Rabies Vaccination

Field Observations During Epizootics in Dogs

Texas has been a testing ground for rabies vaccines in recent years because of the extensiveness of the disease within this state. A high level of wildlife rabies along with subsequent "spillover" into domestic animals and localized rabies epizootics along the US-Mexico border have kept much of Texas' dog population at risk. Followup studies of naturally challenged dogs have afforded the opportunity to assess the effectiveness of rabies vaccines under field conditions. Such studies are uniquely valuable because they include countless combinations of variables not generally reproducible in the laboratory and because field experiences in some instances have invalidated conclusions derived solely from laboratory experiments. Experiences with vaccination during epizootics may also provide information applicable to the handling of dogs known to have been exposed to rabies virus.

Studies of Two Epizootics

Epizootics of canine rabies occurred in Laredo, TX, in 1976-1977 and in Eagle Pass, TX, in 1979. The Laredo outbreak began in November, 1976 and ended in March, 1977. During that interval 54 cases of rabies were diagnosed in dogs. Between
March 14 and September 17, 1979 there were 19 cases diagnosed in Eagle Pass. In Figures 1A and 1B the temporal occurrence of these canine rabies cases is shown.

In 1976 prior to the epizootic an inactivated rabies vaccine (Monorab: Jen-Sal) was used in Laredo for mass vaccination of dogs. Another inactivated vaccine (Trimune: Ft Dodge) had been used for mass vaccination in 1974 and 1975. It was estimated that 38% of the dogs in the city had been vaccinated at the beginning of the epizootic. High-egg-passage, Flury-strain vaccine of canine cell line origin (Endurall-R: Norden) was used exclusively for control during the Laredo and Eagle Pass epizootics. Almost 20,000 dogs were vaccinated during the 2 epizootics. In Laredo, 16,254 dogs, which represented 88.8% of the estimated canine population, were vaccinated or revaccinated. In Eagle Pass, 3331 dogs or about 74% of the estimated canine population were vaccinated or revaccinated during the epizootic.1

Detailed records were maintained during the epizootics and all known cases of canine rabies in Texas were investigated from 1976 through 1980. Special attention was given to the infested dog’s vaccination status. The following definitions were used for vaccination status:

*Vaccination failure* was applied to cases confirmed by immunofluorescence by the Texas Department of Health in dogs known to be currently vaccinated.

*Current vaccination* was defined as vaccination with an approved rabies vaccine not less than 30 days nor more than 1 year previously.

*Incompletely immunized* was defined as the occurrence of laboratory-confirmed rabies in a dog less than 30 days after initial vaccination.

The state’s health department records were studied retrospectively to determine the number of rabid dogs that were unvaccinated, currently vaccinated with only one vaccination, and currently vaccinated with more than one vaccination. Frozen brain tissue from one “incompletely immunized” dog was sent to the Center for Disease Control in Atlanta, GA, to determine whether street virus or vaccine virus was responsible.

The epizootics of canine rabies in Laredo and Eagle Pass were controlled by a combination of intensive educational programs, rigid control of stray animals, and extensive low-cost vaccination.1

No dogs vaccinated during the epizootics developed rabies after the 29th post-vaccination day.

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**Table 1. Rabies Vaccination Failures in Dogs**

<table>
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<tr>
<th>Case Number</th>
<th>Age (Years)</th>
<th>Number of Previous Rabies Vaccinations</th>
<th>Vaccine(s) Used in Last 3 Years*</th>
<th>Interval Between Last Vaccination and Onset of Disease (Months)</th>
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*1 - Monorab, 2 - Trimune, 3 - ERA (Jen-Sal), 4 - Raboid (Fromm)
Three vaccination failures occurred during the Laredo epizootic; though there was evidence that 2 others occurred, proof of vaccination was lacking. There were no documented vaccination failures in the Eagle Pass epizootic, but 5 occurred in other parts of the state during 1979 and 1980. The 3 cases in Laredo and 2 near the US-Mexico border may have resulted from contact with other infected dogs. In the other 3 cases the dogs were probably infected by wild animals. The pertinent data on these cases are contained in Table 1.

Seventeen "incompletely immunized" dogs developed laboratory-confirmed rabies during the 2 epizootics. They all developed clinical signs of rabies within 3 to 29 days after vaccination. Seven (41%) of the Laredo dogs developed rabies within 1 week after vaccination.

Ninety-two percent (162/176) of the canine rabies cases in Texas occurring from 1976 to 1980 involved unvaccinated dogs. Eight percent (14/176) of these dogs were currently vaccinated and 29% (4/14) of the vaccinated dogs had been vaccinated more than once. The viral study performed at CDC indicated that the causal agent was probably a street strain.

Discussion
The efficacy of rabies vaccination has been demonstrated repeatedly under laboratory conditions in which all the vaccinated animals were healthy and well-nourished. Under field conditions, however, there are many variables that may adversely affect immunologic responses. Thus the information obtained from field epizootics is extremely valuable. The effectiveness of vaccination with a high-quality MLV vaccine used in conjunction with other control measures was adequately demonstrated in these 2 epizootics.

The vaccination failures emphasize the fact that protection against rabies is not absolute. This should not be construed as an indictment against vaccination, however, because such factors as inherent lack of potency, loss of potency due to mishandling, improper administration, or immunologic unresponsiveness of the recipient animal can result in inadequate immunity.

"Incomplete immunization" as used here applies to dogs that did not develop protective immunity following vaccination presumably because inadequate time had elapsed. Though relatively high neutralizing antibody titers have been found 3 weeks after administration of MLV vaccine, that study did not distinguish between classes of antibodies. IgG antibodies are probably protective in vivo, but IgM antibodies, which are produced first, are probably not protective in vivo. (This may be due to their confinement in intravascular spaces because of their large molecular size and consequent inability to reach the virus in tissues.) The roles of cell-mediated immunity and interferon in rabies immunity are unclear.

The available evidence indicated that vaccine-induced rabies was unlikely in the "incompletely immunized" dogs. This evidence included the following facts: 1. The incubation time in 7/17 (41%) of the cases was shorter than that specified by the California Department of Health.2 2. One of the affected dogs had received inactivated vaccine only. 3. Studies at CDC indicated that the virus was a street strain. 4. This phenomenon was observed only during epizootics. 5. The safety record of the vaccine used in the mass vaccination programs had been unblemished for 8 years and after 70 million administrations.

The large number (41%) of incompletely immunized dogs that developed rabies within the first week after vaccination was somewhat unexpected. It suggests that vaccination may evoke clinical signs in dogs that are in the incubation stage. This is compatible with the "early death" phenomenon observed in rabies infections in which animals immunized with non-protective doses of vaccine die sooner than do unvaccinated controls. Possible mechanisms for this phenomenon include (1) increased viral activity caused by diversion of immune mechanisms to react with vaccine virus and (2) immunologically mediated injury to host cells.

Post-exposure anti-rabies treatment in man is designed to exploit the usually long incubation of rabies by inducing immunity during the incubation period and thus aborting the infection. In mass
Fig 1A. Occurrence of cases in Laredo epizootic.

Fig 1B. Occurrence of cases in Eagle Pass epizootic.

Fig 2. Occurrence of rabies in dogs following vaccination.
vaccination programs for dogs during rabies epizootics, some animals in the incubation stages of the disease will undoubtedly be vaccinated. In view of the variable incubation period usually associated with rabies, it is questionable that all such dogs in a population of 20,000 would develop the disease within 30 days of vaccination. This suggests that an undetermined number of incubating rabies infections may be aborted by post-exposure vaccination. This observation has important implications when formulating recommendations for management of exposed animals because it suggests that post-exposure vaccination may be successful in some cases.

Because none of the nearly 20,000 dogs vaccinated during these 2 epizootics developed rabies 30 days or more after vaccination, the current recommendations for dogs exposed to rabies may be unnecessarily conservative. In Texas it is currently recommended (when owners elect not to have their animals destroyed following exposure to rabies) that currently vaccinated animals receive a booster injection as soon as possible and be confined for 90 days. Because of the experience gained in these 2 epizootics, immediate vaccination is recommended for unvaccinated animals, followed by 6 months confinement and a booster injection administered 30 days prior to their release. Future modifications of these recommendations will be based on additional experimental and epidemiologic information.

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References