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MANAGEMENT OF WARTS: AN UPDATED OVERVIEW

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ABSTRACT

Background: Mucocutaneous warts are mostly asymptomatic and usually attract the attention of patients by the cosmetic problems that they cause. This disease should be treated because it can influence strongly on the patients quality of life by causing shame, fear, and anxiety about developing negative attitude in other people and disillusionment due to disease chronicity or relapse. Treatment options for cutaneous warts vary in effectiveness and often result in recurrence. Therapies can also be painful, which especially limits their use in children. Primary treatments include topical salicylic acid, topical imiquimod, bleomycin injections, cryotherapy, excision, electrocautery, and laser vaporization. Topical therapies require frequent treatment applications but are more tolerable to patients. Traditional treatment modalities are limited to local application and do not act systemically. Therefore, they are inconvenient for patients with multiple distant lesions. Various systemic immuno-therapies including interferons and contact sensitizers have been attempted to stimulate the host immune response. Intralesional injections of vaccines and organic antigens such as Candida albicans, measles, and mumps, measles and rubella (MMR) vaccine have also been studied extensively with variable degrees of success

Key words: Warts, Viral Vaccines, Intralesional injections

Warts:

The last 30 years have witnessed the discovery of many different types of human papillomaviruses

Warts are the cutaneous manifestations of HPV infection. Warts may exist in different forms according to the epithelial surface and HPV type responsible for the infection. Common warts (Verruca vulgaris), plantar warts (Verruca plantaris), flat or plane warts (Verruca plana) and genital warts (Condyloma acuminata) are some of the clinical manifestations of HPV infection (1).

Transmission of warts

Warts are spread by contact, either directly from person to person or indirectly via fomites on left surfaces. infection via the environment is more likely to occur if the skin is macerated and contact with roughened surfaces, the conditions which are common in swimming pools and washing areas (1)

I. CLINICAL FEATURES:

Cutaneous warts

Common Warts

Common warts (verrucae vulgaris) are irregularly surfaced, domed lesions that can occur almost anywhere on the body. Multiple warts are common and are spread by skin-toskin contact or contact with a contaminated surface. After initial infection, warts frequently are spread by autoinoculation from scratching, shaving or other skin trauma. On exposed skin, these warts tend to be hard and, if not affected by mechanical forces, they develop the typical carpet-like (verrucous) surface. On areas that receive frequent friction, such as the hands, the firm, nodular aspect predominates. On areas that are moist or occluded, warts tend to be softer and more polypoid. Characteristic

features are punctuating black dots representing thrombosed capillares and capillary bleeding that follows shaving of the hyperkeratotic surface **(2).**

Filiform warts

Filiform or digitate wart is a variant of comman warts and are characterized by their long, finger like projections. It is most frequently encountered on the face and demonstrates a predilection for circumoral skin, eyes, ala nasi and the area of the beard **(3).**

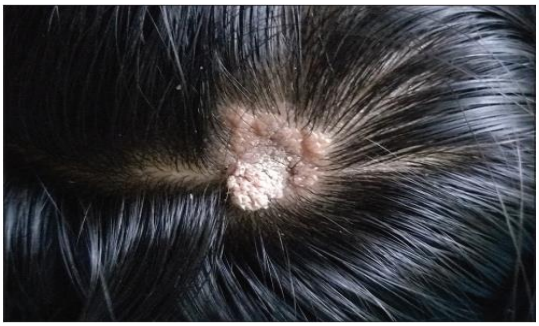

Figure 1: Filiform wart on the frontotemporal part of the scalp **(4).**

Periungual warts

Periungual warts occur at the nail margins. As with other warts on the hands and feet, they often show peeling and roughening of the surface and tend to be somewhat abraded although not as much as palmar warts. They can affect the shape of the nail by undermining its side and pushing the nail up or causing partial detachment, sometimes mimicking the changes that occur with onychomycosis. Occasionally, when the wart affects the nail matrix or when destruction of the wart injures the nail matrix, permanent nail deformity can result **(5).**

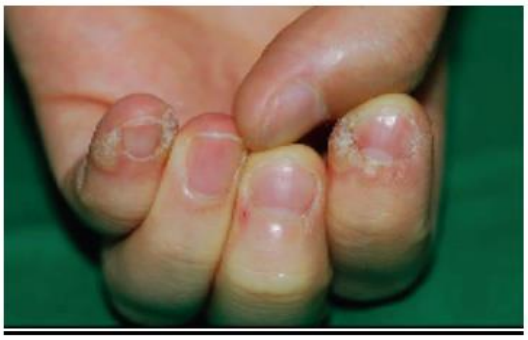

Figure 2: Periungual wart **(6).**

Palmar and plantar warts

They present as thick painful endophytic plaques located on the soles and/or the palms. The lesion is often covered by a thick callous. Plantar warts tend to be painful on application of pressure from either side of the lesion rather than direct pressure, unlike calluses which tend to be painful on direct pressure instead. Feet are covered by skin striae, which are akin to fingerprints on the feet. Skin striae go around plantar warts; if the lesion is not a plantar wart, the cells' DNA is not altered, and the striations continue across the top layer of the skin **(7).**

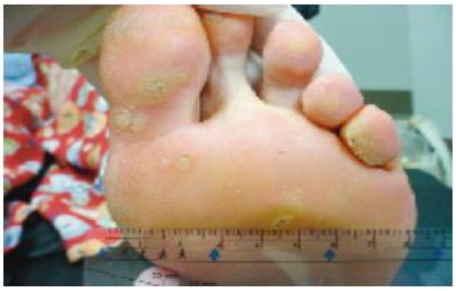

Figure 3: Multiple plantar warts **(8).**

Autoinoculation of the virus into opposed lesions is common. The HPV can survive for many months and at low temperatures without a host. Therefore an individual with plantar warts can spread the virus by walking barefoot. Clinically detectable verrucae develop from a few weeks to 18 months after inoculation. In most infected individuals, the virus is carried subclinically and never produces apparent lesions **(9).**

Flat warts or verrucae planae

Skin colored or reddish, smooth surfaced, slightly elevated and flat topped papules most commonly located on the dorsal hands, arms or face, often in a linear array. They are usually caused by HPV types 3 or 10 and less often by 28 and 29 **(10).**

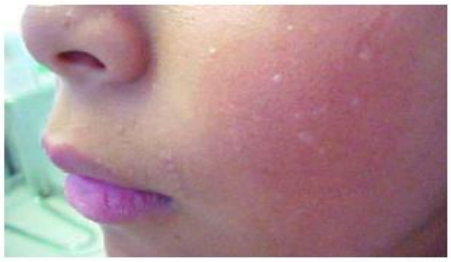

Figure 4: Plane warts on the face **(11).**

Epidermodysplasia verruciformis (EDV)

It is a very rare, chronic disease characterized by a unique susceptibility to cutaneous infections by a group of phylogenetically related HPV types, referred to as EDV types. The disease usually manifests in childhood with highly polymorphic, wide spread lesions. EDV-specific HPV types have been described as HPV 5, 8, 9, 12, 14, 15, 17, 19, 25, 36 and 38, but mainly types 5 and 8 are detected in EDV associated skin cancers and in most EDV affected family's inheritance follows an autosomal recessive pattern **(12).**

EDV patients present with wide spread, discrete or confluent lesions that clinically resemble flat warts and scaly, guttate, reddish or hypopigmented macules and thin plaques that resemble pitryasis vercicolor and recently a susceptibility locus for EDV has been mapped to chromosome 17 q25 and 2p21-p24. Actinic keratosis usually arises after the age of 30 years and slowly transform into invasive squamous cell carcinomas in approximately half of the patients **(13).**

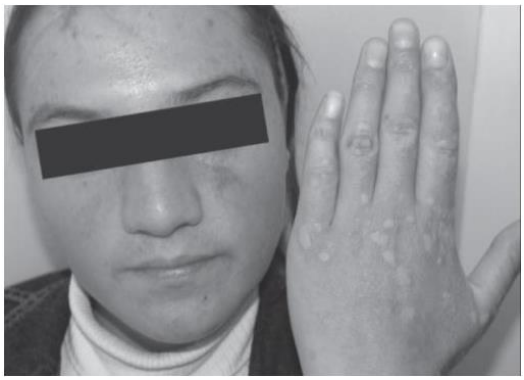

Figure 5: Multiple hyperkeratotic, pinkish red papillomatous lesions and tan-coloured macular lesions on her hands **(14).**

II. MUCOSAL FORMS

Condyloma acuminate

Genital warts (condyloma acuminatum, venereal warts) are common highly contagious benign epithelial lesions occurring on the genitals, perianal area and inguinal folds and are caused by human papillomavirus (HPV). Diagnosis is based largely on the clinical appearance of lesions. The main manifestations of anogenital warts are

cauliflower-like condylomata acuminata that usually involve moist surfaces, keratotic and smooth papular warts, usually on dry surfaces and subclinical "flat" warts, which can be found on any mucosal or cutaneous surface **(15).**

Diagnosis is primarily clinical. However, it is hard to detect lesions such as those on the cervix, so the diagnosis can be aided by the application of 5% acetic acid solution to the suspected region. Within minutes condylomata should appear as whitish patches on the mucosa. However, this aceto-whiting technique is associated with a high number of false negative and false positive results **(16).**

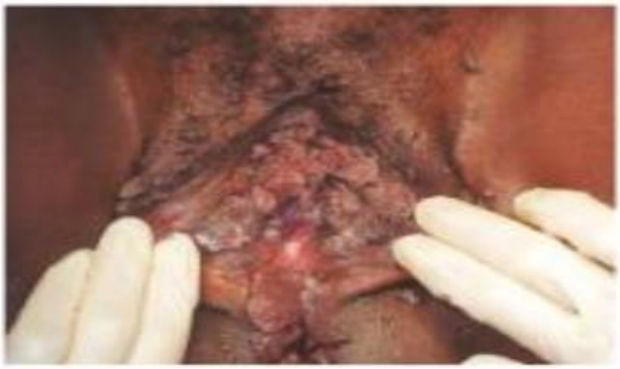

Figure 6: condyloma acuminata **(7).**

Bowenoid papulosis

Bowenoid papulosis (BP) is a disease characterized by multiple brown to black papules on the genitalia and histological changes similar to Bowen's disease, ranging from low to severe dysplasia. The high-risk, oncogenic HPV type 16 has been found in most cases of BP **(17).**

Several studies have shown that the transition of intraepithelial precursor lesions to carcinoma (in situ) is associated with integration of the virus into the cellular genome. Extragenital BP is usually associated with concomitant genital involvement, but there have been rare reports of isolated extragenital BP **(18).**

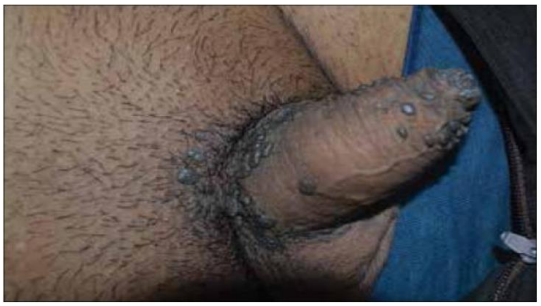

Figure 7: Bowenoid papulosis on the genitalia **(19).**

Oral warts

Appear as small, soft, pink or white, slightly elevated papules and plaques on the buccal, gingival or labial mucosa, the tongue or hard palate. Oral condylomata are associated with HPV types 6 and 11 and may result from digital or oral-genital sexual transmissions **(20)**.

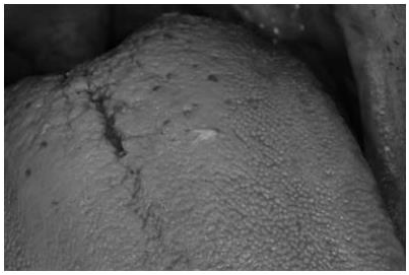

Figure 8: Oral wart of the dorsal surface of the tongue **(21).**

Oral florid papillomatosis

Multiple, confluent warty or verrucous lesions associated with HPV types 6 or 11 are found in the oral cavity or the nasal sinuses. The development of these lesions is believed to be promoted by smoking, irradiation and chronic inflammation. Patients with oral papillomas need frequent examinations and repeated biopsies for early diagnosis of progression to a well differentiated verrucous carcinoma **(22)**.

Focal epithelial hyperplasia

Focal epithelial hyperplasia (FEH) or Heck's disease is a rare contagious disease caused by human papillomavirus that was first described in 1965 from the observation of isolated or multiple soft papular and nodular eruptions on the oral mucosa of Navajo Xavante Indian and Alaska Eskimo children **(23).**

FEH manifests on the mucosa as multiple or unique soft papules of whitish or normal color with a smooth surface and measuring 1 to 10 mm in diameter. The lesions are painless, tend to disappear spontaneously and are predominantly found on the lower lip, buccual mucosa and tongue and less often on the upper lip, gingiva and palate **(23).**

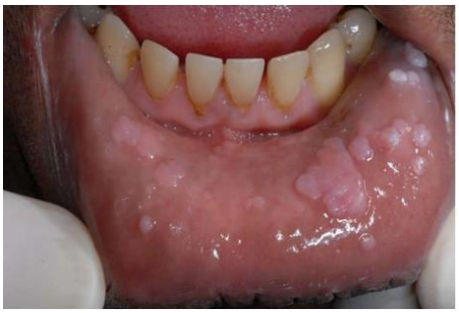

Figure 9: Focal epithelial hyperplasia on lower lip **(24).**

III. RECCURENT RESPIRATORY PAPILLOMATOSIS

This lesion is characterized by recurrent proliferations of benign squamous papillomata within the respiratory tract. Histologically, the papillomata consist of multiple finger-like projections with a central fibrovascular core, which is typically covered by stratified squamous epithelium. Although benign histologically, respiratory papillomatosis may behave aggressively and can precipitate sudden airway obstruction. They clinically present with hoarseness of voice and aphonia, repeated episodes of respiratory distress and recurrent pneumonia. In addition, there can be associated inspiratory stridor, asthma-like symptoms and hemoptysis **(25).**

The most common site of involvement by respiratory papillomatosis is the true vocal cord, followed by the trachea, bronchi, palate, nasopharynx and pulmonary parenchyma**.** Pulmonary lesions include nodule formation, atelectiasis, pneumonia, bronchiectasis, cavitations and carcinomatous transformation or may even be fatal**.** Pulmonary papillomatosis usually occurs 10 years after the initial diagnosis and malignant transformation into an invasive squamous cell carcinoma and adenosquamous carcinoma have been reported. Molecular markers of transformation include increased topoisomerase alpha II and p53 expression along with retinoblastoma (RB) gene protein product and p21 expression **(26**).

Diagnosis:

The diagnosis of cutaneous warts is usually based on typical clinical appearance. Extra tests should be finished to completely evaluate. the tests which will be done regularly for the diagnosis of HPV are The Papanicolaou (Pap) smear test that is cytologic technique routinely employed to detect HPV disease of the cervix and vagina **(27).**

And PCR-based detection is both highly sensitive and specific. Since PCR can be performed on very small amounts of DNA, it is ideal for use on specimens with low DNA content. Molecular detection methods of human papillomavirus (HPV). Acetic acid test, after application of 3-5% dilute solution of acetic acid to the cervix using cotton swab or spray. Detection of well-defined aceto-white areas close to the squamocolumnar junction indicates positive test **(27).**

Dermoscopy: -

human papillomavirus infections are among the most common cutaneous infections in human beings, as the human papillomavirus is ubiquitous, and its clinical expression can be extremely variable. From this clinical variability, a variegate presentation of dermoscopic findings derives. There is a constant feature that can often be observed in warts, ie, dotted vessels and/or hemorrhagic points that can be variably found in different kinds of viral warts **(28).**

Common warts

Common warts are the most frequent type of warts. They can appear on any part of the body, although hands represent the most affected area. Common warts usually show at dermoscopy as grouped papillae, with dotted or loop vessels, and/or hemorrhagic points and lines often surrounded by a whitish halo, assuming a "frogspawn appearance **(29).**

Plantar warts

Among the most common type of warts, plantar warts show at dermoscopy as small dotted hemorrhagic structures corresponding to thrombosed vessels, visible in the context of whitish or yellowish papillae which interrupt cutaneous dermatoglyphics. Easy to recognize, plantar warts are sometimes misdiagnosed as tylomas (hyperkeratosis without interruption of dermatoglyphics) and must be distinguished from acral melanoma, sometimes unfortunately misinterpreted as wart **(29).**

Histopathology of warts

Warts are usually diagnosed by their clinical appearance, but a histological examination may need to be performed for warts resistant to treatment and for verrucous lesions in immunocompromised individuals. Histologically, a wart demonstrates acanthotic epidermis with papillomatosis, hyperkeratosis and parakeratosis with elongated rete ridges often curving towards the center of the wart. Dermal capillary vessels are prominent and may be thrombosed and mononuclear cells may be present. HPV-associated papillomas are characterized by large keratinocytes with an eccentric, pyknotic nucleus surrounded by a perinuclear halo (koilocytes) **(30).**

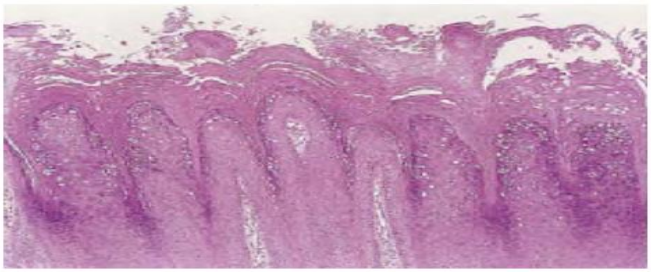

Figure (10): Verruca vulgaris, medium power. Although no granular cells are seen overlying the papillomatous crests, they are increased in number and size in the intervening valleys and contain heavy, irregular clumps of keratohyalin granules **(31).**

In filiform warts, the papillae are more elongated than in verrucae vulgaris. Whereas superficial, mosaic-type palmoplantar warts have a histologic appearance analogous to that of verruca vulgaris and represent human papillomavirus-2 (HPV-2) or HPV-4, deep palmoplantar warts represent type HPV-1. These lesions, also known as myrmecia or inclusion warts, are characterized by abundant keratohyalin, which differs from normal keratohyalin by being eosinophilic **(32).**

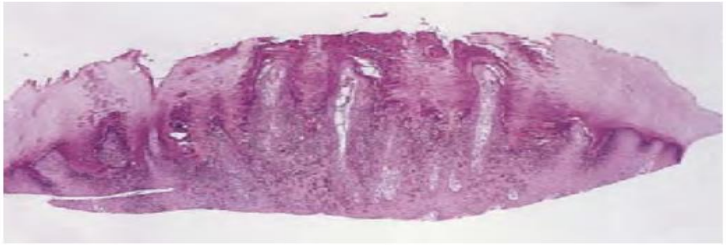

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Fig. (11): Deep plantar wart (myrmecia), low power. There is papillomatosis and thickening of the epidermis with a thickened stratum corneum **(31).**

Flat warts have less acanthosis and hyperkeratosis and do not contain parakeratosis or papillomatosis, but they do have abundant koilocytes**.** Anogenital warts may express slight to extensive acanthosis and parakeratosis since they are within or adjacent to a mucosal surface and do not have a granular layer. Koilocytes are often observed in anogenital warts, and the rete ridges often form thick bands extending extensively into the underlying, highly vascular dermis **(33)**.

IV. TREATMENT OF WARTS

Although the spontaneous resolution rate for warts is 65–78%, the cosmetic disfigurement, tendency to spread and associated poor quality of life warrants quick intervention. However, the management of different types of warts still continues to annoy both patients and dermatologists. The main goal when treating warts is to eradicate the lesions, while attempting to minimize pain, avoid scarring and prevent recurrence. Choice of treatment will depend on the location, size, number and type of warts, as well as on the age and level of cooperation of the patient **(34).**

The treatment of warts depends on two main therapeutic options: the first is the conventional destructive and aggressive method, which includes treatment with chemical cautery, cryotherapy, electrocauterization, surgical excision, and laser ablation, and the second is immunotherapy, which is based on the activation of the immune system to deal with the virus and suppress its activity **(35).**

No single treatment is completely effective in all patients and the success rate of both destructive and immunological procedures varies from 65% to 85%. Ideally, the treatment should be simple and cheap with the least possibility of undesired side effects **(36).**

Table (1): Treatment for common warts **(20)**

A)	**Destructive treatments**
	• Salicylic Acid • Cryotherapy • Cantharidin • Trichloroacetic acid • Surgery • Phototherapy • Laser • Retinoids
B)	**Antimitotic Drugs**
	• 5-Fluorouracil • Bleomycin • Cidofovir • Podophyllin
C)	**Other Treatments**
	• Local hyperthermia • Duct tape • Garlic extract • Hypnosis • Sinecatechins • Glutaraldehyde • Formaldehyde
D)	**Immunotherapy**
	• Topical immunotherapeutic agents • Systemic immunotherapeutic agents • Intralesional immunotherapy

A) Destructive Treatments

1. Salicylic acid:

Salicylic acid, a keratolytic that lyses the epidermis, is prepared in concentrations from 10% to 60%. Over-the-counter preparations are available as 17% salicylic acid combined in a base of flexible collodion or as a 40% salicylic acid plaster patch. Because it is cost effective and not often painful, it presents as an effective initial therapy for many patients **(37).**

2. Cryotherapy

Cryotherapy with liquid nitrogen is a favorable and alternative treatment in most patients, resulting in treatment of up to 50–70% of lesions after three or four sessions **(36).**

3. Cantharidin

Cantharidin is a topical keratolytic agent and vesicant that induces acantholysis and intra-epidermal skin blistering within 24–48 h of application via degradation of desmosomal attachments, leading to exfoliation of virus-containing tissue. Cantharidin in combination with podophyllotoxin and salicylic acid has shown a high clearance rate of plantar warts across numerous studies, often after one application **(38).**

***4*. Trichloroacetic Acid and Monochloroacetic Acid**

Trichloroacetic acid (TCA) and monochloracetic acid (available as 80, 90, 100% solutions) cause a superficial necrosis by chemical dehydration of the affected tissue **(39).**

5. Surgery

Surgical treatment of warts involves the radical eradication of lesions by conventional surgery, electrosurgery, or curettage. One of the advantages of surgery is that it provides a rapid solution and can therefore be beneficial in the case of recalcitrant or isolated warts. It is, however, associated with high rates of bleeding, scarring, and bacterial infections, and estimated recurrence is around 20% **(40).**

Curettage and cautery is now less commonly used because of the requirement for local anaesthetic injection, the risk of scarring, and high rates of recurrence **(41)**.

6. Phototherapy

The mechanism of action of photodynamic therapy (PDT) is tissue destruction secondary to an inflammatory response induced by a phototoxic reaction. The recommended procedure involves applying 5-aminolevulinic acid 20% cream on the wart and covering this with an occlusive polyurethane dressing for 4 hours. The wart is then irradiated for 20 minutes with a light source with a wavelength of between 590 and 700 nm **(42).**

7. Laser Therapy

Laser therapy is considered a promising treatment method for recalcitrant warts. Different types of lasers have been evaluated for treatment of warts including carbon dioxide (CO2) laser, pulsed dye laser (PDL), erbium-yttrium aluminum garnet (YAG) laser and neodymium (Nd): YAG laser. Long-pulsed Nd: YAG lasers were reported to be a safe and effective treatment for warts, with response rates higher than those obtained with conventional therapies **(43).**

8. Retinoids

Retinoids influence the process of vitamin A by interacting with specific cellular and nuclear receptors of skin. In that way retinoids control cell proliferation and

differentiation and potentially interfere with the tumor promotion phase of carcinogenesis by inducing apoptosis **(44).**

B) Antimitotic Drugs:

1. 5-Flurouracil (5-FU)

It is a structural analogue of thymine that blocks DNA synthesis by inhibiting thymidylate synthetase **(45).** Topical 5-FU has been used with high efficacy for treatment of both plane warts and common warts on the hands and feet. When used topically or intralesionally, it produces inflammation and occasionally erosions. Also, hyperpigmentation or less frequently hypopigmentation can occur **(20).**

2. Bleomycin

Bleomycin is an antimitotic agent that acts by forming free radicals from binding to guanosine-cytosine-rich portions of DNA that cause DNA single-strand breaks, ultimately resulting in cytotoxicity. Bleomycin is typically

administered as a subdermal injection or by pricking the lesion with a bifurcated needle. Bleomycin is a physician applied treatment with a maximal dose of 4 injections **(46)**.

Concerning side effects, injection pain is the most commonly described **(47).**

3. Cidofovir

Cidofovir- cytosine is a nucleoside analog with strong activity against a broad spectrum of DNA viruses. The drug is active against all herpes virus and papillomavirus **(48).**

Topical cidofovir is reconstituted from the parenteral form, as either a 1% or 3% cream **(20).**

4. Podophyllin and Podophyllotoxin

Podophyllin is an antimitotic agent derived from the plant podophyllum peltatum. It is used at a concentration of between 10% and 25% in alcohol or benzoin, and causes tissue necrosis. It must be left on the affected area for 1 to 4 hours, and then removed. It is reapplied weekly for up to 4- 6 weeks **(49).**

C) Immunotherapy

Immunotherapy is defined as a type of biological therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. Types of immunotherapy include cytokines, vaccines, and some monoclonal antibodies. It may either be an activation immunotherapy, where immunity is induced or enhanced (used in infections, cancers), or a suppression immunotherapy, where immunity is suppressed (used in autoimmune diseases) **(50).**

Many immunotherapeutic modalities have been investigated to overcome the challenges associated with the use of destructive therapies. These include: immune enhancers either systemic such as zinc sulfate or topical such as imiquimod, immunosuppressives such as sirolimus and proinflammatory cytokines such as interferons and interleukins. Inducers of cell-mediated immunity (CMI), such as Candida and mumps antigens, topical contact sensitizers such as diphencyprone and a combination of the agents are other immunotherapeutic options **(51).**

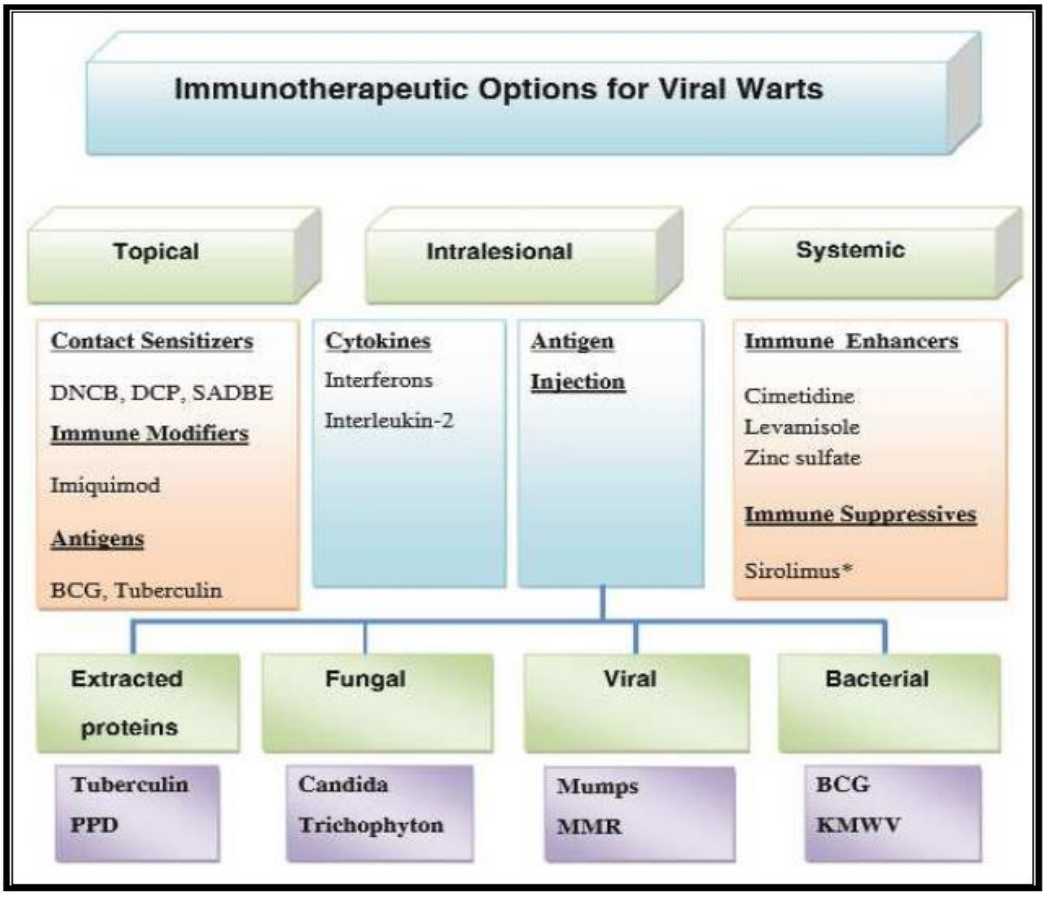

Figure (12): Immunotherapeutic options for viral warts. DNCB dinitrochlorobenzene, (DPC) diphencyprone, (SADBE) squaric acid dibutylester, (MMR) measles, mumps, rubella, (BCG) Bacillus Calmette Gue´rin, (KMWV) killed Mycobacterium w vaccine, (PPD) purified protein derivative **(51).**

B 1. Topical Therapy

Contact Sensitizer: contact immunotherapy is classically performed with contact sensitizers such as dinitrochlorobenzene (DNCB), diphenylcyclopropenone (also known as diphencyprone [DPC]), or squaric acid dibutylester (SADBE). It is postulated that these agents act through activation of the host adaptive immune system with a resultant antiviral state-inducing clearance of the wart **(52).**

A. Dinitrochlorobenzene (DNCB)

Dinitrochlorobenzene was the first topical sensitizer to be extensively studied for the treatment of warts. It contains contaminants that are mutagenic and carcinogenic to animals, so it is no longer use in clinical settings **(53).**

B. Diphencyprone (DPC)

Diphencyprone (DPC) is a more potent contact sensitizer than dinitrochlorobenzene (DNCB) for the same concentration **(53).**

Patients with recalcitrant plantar, palmar, periungual and digital warts are candidates for DPC treatment **(54).**

C. Squaric Acid Dibutylester (SADBE)

Acting by induction of a type IV delayed hypersensitivity reaction, SADBE stimulates a cell-mediated response against the hapten-bound viral proteins on antigen-presenting cells, which can ultimately lead to wart resolution. Warts not directly treated using SADBE can also resolve during treatment of a distant wart, suggesting stimulation of a systemic immune response as well **(55).**

Immune Modifiers

1. Imiquimod

Imiquimod, a synthetic imidazoquinoline derivative that is US FDA approved for the treatment of external genital and perianal warts, actinic keratoses, and superficial basal cell carcinomas. It is thought to have both antiviral and anti-tumoral effects. The mechanism of action is presumed to be through the activation of both innate and cell mediated immune responses by the induction, synthesis, and release of interferon-α, interleukin-1, interleukin-6, and tumor necrosis factor-α.
This leads to a cell-mediated immune response via toll-like receptors 7 and/or 8 (56).

Antigen

2. topical Bacillus Calmette-Guerin (BCG)

BCG is one of the agents used for immunotherapy in warts. Its precise mechanism of action is not known, but it is speculated to upregulate the Th1 type of cytokine response IFN-α, IL-2, 12, 18, IFN-γ, and TNF-α as well as induce a nonspecific inflammatory response against the virus. Most of the researchers used intralesional injections of the BCG vaccine to treat recalcitrant warts, and a few of them used the intradermal route (57).

3. Systematic Therapy

Immune Enhancers

- Levamisole

Levamisole is a synthetic antihelminthic belonging to the class of imidazothiazole derivatives, possessing potent immunomodulatory activity. It has been extensively used in dermatology practice for the management of various dermatoses ranging from infections such as warts and leprosy to inflammatory dermatoses such as lichen planus and Behcet's disease (26).

- Zinc Sulphate

It acts as an immune modulator. Zinc is a trace element that is essential for the functioning of many enzymes and transcription factors. It is crucial for all highly proliferating cells in the human body, especially the immune system, and innate and acquired immunity can be compromised by zinc deficiency (58).

Immune Suppressive

- Sirolimus

New immunosuppressive drugs belonging to the target of rapamycin (TOR) inhibitors family (sirolimus, everolimus) have been successfully developed for the prevention of organ rejection after transplantation. Recent reports support the hypothesis that TOR inhibitors may also actually interfere with virus replication in the host. It was noticed that cases of organ transplant recipient in whom sirolimus monotherapy conversion was followed by a rapid improvement in cutaneous warts **(59).**

D) Other Treatments

Local Hyperthermia

The exact mechanisms of thermotherapy in the treatment of warts are not yet clear. Hyperthermia increases the number of apoptotic keratinocytes in warts and normal skin. The expression of Fas increases in both lesion and normal skin with high temperature. Bcl-2 expression in warts decreases after hyperthermia. It can alter cytokines profiles and modify the cellular immune response **(60).**

Thermotherapy with local hyperthermia of 44°C for 30 min. has been reported with success in the treatment of various warts including vulgaris and facial warts (**61).**

Duct Tape

The mechanism of action underlying the use of duct tape to treat warts is not known, but like other treatments, it would appear to involve the stimulation of the immune system in response to local irritation. The wart is covered with duct tape (or a plaster) for 6 days, after which it is soaked in water, pared down, and left uncovered for 12 hours. The cycle is repeated until the wart disappears (49).

Garlic Extracts

Ancient Egyptians, Greeks and Chinese used it for the treatment of various diseases. Besides, components of garlic have been shown to have antiviral and anti-carcinogenic effects (62).

Hypnosis

Hypnosis has been used to treat warts in children and adults for years. It is believed to stimulate the immune system, leading to the resolution of lesions. No studies, however, have determined whether the warts heal because of hypnosis or simply because of spontaneous regression (49).

Sinecatechins

Sinecatechins ointment, a green tea derivative, is a novel agent approved for the treatment of anogenital warts in immunocompetent adults and has been reported to be effective in treating extragenital warts as well (63).

Formaldehyde

Formalin (formaldehyde) is a virucidal agent and has strong disinfectant properties, and exerts its effects by causing damage to the upper layers of epidermal cells that contain the virus, and thus destroying viruses. The most common side effects of formalin include redness, irritation and dryness of skin. Severe allergic reactions are rare (64)

Glutaraldehyde

Glutaraldehyde is an antiviral agent. A 10% or 20% solution is applied daily over a period of 3 months. A cure rate of 72% was reported in a series of 25 patients with recalcitrant warts. There have been reports of deep necrosis after repeated application and of contact dermatitis (20).

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