EDITORIAL

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TREATMENT OF WARTS

The treatment of warts is at once simple as well as difficult. It is simple because the lesions can be easily destroyed by anything available at hand; at the same time it is difficult, because frequent recurrences are a common cause of frustration both to the patient and the treating dermatologist. The very fact that a variety of methods have been tried and are still being looked for, is a proof that there is no satisfactory method available so far.

Most reports mention that a significant proportion of warts disappear spontaneously within a period of 2 years[1-8], and therefore, one should play for time in the treatment of warts. The clinical indication of a spontaneous regression has been reported to be darkening of the wart or appearance of dark spots on its surface[4]. It is, however, also known that in the same patient, new lesions may continue to appear, when some of the old lesions are disappearing. Thus, as a practical approach, it may be difficult to convince a patient just to wait for the warts to disappear when it may not happen at all. Moreover, at a latter date a wart may become more difficult to treat, particularly if it extends under the nail plate or into the eye-lid margin. Therefore, the only reasonable indication for leaving the warts alone for spontaneous regression may be when the treatment seems likely to leave behind unwelcome sequelae, or when the patient refuses treatment.

The most logical method of treating warts seems to be the use of a specific anti-viral agent, but unfortunately no such agent is available to date. Trials with 5-fluorouracil (5-FU), a flourinated pyrimidine which can interfere with the synthesis of DNA showed cure rates of 67%[5] and 46.5 to 53%[6]. Topical as well as intralesional 5-FU resulted in success in 75% cases[7]. In a controlled trial[8] where the effect of 5-FU was compared in a double blind manner with a placebo, 5-FU was successful in 60% of the cases compared to 20% success with placebo. The method of using 5-FU consisted of applying a 5% ointment on the lesions and covering the lesions with a water-proof adhesive plaster for 24 hours. This treatment was repeated daily for 4 weeks. Although the results are encouraging, the method seems to be tedious and slow. Morison[9] used 25% hydroxyurea in dimethyl sulphoxide (DMSO) and 40% idoxuridine (IDU) in DMSO for warts, but neither of these agents was effective. This failure being attributed to the effect of DMSO which leads to a very quick absorption of the compounds and thus allows very little time for the active ingredients to act on the wart tissue, IDU 40% was tried in a cream base with occlusion with very good results. Similar success was obtained with 20% IDU, but further lowering the concentration of IDU to 10%, made it much less effective. The duration of treatment in each case was 4 weeks. Bleomycin, a group of cytotoxic glycopeptide antibiotics derived

from *Streptomyces verticillus*, was used intravenously in 3 cases by Mishima and Matunaka[10] with complete success. Bremner[11] used it intralesionally as a 0.1% solution in normal saline and found a cure rate of 63%; the lesions disappearing within 4 weeks. In most cases, a single injection was sufficient though in a few, a second injection was given after 4 weeks. The method is promising though availability of bleomycin could be a limitation. Podophyllum is the only antimitotic agent with an established role in the treatment of warts, but it is effective only in the genital warts. A 20-25% concentration in tincture benzoin is applied on the surface of the lesion after protecting the adjoining normal skin. After 2 hours, it can be washed off. The applications can be repeated once or twice a week if required[2]. It is not effective in other types of warts because it is probably unable to penetrate the thickened stratum corneum.

In the absence of a specific and thoroughly evaluated anti-viral agent, the oldest and still the most widely used method for the treatment of warts consists of non-specific destruction of the infected tissue which automatically leads to elimination of the virus as well. Freezing of the tissue (Cryotherapy)[12,13] with liquid air, liquid nitrogen or carbon dioxide snow can be used wherever facilities are available. The method consists of applying the agent on the wart for a period long enough to cause severe vasoconstriction and necrosis of the tissue. Freezing by itself leads to destruction of the tissue. Sanders and Strectcher[8] stress the importance of formation of an 'ice ball' extending several millimeters beyond the wart. This leads to formation of a blister followed by crusting. Healing occurs in 7-10 days. Destruction of the tissue can also be achieved by local applications of strong acids or alkalis[12]. The choice obviously depends upon whatever is available and is strong enough to cause necrosis of the tissue, but carbolic acid (phenol) and trichloroacetic acid are the ones used most frequently. The agent has got to be pricked into the lesion by means of a hypodermic needle, because these acids as a rule, have only a limited capacity to penetrate the thickened stratum corneum. In case the lesions are big, surgical scooping of the main wart followed by cauterization of the base with phenol or trichloroacetic acid is necessary to destroy the left-over infected tissue[14]. The rate of success depends upon the thoroughness with which the infected tissue has been removed. It is necessary to examine the patient again within 2-3 weeks to detect recurrence of the treated lesions if any and also the appearance of new lesions which escaped detection earlier. For complete eradication, each lesion must be treated at the earliest, because the longer a lesion stays on the skin more likely it is to give rise to new lesions. This is particularly so when the lesions occur on the beard region where shaving facilitates cutting off of the wart tissue and its transplantation on new abraded areas. Warts can also be destroyed by electro-coagulation or electric cauterization in which case an electric electrode coagulates or chars the tissue. This procedure also requires the same precautions as cauterization with acids or alkalis. The amount of tissue destroyed with these procedures has got to be carefully regulated, because if the destruction is incomplete, the warts are likely to recur and if the destruction is more, the resultant scarring is likely to be unpleasant. For the same reason, surgical excision of the entire wart is not necessary, because it almost always leaves behind a scar which can be extremely painful when situated on the sole. Genital warts however, can sometimes be very big, particularly

during pregnancy. In such a situation surgical excision seems to be a preferred method of treatment.

Since infection with warts is limited to the epidermis only, the most logical non-specific destructive procedure would be use of agents which can cause dermo-epidermal separation. Such an agent will ensure total removal of the infected tissue without any risk of residual scarring. Cantharidin, a powerful acantholytic agent was first used by Epstein and Kligman[15] and recently by Rosenberg et al[16] as a 0.7% solution in a collodion base for local application on warts daily till a blister formed or the lesion disappeared. The lesions have been reported to heal within 10 days or so.

Limitation of the warts to the epidermis only and absense of an inflammatory reaction had led many workers to believe that the virus does not incite an immunological reaction. But the facts that (1) the infection is most frequent during childhood, it becomes less during adolescence and still less as the age advances, (2) the warts can regress spontaneously particularly after electro-coagulation of a few lesions[17], (3) histopathological demonstration of round cell infiltrates at the base of some warts[18,19] and (4) preponderance of warts in patients with immunosuppression[20-23] did suggest that immunologic mechanisms may be playing a role. Antibodies to the warts virus were demonstrated by many workers[24-30], but in general, no correlation could be found between the antibody levels and regression of the warts. Morison[23,31] however, considered depression of the cell mediated immunity to be responsible for propagation of the warts. Levamisole, as a stimulant of cell mediated immunity, was tried by Helin and Bergh[32] and also by Sutton[33] with apparent success in several cases. The treatment schedule used by Helin and Bergh consisted of 50-150 mg levamisole on 3 conceeutive days every 2 weeks for 6-18 weeks and that used by Sutton was 150 mg on 2 consecutive days per week for 7 months. Further trials on a larger number of cases perferably in a double blind manner are necessary to establish the usefulness of the agent because spontaneous regression of warts remains a possibility in all uncontrolled studies, and the record of levamisole as a stimulator of CMI is not uniformly good. Repeated small-pox vaccination was also tried in the past[34] probably on the basis of a similar mechanism but the practice has been given up because of serious side effects[3].

Another interesting method to induce regression of the warts was tried by Greenberg et al[35]. The patient was first sensitized by applying a 3 sq cm filter paper soaked with 0.05 ml of 30% DNCB in acetone on the patient's forearm for 24 hours. After 10 days the wart was challenged with 1-10 ug DNCB in acetone applied directly on the wart. In 4 out of 5 patients thus treated, the warts disappeared in 4-7 days. In 2 cases, even the unchallenged warts disappeared in 10-14 days. This method however, is risky and cannot be recommened for general adoption.

Other agents used for the treatment of warts include (1) soaking the wart bearing area (especially in the case of plantar warts) in 10% formaline[12] or 2% glutaraldehyde[36] for 15 minutes every day or applying 10% glutaraldehyde in ethanol or 5% glutaraldehyde in collodion on the lesions twice a day[36-39]; (2) local applications of retinoic acid[40] on the warts once or twice a day, and (3) oral griseofulvin in 500 mg dose daily for 12 weeks[41], but each of these methods needs further evaluation in properly controlled trials before they can be recommended for general adoption. The fact remains that the most ideal treatment must be

effective in almost all the patients, it should be simple and safe and should not leave behind residual scars.

Finally, it is also worthwhile to consider if a vaccine can be prepared to protect patients from warts. Theoretically, it seems possible to develop a vaccine which should enhance the cell mediated immunity against the virus, but for a disease which is neither lethal nor seriously disfiguring, necessity of a vaccine can be a debatable issue.

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