Evaluation of safety and potency of rabies vaccines

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Summary: To avoid the risks entailed by uncontrolled vaccines, the safety and potency of rabies vaccines should be controlled at two levels, by the manufacturer and by a national control authority. The methods for evaluation of modified live vaccines and of inactivated vaccines are presented. According to the NIH test, there is a correlation between vaccine potency and protection.

KEYWORDS: Immunity - Quality control - Rabies - Vaccines - Viral diseases.

1. Necessity of vaccine control

The designation “rabies vaccine” without any control measurement is no proof of safety or potency. Quality control of rabies vaccines is of the utmost importance in any programme of rabies control: vaccination using uncontrolled vaccines should be avoided under all circumstances, because of the severe consequences of false confidence in an animal’s immunity.

Quality control of rabies vaccines should be conducted at two levels, by the manufacturer and by a national control authority, e.g. the national rabies laboratory or national Veterinary Service laboratory. The methods for quality control of rabies vaccines were revised by a WHO Expert Committee in 1983. They are summarised in the Seventh Report of the WHO Expert Committee on Rabies (Technical Report Series 709, 1984).

In 1980, the OIE, WHO and FAO recommended that in countries with low rabies incidence, as is the case in Europe, only inactivated rabies vaccines should be used. But in a 1985 questionnaire, 8 of 16 countries indicated that they still used live attenuated vaccines.

2. Modified live vaccines

Safety is tested by injection of guinea pigs or target animals by the i.m. route. Potency is tested by inoculation of the vaccine into guinea pigs. Sufficient potency has been attained when 70% of vaccinated animals survive a challenge which kills 80% of the unvaccinated controls.

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3. **Inactivated rabies vaccines**

   **Evaluation of safety**

   Safety of rabies vaccines is the absence of adverse reactions after vaccination in the vaccinee. The content of unspecific protein/dose is one parameter for the quality of a vaccine. Purified inactivated tissue culture vaccines have the lowest content of unspecific protein. They are almost exclusively composed of rabies virus particles. This cannot be achieved with brain rabies vaccine. In addition, vaccines prepared from adult central nervous tissue contain neuroparalytic factors such as myelin. The neuroparalytic factors in vaccines of avian tissue origin are further reduced, but they may still be allergenic. Control of innocuity is carried out by injection of the vaccine into mice or target species. Vaccine batches can be considered for licensing only when they meet the criteria of microbiological sterility, rabies inactivation and absence of abnormal toxicity.

   **Evaluation of potency**

   Potency is the capacity of a vaccine to protect the vaccinee against rabies. The potency of rabies vaccines is determined, on the one hand, by the cross-reactivity of the rabies virus strain and, on the other hand, by the amount of immunising viral antigen in the vaccine. The potency of inactivated vaccines should be evaluated by measurement of the protection after vaccination of the target species being exposed (man) or challenged with infectious virus (animal). Potency may be evaluated in the target species, in the laboratory animal or in the test tube. The minimal requirements of potency are defined in IU values. For animal vaccines in general a potency of 1 IU/dose is required. In developing countries in which vaccination campaigns in dogs are carried out every two years, the WHO recommends a potency of 2 IU/dose.

4. **Correlation of potency and protection**

   The IU values obtained in the NIH test can be correlated with the protection in dogs and foxes for inactivated tissue culture rabies vaccine. The vaccine efficiency of an inactivated tissue culture vaccine of 2.5 IU for man is better than 99.999%. In other words, with a statistical significance of 0.1 > \( \alpha \) > 0.01 no vaccine failure will be observed in 1 to > 1 million vaccinations.