

A COMPARISON OF PREEXPOSURE RABIES PROPHYLAXIS REGIMENS USING DUCK EMBRYO VACCINE¹

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In preexposure rabies prophylaxis the recommended practice is to administer four doses of duck embryo vaccine subcutaneously. The findings reported in this article indicate that equally effective results can be achieved with smaller intradermal doses if personnel competent to administer the vaccine by this route are available.

Introduction

Following Pasteur's initial development of rabies vaccine, a variety of rabies vaccines were prepared from nerve tissues. Such nerve tissue vaccines (NTV) proved highly effective, but were also associated with occasional neuroparalytic reactions. The development of duck embryo vaccine (DEV), which is not prepared from nerve tissue, led to a fall in the rate of serious reactions in rabies prophylaxis. Though the postexposure treatment failure rates for NTV and DEV do not differ significantly, the significantly lower incidence of central nervous system reactions with DEV has made its use preferable to that of NTV (1,2).

The present recommendations of the U.S. Public Health Service Advisory Committee on Immunization Practices (ACIP) for pre-exposure rabies prophylaxis call for three subcutaneous injections of DEV (1 ml each) at weekly intervals, followed by a fourth 1 ml dose three months later. Three to four weeks after the last injection a serum sample should be collected for rabies antibody testing.

This article reports on a study designed to determine whether a difference in the antibody response to DEV would be observed if the preexposure method of administering the vaccine were altered.

Methodology and Results

A total of 203 veterinary students with no previous history of rabies vaccination were randomly divided into three groups of 70, 67, and 66. Although these three groups were of almost equal size, the final groups of subjects differed considerably (see Table 1) because some individuals failed to complete their prescribed regimen.

Each student was given the first three recommended doses of DEV at weekly intervals. In order to accommodate student schedules the fourth dose was given one month later, instead of the three months later recommended by ACIP. Group I received four 1.0 ml doses of DEV subcutaneously; Group II received four 0.1 ml doses intradermally; and Group III received four doses of 0.1 ml intradermally and 0.9 ml subcutaneously. A serum sample was collected from each subject two to three weeks after the fourth injection.

Table 1 shows the resulting antibody responses observed. All antibody determinations were performed by the U.S. Center for Disease Control, utilizing the rapid fluorescent focus inhibition test (3). The percentages of positive responses obtained with

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Table 1. Antibody responses to duck embryo rabies vaccine (DEV), considering a titer over 1:5 to constitute a positive response.

Method of Administration	Positive responses (titer > 1:5)		Negative responses (titer ≤ 1:5)		Total No.
	No.	%	No.	%	
Subcutaneous (1.0 ml)	63	90.0	7	10.0	70
Intradermal (0.1 ml)	38	90.5	4	9.5	42
Intradermal (0.1 ml) and subcutaneous (0.9 ml)	42	82.4	9	17.6	51
Total	143	87.7	20	12.3	163

$$\chi^2_{(df = 2)} = 1.992; p > 0.05.$$

subcutaneous administration and intradermal administration were practically identical, while the combination of the two methods appears to have elicited a slightly lower rate of positive response. None of the observed differences are statistically significant.

Although the Center for Disease Control

considers a titer greater than 1:5 to constitute a positive response, the authors feel that a titer greater than 1:15 should be considered positive for high-risk individuals—veterinarians, animal handlers, etc. (4). Table 2 shows the rates of positive response obtained in terms of this higher standard. It can be seen that the trend observed in Table

Table 2. Antibody responses to duck embryo rabies vaccine (DEV), considering a titer over 1:15 to constitute a positive response.

Method of administration	Positive responses (titer > 1:15)		Negative responses (titer ≤ 1:15)		Total No.
	No.	%	No.	%	
Subcutaneous (1.0 ml)	49	70.0	21	30.0	70
Intradermal (0.1 ml)	31	73.8	11	26.2	42
Intradermal (0.1 ml) and subcutaneous (0.9 ml)	30	58.8	21	41.2	51
Total	110	67.5	53	32.5	163

$$\chi^2_{(df = 2)} = 2.711; p > 0.05.$$

1 appears to persist and that, as before, the differences in the rates of positive response are not statistically significant.

Discussion

In accordance with our findings, it is considered that preexposure rabies prophylaxis by intradermal inoculation with 0.1 ml doses of DEV is effective, as is subcutaneous inoculation with 1.0 ml doses of DEV. The former method of administration requires greater precision and expertise than the latter. It also greatly reduces vaccine costs, but since the cost of DEV is relatively low, this should not be an important consideration in the decision-making process. Should there be an opportunity to receive the intradermal dose, this method is considered completely feasible and is recommended.

The combined subcutaneous/intradermal method is not recommended because of the cumbersome nature of the adminis-

tration technique and the apparently lower immunogenic response.

Although the numbers of subjects involved in this study were large enough to make valid comparisons among groups, the authors consider these numbers too small to provide valid extrapolations to the general population with regard to vaccine reaction and/or failure rates.

Serious (neurological) reactions to post-exposure subcutaneous inoculation have been reported to occur at a rate of 1 case in 33,385, and postexposure treatment failure is said to occur at a rate of 1 instance in 25,800 (1,2).

In our preexposure studies with 163 students, there were no serious reactions to vaccination by any of the three methods employed. Non-neurological reactions such as erythema, pain, and swelling were minimal. Overall, only six students requested medical consultation because of localized reactions. One of these was in the group vaccinated intradermally, two were in the intradermal/subcutaneous group, and three were in the subcutaneous group.

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administering the vaccine and collecting serum samples. The cooperation of the Viral Zoonoses Branch, Bureau of Laboratories, Center for Disease Control, was essential in determining serum antibody levels for participating subjects.

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SUMMARY

For some time subcutaneously administered duck embryo rabies vaccine (DEV) has been used for preexposure rabies prophylaxis in order to elicit an immunogenic response. This article

reports the results of tests designed to determine whether administration of DEV by the intradermal route, or by both intradermal and subcutaneous routes, might be equally effective.

For this purpose veterinary students were given four doses of DEV via each of these routes and via a combination of both. The results indicate that the intradermal doses (0.1 ml) and

the subcutaneous doses (1.0 ml) were equally effective. However, the intradermal route is recommended only where a staff competent to administer DEV in this manner is available.

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SMALLPOX: \$1,000 GLOBAL REWARD

The World Health Organization is to offer a global reward of US\$1,000 for the first report of an active case of smallpox, under the terms of a resolution passed by the Thirty-first World Health Assembly in Geneva. The aim of the reward offer is to strengthen worldwide vigilance against smallpox and to assist national surveillance programs in countries where eradication of the disease has not yet been officially certified.

The reward offer will stipulate that any smallpox case reported must be confirmed by laboratory tests and should have resulted from person-to-person transmission. No case of smallpox has been reported anywhere in the world for over six months. The last confirmed case, with onset of rash on 26 October 1977, occurred in Merka Town, Somalia.

Commenting on the reward offer, Dr. Halfdan Mahler, WHO Director-General, said active search and surveillance programs must be maintained at least two years after the last confirmed case in any country, since "only after that period has elapsed can we be fully certain that no hidden foci of smallpox remain."