 2 and 8% of the total population. The disease is most prevalent in the 20- to 30-year-old age group and affects men and women equally. There is an increased incidence of disease in heterosexual populations compared to homo- and bisexual populations.41–43 Additionally, there is an increased prevalence of sexually transmitted molluscum in married patients.

Sexually transmitted molluscum is diagnosed primarily through an evaluation of patient history and physical examination, noting the localization of the molluscum lesions to the genital and perianal regions. Although single lesions may occur, sexually transmitted molluscum lesions are typically found in clusters of 30 papules or fewer in otherwise healthy individuals.43 Molluscum can be identified by its characteristic central umbilication, but in cases where the clinical picture is not clear, laboratory testing may be used to confirm the diagnosis.42 Patients testing positive for genital molluscum infection should be tested for other concurrent STIs as a precautionary measure.43 Although the efficacy of therapeutic interventions continues to be debated in conventional, non–sexually transmitted cases of molluscum, active treatment in sexually transmitted cases is unequivocally indicated.41 This course of action is favored to reduce the risk of further sexual transmission, to prevent additional autoinoculation, and to improve a patient’s quality of life.42 An Indian study notes that evidence is accumulating that STIs, including molluscum, augment HIV infectiousness and promote its transmission.42 This further demonstrates the need for prompt management of sexually transmitted molluscum contagiosum.

The standard treatment for molluscum lesions is generally the same as the treatment for the genital warts caused by the human papillomavirus. Physical ablation of the infected tissue via curettage, electrocautery, or cryotherapy is considered to be first-line therapy in the treatment of sexually transmitted molluscum.43 One study reported clearance of infection in 92.3% of patients after 15 days of ablative treatment.44 However, as noted above, in patients concurrently infected with molluscum contagiosum and HIV, destructive therapies may not be effective. Instead, other treatment strategies should be developed, particularly in cases of giant, recalcitrant, or extensive molluscum infection that are often seen in immunocompromised patients.44 Physicians may alternatively use chemical ablation such as trichloroacetic acid or
podophyllin to destroy infected tissue. However, because of the low efficacy and high toxicity of these treatments, they are not commonly used.\textsuperscript{43}

In addition to physician-administered physical and chemical ablation, there are a number of treatment options that may be self-administered by the patient. Podofilox, which is the active ingredient in podophyllin, and retinoic acid have been shown to have varying success in treating cutaneous warts and may be effective in treating molluscum lesions.\textsuperscript{43,45} The most common side effects noted in these self-administered ablative treatments are xerosis, burning, irritation, itching, inflammation, and erosion.\textsuperscript{43} Self-administered topical treatments that modulate the local immune response have been used in the treatment of genital molluscum lesions. In clinical trials, treatment with 5\% imiquimod 5 days a week for 4 to 16 weeks led to complete clearance in 80\% of study patients and a 50\% reduction in molluscum lesions in the remaining 20\%, with very low recurrence rates at 32 weeks posttreatment.\textsuperscript{46} An additional double-blind study found that three times daily application of 1\% imiquimod for 4 weeks resulted in a clearance rate of 86\%.\textsuperscript{47} In our clinic, we frequently use 3.75\% imiquimod cream as well as sinecatechin ointment to treat genital molluscum (data forthcoming). The most common side effects of imiquimod treatment were erythema, erosion, and pruritus.\textsuperscript{43}

As previously mentioned, molluscum can occasionally spread to the oral mucosa. Although it is most commonly observed in epidermal tissues, a review of the literature found six reported cases of molluscum infections of the oral cavity in immunocompetent individuals. These cases presented as single or multiple papules with the characteristic central umbilication, although case reports note a great deal of variance in the appearance of intraoral molluscum lesions.\textsuperscript{48–51} Intraoral molluscum papules have been described as skin colored, yellowish white, and waxy. In one case, a smooth nodule 2.5 cm in diameter initially suspected to be squamous cell carcinoma was found to be a molluscum lesion on histologic analysis.\textsuperscript{51} Intraoral molluscum lesions are typically localized to the labial and buccal mucosa as well as the hard palate. Mild erythema is often observed surrounding the papule clusters.\textsuperscript{48–51} Multiple studies have reported complete clearance of molluscum lesions with minimal scarring within 2 weeks of curettage or excisional biopsy.\textsuperscript{48–51} In one of these studies, no additional or recurring lesions were found during a follow-up examination 2 years later.\textsuperscript{48}

Ocular and periocular molluscum infections can occur in pediatric, adult, and immunosuppressed patients. Molluscum lesions in these regions can be difficult to identify or are unusual in appearance. One retrospective study of several histologically proven cases of molluscum contagiosum found that molluscum was not diagnosed during the initial visit in up to 40\% of the cases.\textsuperscript{52} As in most cases of molluscum infection, diagnosis of ocular or periocular molluscum is made based on the presence of the characteristic molluscum lesions in the eye and orbital regions with or without additional lesions on the face or body. Rarely, molluscum lesions may be found in the conjunctiva or epibulbar region of the cornea. Chronic conjunctivitis or keratoconjunctivitis secondary to molluscum infection has been associated with both ocular and periocular molluscum lesions. In most cases, patients present with chronic conjunctivitis as their primary complaint, and a diagnosis of molluscum contagiosum is made on physical examination.\textsuperscript{52,53} However, the conjunctivitis is believed to be secondary to molluscum infection and is hypothesized to result from either a host hypersensitivity reaction to MCV proteins or toxic damage mediated by MCV.\textsuperscript{52} The most common treatment for ocular and periocular molluscum infections is surgical excision of the lesions, which has generally led to rapid and dramatic resolution of the disease.\textsuperscript{52–54} The concurrent conjunctivitis has been frequently observed to resolve simultaneously with the clearance of the molluscum lesions, which provides further evidence that conjunctivitis occurs as a secondary disease.\textsuperscript{52}

**Conclusion**

There is no FDA-approved standard of care and no widely accepted form of treatment for molluscum contagiosum. Further research is needed for identifying and standardizing therapies that are effective and associated with limited side effects. Additionally, future studies should investigate outcome measures, such as transmission rates, recurrence, and disease-related quality of life. A standardized outcome measure for each treatment would likely facilitate comparative assessment. Molluscum contagiosum is an uncomplicated, self-resolving infection for most healthy patients, which explains why this disease has diminished in attention and investigation. However, molluscum has myriad clinical presentations based on the patient population and/or anatomic location affected. If these multifarious clinical scenarios are not managed properly with case-specific treatment, there is the potential for debilitating infection. This information should highlight the urgency of finding effective therapeutic strategies for molluscum contagiosum.
Acknowledgment

Financial disclosure of authors and reviewers: None reported.

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