Pediatric Warts: 2023 Update

ABSTRACT

Cutaneous warts or verruca are benign growths of the skin that affect 30 to 70% of school-age children and has a lifetime prevalence of 10 to 22% in children. It is caused by human papillomavirus (HPV) which spreads from skin-to-skin contact or fomites and infects squamous cell in areas like the hands and feet. There are different HPV subtypes that cause different types of warts including common warts (verruca vulgaris), plantar warts (verruca plantaris), flat warts (verruca plana), mosaic warts, filiform/digitate warts, epidermodysplasia verruciformis, and condyloma acuminata (genital or venereal warts). Most warts will spontaneously clear within 2 years. Diagnosis is based on history and physical examination features which may include dermoscopy and rarely, histological confirmation. Management includes treatment with topical salicylic acid and cryotherapy, the two most common and effective modalities.

KEYWORDS: warts (verruca), human papillomavirus (HPV), common warts (verruca vulgaris), plantar warts (verruca plantaris), flat warts (verruca plana), mosaic warts, filiform/digitate warts, epidermodysplasia verruciformis (EV), condyloma acuminata (genital or venereal warts)

Introduction

Warts or verrucae are caused by the human papillomavirus (HPV) which is a double-stranded DNA virus with over 200 distinct subtypes and is one of the most frequent viral mucocutaneous infections.[1] HPV can be transmitted through skin-to-skin or surface-to-skin contact and cause proliferation and growth of epidermal cells of the skin.[1,2,3] Warts are seen worldwide and can affect all age groups with a higher incidence in children and young adults and are rarely present before the age of 5.[1,2,4] Immunocompromised individuals are at an increased risk with higher incidence, resistant to treatment, and progression to intraepithelial neoplasms.[1,2] About 30% of warts will clear in 12 months and 60% clear in 24 months.[3,5] Different HPV subtypes can lead to different types and location of warts including common warts (verrucae vulgaris), plantar warts (verrucae plantaris), flat warts (verruca plana), mosaic warts, filiform/digitate warts, epidermodysplasia verruciformis, and condyloma acuminata

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(genital or venereal warts).[1,3,6] This paper will review warts including the various subtypes in the paediatric population.

Epidemiology

Warts occur throughout the world and in all ages with cutaneous warts being most common in childhood affecting 30% to 70% of school-age children. Anogenital warts, more commonly spread through sexual contact, are less common in children.[7] Spread of HPV infection can be through direct skin-to-skin contact or through fomites.[7,8] Vertical transmission may also occur in utero or during delivery and autoinoculation is common in younger children.[8] Vertical infection may be latent for 2 or more years and warts are rare before the age of 5 years.[8,9]

Overall, it is estimated that 10 to 22% of children will be infected with warts in their lifetime with a gradual increase in incidence after 5 years of age, peak occurrence at 9-10 years of age, plateau between 11-17 years of age, and decline after 17 years of age.[9,10,11] Cutaneous warts are frequently caused by HPV types 1, 2, 3, 4, 27 and 57, and in children. Common warts represent 70% of all skin warts and are more frequently seen than plantar warts (24%), flat warts (3.5%), filiform warts (2%) and condyloma acuminata (0.5%).[9,12] Anogenital warts, commonly seen with HPV types 6, 11, 16, and 18, should raise consideration about sexual abuse in children.[7,9] Most warts in children will spontaneously clear with 33% clearing within the first 6 months, 66% within the first 2 years, and 90% within the first 5 years and this clearance is mediated through T-cell host defence mechanisms.[7,8,10] Regardless, there is still a risk of progression and recurrence.[8,10] There is no difference in prevalence of warts between males and females. However, there is a higher prevalence in those exposed to places with easier transmission such as schools and swimming pools.[7,12] Immunocompromised individuals are also at increased risk of developing warts and reoccurrence as seen with higher incidence in renal transplant patients and patients with HIV.[2,7]

Pathophysiology

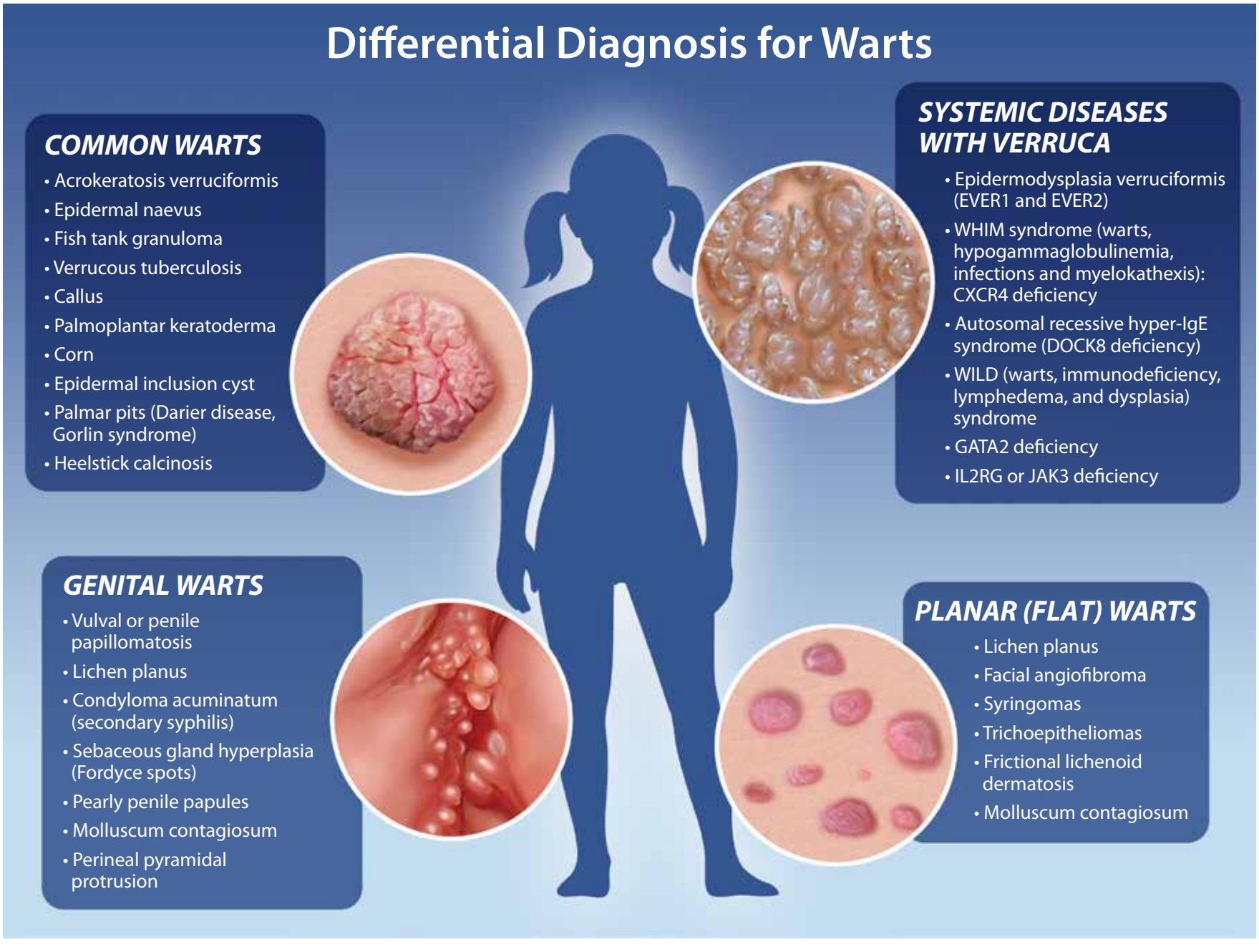
HPV is a coiled, double stranded DNA virus that infects squamous cells through insertion of viral DNA into the host genome.[11] HPV infection occurs when viral particles reach exposed basal cells often by microtrauma of the epithelium. The locations of most common infection in children include the hands, legs, and feet.[13,14] Most infections are cleared within 7-9 months, however in many cases the virus will integrate into host DNA.[15] HPV completes its life cycle in epithelial cells and does not produce viremia, cell lysis, or inflammation and remains protected by evading the immune system's innate immune response.[13]

HPV may also carry two oncogenes, E6 and E7, that aid in tumor

growth and carcinogenesis through unregulated cell growth via inactivation of the tumor suppressor gene p53.[15]

Classification of HPV is based on the DNA sequence of the L1 gene with 5 genera that affect humans: alpha-papillomaviruses (α-HPV) which produce macroscopic visible lesions and compromises viruses of low skin risk and high mucosal risk, beta-papillomaviruses (β-HPV) that produce subclinical infections mainly in childhood and are involved in skin tumors in immunocompromised patients with epidermodysplasia verruciformis, gamma-papillomaviruses (γ-HPV) that produce subclinical infections in childhood and clinical lesions in immunocompromised patients, mu-papillomavirus (μ-HPV), and nu-papillomavirus (ν-HPV).[13]

The L1 protein is the main component of the viral capsid, is highly immunogenic, and is targeted by vaccines that prevent HPV infection.[13] The viral replication cycle has 3 phases: initial amplification of DNA, maintenance of viral replication that occurs in proliferating cells, and a genome amplification phase



that involves the formation of new viruses.[13] Initial HPV infection does not recruit Langerhans cells and thus does not produce an antigen-specific immune response. However, clinically evident lesions involve a local immune response with CD8+ cytotoxic T lymphocytes and T helper 1 CD4+ cells which produce interleukin 2 and interferon-gamma.[13]

Differential Diagnosis for Warts

History

A detailed history is important as infection occurs through surface contact and skin-skin contact and more commonly impacts individuals who are immunocompromised. Trauma to the skin facilitates inoculation of the virus, and family history is relevant especially in anogenital warts and epidermodysplasia verruciformis (EDV).[1] Maternal history of genital condyloma at time of delivery can lead to warts in children and there is often a family history in cases of EDV.[13,15,16] It is also important to discuss risk factors for sexual abuse in children with anogenital warts.[8,16]

A history should include the duration of warts, location of warts, and current and past treatments. In adolescents, this history should include any sexual partners or potential abuse.

Physical Examination

Classic examination features include absence of normal dermatoglyphics of the skin and presence of pinpoint areas of bleeding when the lesion is pared down. Warts are rough to touch which helps distinguish them from other skin conditions.[11,17]

Warts are classified by their clinical location and morphology and different types have distinct features seen on physical examination.[18] Common warts are skin colored, hyperkeratotic, exophytic, contain dome-shaped papules ranging from 1 to 10 mm, may contain mild erythema, and are more commonly seen on hands. Plantar warts contain verrucous or endophytic papules ranging from 1 to 10 mm, may contain black or brown dots on the surface from thrombosed capillaries, and are commonly seen on the plantar surface of the foot. Mosaic warts are clusters of small warts commonly seen on the palms and soles. Flat warts are smaller, ranging from 1 to 3 mm flat-topped papules, and are commonly seen on the face and dorsal hands. Filiform/digitate warts contain pedunculated papules with finger-like projections arising from the skin's surface and are commonly seen on the face and neck. Condyloma acuminata are sessile, have a smooth surface with exophytic papilloma, can be skin-colored, can form confluent plaques, and may extend into the vagina, urethra, or anal canal.[1,18]

Investigations

Warts can usually be diagnosed clinically and often does not require histological confirmation. The diag-

nosis can be facilitated by visualizing thrombosed capillary loops which present as black dots.[7,11] If the diagnosis is questionable or uncertain, genotyping, and histopathological testing can determine HPV type and aid with confirming clinical diagnosis.[17] Dermoscopy may also be used to aid in diagnosis and cutaneous warts have unique dermoscopic features.[13,17,19] Common and plantar warts appear as papillomatous hyperkeratotic dome-shaped papules that interrupt the skin lines with linear, hairpin-like and dotted vessels. Flat warts appear as light brown to yellow patches with dots or globular vessels.[19,20]

Management

Management of warts in children aims to destroy the infected epithelium, disrupt the virus life cycle, or stimulate an immune response.[7,11] Some of the most common treatments are destructive therapies which entail topical salicylic acid (SA), cantharidin, duct tape, cryotherapy and light-based modalities which include CO2 laser and photodynamic therapy. Immunotherapy options include oral cimetidine, zinc, intralesional Candida antigen, topical imiquimod, and topical contact sensitizers like squaric acid and diphencyprone. Antimitotic therapies include topical 5-fluorouracil (5-FU), bleomycin, cidofovir, podophylin resin and podophyllotoxin, sinecatechins, and topical retinoids.[21]

Efficacy of wart therapies differ, and destructive therapies are the most commonly used, specifically topical SA and cryotherapy.[7] Although SA products are the only treatments that have shown consistent efficacy in controlled trials other treatment modalities have a variable amount of success as well.[1,11] The most recent Cochrane review demonstrated that SA and cryotherapy are the most safe and effective treatments with SA having the most consistent evidence. Therapy with SA showed more effective clearance of warts at all sites but showed better results for warts on the hands as opposed to those on the feet. Cryotherapy also showed effective clearance with better results for hands than feet and aggressive therapy was better than gentle cryotherapy but included more adverse effects. When SA and cryotherapy are used together, better results were seen compared to either modality used alone. Duct tape showed no advantage over placebo and although safe, simple, and cheap, seemed to be less effective than previously reported. Other treatments such as 5-fluorouracil, dinitrochlorobenzene, intralesional bleomycin, intralesional interferon, photodynamic therapy, topical cantharone and intralesional antigen were not as effective.[22] There are side effects for different treatment modalities, such as pain, blistering, dyspigmentation, and scarring for cryotherapy.[11,23] HPV vaccines are useful in preventing infection with the HPV subtypes associated with

SUMMARY OF KEY POINTS

Cutaneous warts are a benign growth caused by human papillomavirus (HPV) infection that can cause discomfort. These are most common in school-aged children and in adolescents.

HPV infection is acquired through skin-to-skin contact, contact with fomites, or through maternal transmission during birth. The virus infects squamous cells on the skin and inserts its viral genome into the cells causing survival and proliferation of the virus.

History and physical examination help diagnose warts in children. Dermoscopy and histology may also aid in diagnosis, especially in more challenging presentations. A history of genital warts in children mandates ruling out sexual abuse.

There is a wide range of treatment modalities that can be used for warts. The most well-studied are destructive therapies such as salicylic acid and cryotherapy. There are side effects from treatments such as pain, blistering, scarring and dyspigmentation from cryotherapy. HPV vaccination in children is useful in preventing certain subtypes of genital warts and those that may cause cancer.

genital warts and cervical cancer. The data on treatment of common cutaneous warts is less robust.[1,11,13]

Conclusion

Warts are a type of benign growth of the skin that arise from HPV infection of skin cells which is transmitted through skin-to-skin or skin-to-surface contact. There are multiple types of warts that include common warts, plantar warts, flat warts, mosaic warts, filiform/digitate warts, epidermodysplasia verruciformis, and condyloma acuminata (genital or venereal warts). Each type of wart is unique in its appearance, location, and HPV subtype. Most warts are benign, but genital warts with HPV subtypes, 16 and 18 cause 70% of cervical cancers, and subtypes 12, 31, 33, 45, 52, and 58 together cause an additional 20%. Patients with EDV can have HPV subtypes 5, 8, 17, 20

CLINICAL PEARLS

Warts often spontaneously resolve with 33% clearing within the first 6 months, 66% within the first 2 years, and 90% within the first 5 years.

Treatment can hasten resolution of warts and often involve destructive therapies such as salicylic acid and cryotherapy.

HPV subtypes causing cancer are rare. Vaccination can significantly decrease the chance of acquiring HPV subtypes that cause genital warts and cervical, anal, oropharyngeal, penile, vulvar, and vaginal cancer.

and 47 that can predispose to squamous cell carcinoma.[1,13] Warts can affect all ages and ethnicities but are especially more common in the paediatric population. A detailed history and physical examination is usually enough to make the diagnosis, and in some cases may raise suspicion of sexual abuse in children. Most warts will spontaneously resolve within 2 years; however, management includes multiple treatment modalities that aim to remove the wart, with topical salicylic acid and cryotherapy being the most common, simple, safe, and effective treatments. HPV vaccination is also used in children to prevent genital warts and is used for the HPV types that can cause genital warts and predispose to cervical, anal, oropharyngeal, penile, vulvar, and vaginal cancer.

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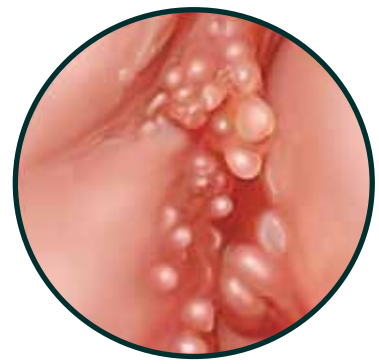
Warts Key Points for the Practitioner

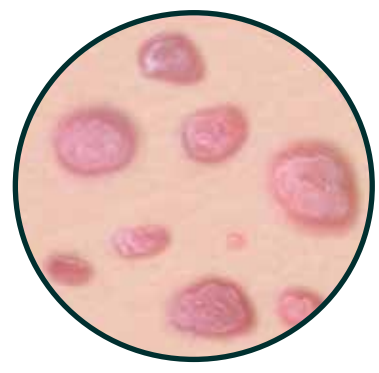
History (key points to cover)

- Medications used (names, duration of use and response to therapy)
- Risk factors for cutaneous warts (family history of warts, history of immunosuppression)
- Risk factors for genital warts (history of maternal genital warts or abnormal Pap smear, cutaneous warts in caregivers, rule-out abuse)
- History of HPV vaccine



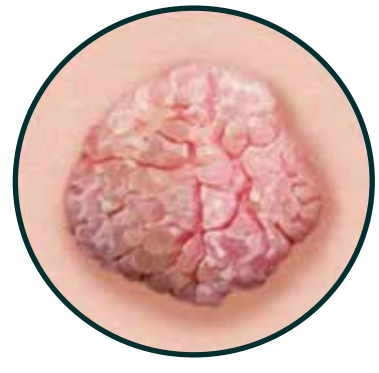
Physical Examination (key features to note)

- Note the morphology and type of warts (plantar, common, flat, mosaic, filiform or genital)
- Note location and number of warts
- On dermoscopy, look for interruption of the skin lines and pinpoint capillaries



Select differential diagnosis (key entities to consider and differentiating features)

- Molluscum contagiosum (pearly papules with umbilication)
- Epidermal nevus (often linear and congenital)
- Heel stick calcinosis (located over the heel in infants and toddlers)
- Callus (skin lines extend over the callus)



Cutaneous Wart Information for the Patient and Family

What are warts?

Warts (also called verruca) are common, harmless, and annoying bumps on the body caused by a virus known as HPV (human papillomavirus). This virus infects skin cells and causes them to overgrow. What we see on the skin as warts is just a bunch of heaped-up skin cells. However, these cells are infectious, and warts can easily be passed on to other people or to other parts of the skin. The body's immune system is able to clear the warts over time, but it can sometimes take years for this to happen.

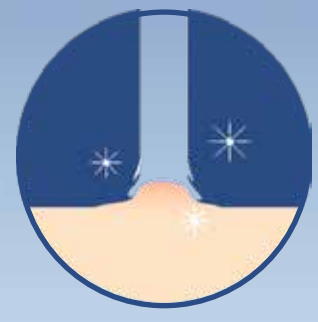
TIPS FOR TREATMENT

Home salicylic acid therapy (Compound W, Dr. Scholls with salicylic acid, Soluver, etc)

- If using medicated bandages, place over the wart and change every 1-3 days
- If using liquid or gel, place over the wart and cover with non-breathable tape (like duct tape, electrical tape or athletic tape) and change every day
- Before each application, you can soak the skin in water and file off the dead skin with a pumice stone or nail file dedicated to the wart

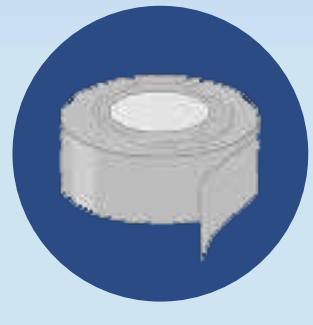
Liquid nitrogen cryotherapy in office

- It's important to note that this treatment can sting, if done properly
- The liquid nitrogen is applied to the wart with a cotton-tip applicator or sprayed onto the wart
- This is done for 3 cycles of around 10 seconds per cycle
- It helps to be distracted by squeezing someone's hand or using a portable electronic device (like a cellular phone)



Other treatments

- If cantharone is used, a bubble usually forms in the area 4 hours later. If the bubble is not popped, it will 'deflate' over the next few days
- If 5-fluorouracil cream is used, put this over the wart and cover with non-breathable tape (like duct tape, electrical tape or athletic tape). Change this every 1-3 days



What can we do to treat warts?

Because warts are harmless and will eventually go away, they do not need to be treated. However, given how noticeable they are, how contagious they are and how warts in some locations can be painful (like if they are on the feet), it's good to know what can be done to make the warts go away faster.

The two most common treatments for warts are home treatment with salicylic acid and in-office treatment with liquid nitrogen.

Home treatment is relatively painless but does involve time and commitment. Salicylic acid is available over the counter as a liquid, gel or as pad and this can be put on the wart. If it is the liquid form, cover up the wart with a non-breathable tape like athletic tape, duct tape, electrical tape or even the sticky part of a Band-aid. This should be repeated every night. The salicylic acid will cause the skin cells to slowly peel off. It can sometime take months to fully clear a wart. Examples of salicylic acid preparations include Soluver, Compound W and Dr. Scholl's. It sometimes helps to soak the area of skin involved in water for about 15 minutes and filing off the dead skin with a nail file or pumice stone dedicated to the wart. Do not use the salicylic acid on warts on the face, neck, or genitals.

Another method is liquid nitrogen, which is applied in doctors' offices. Liquid nitrogen is about -1960 C and can turn the water in the infected cells into ice, which damages and destroys these cells. The liquid nitrogen can be applied with the end of a cotton-tip swab or with a spray. The downside with liquid nitrogen is that it can sting when it is used on the skin. Warts are usually treated about once every 4 weeks. You can combine liquid nitrogen (in the office) with salicylic acid (at home) to help the wart go away faster.

Other treatment options include using a blistering agent called cantharone (applied in office), a cream called 5% 5-fluorouracil (applied daily at home and covered with non-breathable tape) and immunotherapy with an agent known as DPCP (applied in office). For school-aged children, we sometimes get surprising results when we have them look at the wart daily while chanting "wart go away" three times.

It's important to remember that skin warts are harmless and we want to make sure the treatment is not worse than having the wart. With time, even without treatment, warts will go away eventually.