

Orally Administered Specific Transfer Factor for the Treatment of Herpes Infections

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INTRODUCTION

Genital herpes has become a widespread disease in recent years. Because of a lack of effective treatment, herpes patients are treated with various kinds of therapy, ranging from such antiviral agents as acyclovir⁽¹⁾ to vitamin C and isoprinosine,⁽²⁾ but with little success. Nonspecific vaccinations, e.g., polio or BCG, have also been used, and specific vaccines with preventive potential are now being developed.⁽³⁾

It is important to recall that herpes simplex viruses 1 and 2 (HSV1, HSV2) are ubiquitous and that the entire population is exposed to infection. Eight out of ten normal adults shed herpes virus in oral secretions.⁽⁴⁾ The titer of serum-neutralizing antibody, present in 86-90% of the population,⁽⁵⁾ is not correlated with the occurrence of herpetic lesions nor with virus shedding. The humoral immune response to the viral antigens thus seems to be of little importance in preventing the onset of the disease.

We (unpublished) and others^(6,7) have shown that cell-mediated immunity (CMI) to HSV antigens seems to be impaired in herpes patients, as measured by the leukocyte migration test (LMT). The reason for this is unknown, and it raises problems in relation to the efficacy of antiherpes vaccines. It thus seems unclear why some investigators consider the sexual partners of infected patients an appropriate high-risk group for assay of putative vaccines. In our experience, regular partners of some herpes patients have not developed the disease even over periods of up to 20 years. It might, therefore, be more appropriate to test a preventive agent in a large group of sexually promiscuous youths in whom the probability of the existence of a strong immunity to HSV is lower.

METHOD

In an attempt to provide a simple and easy method for enhancing the CMI of herpes patients to HSV antigens, anti-HSV-specific bovine transfer factor (TFdH) was prepared by immunizing 5-6 month old calves with HSV1 or HSV2 viral preparations (Microbiological Associates, Walkersville, MD). The cellular immunity of the animals was assayed 21 days after injection by skin tests, LMT, and lymphocyte stimulation in the presence of the viral preparation. Calves showing immunity were sacrificed, and TFdH was extracted in the conventional way⁽⁸⁾ from the spleens, livers, lymph nodes, and peripheral blood lymphocytes.

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TABLE I. TREATMENT OF HERPES PATIENTS WITH ANTI-HVS TRANSFER FACTOR

Patient N	Before Treatment			Treatment Phase		
	Length of Illness (Years)	Duration of Relapses ^a (Days/Month)	Duration (Months)	Duration of Relapses ^b (Days/Month)	% of Improvement	
1	4	13.5	4	0.08	99	
2	4	18.0	12	0.2	99	
3	4	10.0	5	0.6	94	
4	3	7.5	7	4.5	40	
5	3	6.0	7	1.7	72	
6	4	20.0	9	12.2	39	
7	5	5.8	6	0.5	99	
8	5	15.0	14	5.1	70	
9	2	12.5	4	3.0	58	
10 ^c	2	7.3	5	0.8	89	
11 ^c	10	7.5	3	0.0	100	
12 ^c	15	12.0	6	1.5	87	
13	25	10.0	5	3.0	66	
14	3	14.6	6	1.0	93	
15	5	12.2	6	4.8	59	
16	7	15.0	2	1.0	86	
17 ^d	3	7.50	8	3.3	56	
18	12	4.50	18	2.3	51	

^a"Relapses per month" is the total of days of illness during N months divided by N.

^bThe duration of relapses after treatment was significantly lower ($p < 0.001$), using the Wilcoxon T test).

^cLabial herpes.

^dPatient developed a postnatal encephalitis, with regular skin relapses ever since.

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RESULTS

Eighteen patients suffering from genital or labial herpes for periods ranging from 2 to 25 years and resistant to the various therapies, for example, isoprinosine, idoxuridine, and nonspecific vaccinations, were treated with the TFdH thus obtained. The results are summarized in Table 1. TFdH was originally given intramuscularly but later it was administered orally with equal efficacy. All patients now receive TFdH by oral route.

The results suggest that (1) specific bovine TFdH has a beneficial effect in herpes patients, (2) the full effect is elicited within 3 months of the beginning of treatment, (3) some patients do not relapse when a placebo is administered at the end of the treatment, whereas others do relapse within a few days (Table 2), (4) after the placebo phase, the treatment can be resumed with the same or increased efficacy, (5) the dose and the frequency of administration need to be individually adapted for each patient, although all patients responded to a standard dose of 2 units every 3 days (1 unit is obtained from 10^8 cells), and (6) a correlation with the LMT is not always present but was observed in several cases.⁽⁹⁾

These results are consistent with those of Dwyer et al.,⁽¹⁰⁾ and they warrant additional controlled trials for the evaluation of the full potential of TFdH for treatment of herpes infections. Since TFdH increases CMI to HSV antigens it may be efficacious when used prophylactically. A prospective controlled study in a high-risk group should answer this.

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TABLE 2. TREATMENT OF HERPES PATIENTS: PLACEBO PHASE

<i>Patient N^a</i>	<i>Duration (Months)</i>	<i>Duration of Relapses (Days/Month)</i>
1	3	0.0
2	3	16.6
3	3	2.6
4	3	7.0
5	3	0.0
9	4	6.0
10	3	0.8
11	3	0.0

^aEight patients whose improvement was noticeable under TFdH received a placebo for 3-4 months. Severe relapses occurred in some of these patients, whereas others remained disease-free throughout this period.

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