Current Dermatological Therapy

A series of articles on current dermatological therapy will feature in the pages of the journal this year. This issue presents the second of the series. Articles are contributed by Dr. J. S. Pasricha, M. D., Ph.D., Department of Dermato - Venereology, All India Institute of Medical Sciences, New Delhi.

THERAPEUTIC PROBLEM OF HERPES SIMPLEX INFECTION

The story of the treatment of herpes simplex infection is punctuated with repeated peaks of hope, followed by despair and helplessness. X-ray therapy or repeated inoculations with vaccinia are perhaps the oldest methods of treatment[1,2], but the enthusiasm with which these methods were being pursued with apparent success a few years ago, has now been replaced by the realization that all the benefit attributed to these procedures was perhaps more due to suggestion rather than anything else[3]. The possibility of serious complications following vaccinia[4], particularly in patients with immuno-suppression[5], has dealt the final blow to this procedure.

Trials with specific vaccines prepared from herpes simplex virus were considered successful by some workers[6], but controlled studies showed these vaccines to be hardly better than placeboes[7,8], so much so that Kern and Schiff[9] use inoculations of normal saline every 2-3 weeks for a total of 10 to prevent recurrences of herpes simplex. Attempts to prevent recurrences by stimulating the production of specific antibodies seems off the mark for several reasons. Firstly, most patients having recurrent herpes simplex infection do have adequate levels of antibodies in their blood [6,10] and secondly it is known that the virus spreads from one cell to the other and thus remains protected from the antibody. Moreover, in Lazar's experiments[11], use of patient's own live virus for inoculation at another skin area to prevent recurrences not only failed to acheive the desired result but the patient also started having herpetic lesions on the new sites as well. Lastly, use of a vaccine prepared from a virus which has a possible carcinogenic potential[6,12] needs very careful evaluation before it can be recommended for general use.

Attempts to augment cell mediated immunity by the use of repeated BCG vaccination[8,13,14] or levamisole[8,15] seem more logical, but need further evaluation with appropriate controls to rule out the effect of suggestion. Bierman[8] however, considered BCG inoculations to be of doubtful value.

In 1962, Kaufman et al[16] introduced 5-iodo-2-deoxyuridine (IDU) for the treatment of herpetic keratitis and out of all the anti-viral agents, IDU is perhaps the most widely evaluated drug, but still there is no unanimity on its

effectiveness or otherwise. For occular herpes infections, it is undoubtedly a valuable drug[17,18] but its value in cutaneous herpes has been a variable experience. Whereas some workers[19-23] reported that IDU was useful, others[24-28] concluded that IDU was no better than a placebo. One of the major drawbacks of IDU was considered to be its lack of penetrability in tissues. Goldman and Kitzmiller[29] and Polano[30] therefore, used IDU in dimethylsulfoxide (DMSO) to augment its penetrability and reported good results. Two other anti-viral agents, cytosine arabinoside (ara-C) and adenine arabinoside (ara-A) have some advantages over IDU but they have not as yet been properly evaluated and the possibility of their use for cutaneous herpes seems even less. Attempts have also been made to use interferon, or its inducers to inhibit virus replication, but its utility is quite limited for various reasons[10].

In 1971 Felber et al[31] reported a new method for the treatment of herpes. This method consisted of local applications of 0.1% aqueous neutral red or proflavine on the lesions, followed by exposure to fluorescent light for 15 minutes and is based upon the ability of these heterotricyclic dyes to combine with the guanine portion of DNA; subsequent exposure to light results in excision of the guanine portion of the DNA molecule leading to its disruption[32]. This results in inactivation of the herpes simplex virus. Several clinical studies have reported success with various dyes such as neutral red, proflavine and methylene blue[33-36]. There are, however, several other reports[37-40] which stress that the dye-light treatment is no better than placebo. Moreover, the possibility that the photo-inactivated herpes simplex virus can become oncogenic[41] has led some workers[42] to sound a word of caution in using this method.

In 1973, two brief reports [43,44] one of which was by the author himself suggested the use of ethyl ether for local applications. This method exploits the susceptibility of herpes simplex virus to fat solvents. The method consisted of pressing a cotton swab well soaked in ether on the lesions for 5 minutes on two consecutive days. Following this treatment, the ulcers have been observed to heal much faster and in some cases there were no recurrences for sufficiently long periods of follow-up. The only drawback in this method was the severe pain caused by ether on raw areas. We now press a swab soaked in some local anaesthetic on the ulcers for 5 minutes before applying the ether swab. Following our report, some other workers[42] have also corroborated our experience and consider this method to be free from the risk of oncogenicity. Although these workers have used only ether, theoretically, other fat solvents such as acetone, chloroform or alcohol could also be used. However, a controlled trial with chloroform has shown only an insignificant superiority of chloroform over the placebo[45]. As stressed by us, it is important to press the ether swab over the lesion so that it permeates all the infected cells, otherwise if the virus persists in some cells, it is likely to result in recurrences.

The information that the herpes simplex virus remains latent in the sensory ganglia[46] and not in the skin casts serious doubt on the value of any of the local therapeutic measures. Systemic anti-viral drugs should on that basis be more useful. IDU, Ara-A, Ara-C and the recently introduced phosphonoacetic acid[47-49] are being assessed for systemic therapy but so far it seems that in spite of extensive laboratory studies and clinical trials, we are still groping to find an appropriate treatment for herpes simplex. We are all aware that the lesions of

herpes simplex will heal spontaneously even if nothing is done, while on the other hand, injudicious treatment can certainly prolong the suffering and result in even serious complications. It is, therefore, of utmost importance to know what is potentially harmful, so that nothing is done that can result in more harm than benefit.

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