Effective vaccination against rabies in puppies in rabies endemic regions


Context
In rabies endemic regions, a proportionally higher incidence of rabies is often reported in dogs <12 months of age, which includes puppies <three months of age; this presents a serious risk to public health. The higher incidence of rabies in young dogs may be the effect of low vaccination coverage at this age, partly as a result of the perception that immature immune systems and maternal antibodies inhibit seroconversion to rabies vaccine in puppies <three months of age. Therefore, to test this perception, the authors report the virus neutralising antibody titres from 27 dogs that were vaccinated with high-quality, inactivated rabies vaccine at ≤three months of age, as part of larger serological studies undertaken in Gauteng Province, South Africa and the Serengeti District, Tanzania.

Main conclusion
Dogs ≤three months of age from low-income communities in rabies endemic regions responded well to a single dose of high-quality, inactivated rabies vaccine without any apparent adverse reactions, with all the dogs sampled in this study seroconverting to the vaccine (ie, generated antibody titres ≥0.5 iu/ml).

Approach
Every available puppy (n=68) in the township of Zenzele, Gauteng Province was vaccinated in February 2010 with 1 ml of Rabisin (Merial Animal Health) subcutaneously. In the Serengeti District, a convenience sample of eight puppies brought to a vaccination station in May 2008 were vaccinated with 1 ml of Nobivac Rabies (MSD Animal Health) subcutaneously. None of the puppies were vaccinated before the study. The majority of the 68 puppies in Zenzele were <six to eight weeks of age when vaccinated and deemed too small to bleed sample immediately before vaccination. Therefore, prevaccinal titres were obtained from only four of the puppies. Thirty-seven of the 68 puppies remained in Zenzele 30 days after vaccination, and of these, 19 were big enough to sample to measure postvaccinal peak titres. In the Serengeti, blood samples were collected from all eight puppies immediately before vaccination and 21 days later. Titres were measured by the fluorescent antibody virus neutralisation (FA VN) test.

All of the puppies were examined by a veterinarian at the time of vaccination and blood sampling and/or household visits in Zenzele during March 2010 to collect demographic data.

Results
In Zenzele, titres for the four puppies sampled immediately before vaccination were ≤0.13 iu/ml. Postvaccinal peak (ie, day 30) titres for the 19 puppies in Zenzele ranged from 2 to 90.5 iu/ml, with a geometric mean titre of 20.7 iu/ml. Prevaccinal titres for the eight puppies in the Serengeti were ≤0.29 iu/ml. Postvaccinal peak (ie, day 21) titres for all eight puppies in the Serengeti exceeded 5.9 iu/ml.

There were no reports or clinical signs of type IV hypersensitivity reactions during blood sampling and household visits. Although 14 puppies in Zenzele died before examination, none was reported to have died on the day of vaccination, which would have been suggestive of a type I hypersensitivity (anaphylactoid) reaction.

Interpretation
Canine-mediated human rabies kills approximately 60,000 people every year, particularly in Asia and Africa where domestic dogs are free roaming; there is increasing evidence that the majority of dogs are owned and, thus, generally accessible for vaccination. Mass vaccination of dogs is the key to successful control of canine rabies, and a strong evidence base indicates that vaccinating 70 per cent of the dog population during annual campaigns should be sufficient to control rabies. Effective coverage has been achieved through vaccinating juveniles and adults, given that puppies <three months of age are often excluded from vaccination programmes.

Low vaccination coverage in puppies has important implications for public health, especially as vaccination coverage of the population and, thus, herd immunity declines between vaccination campaigns through natural attrition of vaccinated dogs. A proportionally higher incidence of rabies is often reported in dogs <12 months of age which includes puppies <three months of age; this presents a serious risk to public health given the close relationship between people and puppies.

Puppies <three months of age are generally excluded from vaccination programmes on the assumption that they have immature immune systems and maternal antibodies which may inhibit the immune response to vaccines. Evaluation of the effect of maternal antibody and immune function of puppies on rabies vaccine-induced immune responses is limited. However, under experimental conditions these factors may not limit immune responses to high-quality, inactivated vaccines in puppies <three months of age. Although the vaccination status of the dams in this study was uncertain, these results in free-roaming dogs support these prior observations.

Given the inadequacy of vaccination campaigns, a substantial proportion of dogs in affected communities are never vaccinated or vaccinated only once in their lifetime. Although mortality in puppies <three months of age is generally high in these populations, delaying vaccination until puppies are three months of age may result in these dogs never being vaccinated. On the basis of the results from this study, puppy vaccination should therefore be included in annual rabies vaccination campaigns. However, these efforts should not compromise vaccination of juvenile and adult dogs, which have higher survival rates than puppies and are therefore important in maintaining vaccination coverage between campaigns. As humoral immunity can wane rapidly in young dogs, and puppies are continually acquired by community members throughout the year, it is recommended that all young dogs should also be given primary and booster vaccinations whenever veterinary services are available to owners.

Significance of findings
The results from this study support World Health Organization recommendations that all dogs in rabies endemic regions, irrespective of age, should be vaccinated against rabies.
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