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Vaccination of Small Asian Mongoose (*Herpestes javanicus*) Against Rabies

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ABSTRACT: Oral vaccination of free-ranging wildlife is a promising technique in rabies control. The small Asian mongoose (*Herpestes javanicus*) is an important reservoir of rabies on several Caribbean islands, but no vaccines have been evaluated for this species. Captive mongooses were used to test the safety and efficacy of the commercially licensed vaccinia-rabies glycoprotein (V-RG) recombinant vaccine and a newly developed genetically engineered oral rabies virus vaccine (SPBNGA-S). In one study using V-RG, no vaccinated animals developed detectable rabies virus–neutralizing antibodies, and all but one died after experimental challenge with rabies virus. In contrast, all animals given SPBNGA-S demonstrated seroconversion within 7 to 14 days after vaccination and survived rabies virus challenge. On the basis of these preliminary results indicating the greater efficacy of SPBNGA-S vs. V-RG vaccine, additional investigations will be necessary to determine the optimal dose and duration of vaccination, as well as incorporation of the SPBNGA-S vaccine into edible bait.

Key words: *Herpestes javanicus*, mongoose, rabies, SPBNGA-S, vaccination, V-RG, zoonosis.

The small Asian mongoose (*Herpestes javanicus*) is native to a large geographic area stretching from Iraq to the Malaysian Peninsula. However, in the mid-1800s, mongooses were introduced throughout the Caribbean to control rodent populations in sugarcane fields. Due to their diurnal nature, the mongoose did little to control the rodent populations, most of which had nocturnal habits (Tierkel et al., 1952). In addition to the mongoose's impact upon native bird and reptile populations, by the mid-20th century, rabies was identified among mongoose populations in Cuba, the Dominican Republic, Grenada, and Puerto Rico (Everard and Everard, 1992). Mongooses now serve as the main rabies reservoir in the Caribbean, with numerous human exposures, and infection of other species. Several countries, including Cuba and Grenada, have attempted to control mongooses by population reduction. However, such programs have been met with little long-term success (Nellis and Everard, 1983).

Novel attempts are underway to expand oral rabies vaccination (ORV) programs for some species such as raccoons (*Procyon lotor*), gray foxes (*Urocyon cinereoargenteus*), and other carnivores (Rupprecht et al., 2004). Mongooses present another species for consideration. Preliminary studies indicate that baits can reach up to 96% of a mongoose population on some Caribbean islands (Creekmore et al., 1994). Thus, ORV programs could be implemented to limit the spread of rabies in the Caribbean and minimize the opportunity for domestic animal cases and human exposures. However, no oral rabies vaccine has been shown to be effective in mongoose (Esposito et al., 1992). Development of reverse genetics techniques opens the possibility of creating new oral rabies vaccines that are safer and more potent than current biologicals (Dietzschold et al., 2004).

To this effect we evaluated recently developed rabies virus vaccines for their safety, immunogenicity, and efficacy in the mongoose. Our initial experiment sought to determine the efficacy of the vaccinia-rabies glycoprotein (V-RG) (Raboral V-RG®, Rhone Merieux, Inc., Athens, Georgia, USA) recombinant virus vaccine in mongoose; the vaccine is currently used extensively in ORV programs in the

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United States. Following the results of the experiment with V-RG, a second trial of a new, genetically engineered, oral rabies vaccine was tested to determine its efficacy in mongoose.

Because of the mongoose's status as an exotic pest species, importation of mongoose is limited for research purposes by the US Fish and Wildlife Service. Male mongooses were captured from the wild by the US Department of Agriculture/Wildlife Services (USDA/WS) from the US Virgin Islands. Before any procedures were initiated, all animals were held in quarantine for a minimum of 30 days according to Centers for Disease Control and Prevention Institutional Animal Care and Use Committee policies.

All procedures were performed while the mongooses were under sedation, which was induced with 0.2 ml of Tilatamine HCl and Zolazepam HCl (Telazol®, Fort Dodge Animal Health, Fort Dodge, Iowa, USA). In our preliminary experiment, using V-RG we randomly assigned five mongooses to receive 1 ml of V-RG per os (10^8 tissue culture infective dose [TCID]/ml) and seven controls to receive only media (modified Eagle medium-10 [MEM-10]). Administration of oral vaccine was conducted under light sedation using a syringe. Before the animals were vaccinated, a blood sample was obtained from the jugular vein for serologic evaluation. Following vaccination, blood was collected on a weekly basis for 4 wk (days 7, 14, 21, and 28). On day 28, all animals were inoculated with 500 µl (10^5 mouse intracerebral 50% lethal dose [$MICLD^{50}$]) of rabies virus in the left and right masseter muscles. Challenge virus was obtained from the 10% homogenate of a skunk salivary gland and was typed as California skunk variant. Seven days after virus challenge, blood was collected again. At the first detection of clinical signs of rabies, animals were sedated, blood was collected, and the animals were euthanized by administration of a barbiturate (Beuthanasia®-D, Schering-Plough, Union, New Jersey, USA). The brainstem was collected during necropsy for rabies testing using the direct fluorescent antibody (DFA) test as described elsewhere (http://www.cdc.gov/ncidod/dvrd/rabies/professional/publications/DFA_diagnosis/DFA_protocol-b.htm). All surviving animals were held for 100 days and then euthanized for rabies diagnosis. The presence of rabies virus neutralizing (VNA) antibodies was determined by use of the rapid fluorescent focus inhibition test (RFFIT) as described (Smith et al., 1996).

Following V-RG vaccination, neither vaccinated nor control animals developed detectable VNAs. Following challenge, all but one animal, which received V-RG, succumbed to rabies virus infection and were confirmed rabid by DFA (mean time to death: 25 days). Seven days after rabies virus challenge, the one surviving vaccinated animal had a titer of 0.91 IU/ml.

We next sought to test the efficacy of the experimental SPBNGA-S recombinant rabies virus vaccine (Faber et al., 2005). Five mongooses were randomly selected and given 1 ml of SPBNGA-S vaccine (10^8 TCID/ml) per os, and five remaining mongooses were given 1 ml of media (MEM-10).

Twenty-eight days following vaccination, no adverse events were observed among the mongooses. Three (60%) of the vaccinated animals had detectable VNA by day 7 and all had detectable VNA by day 14 (Table 1). Seven days following challenge with 500 µl of a street rabies virus (10^5 $MICLD^{50}$), in the left and right masseter muscles (the same virus as described above), an anamnestic response (>fourfold rise) was observed among four of the five vaccinated animals, and a titer <0.05 IU/ml was maintained by the nonvaccinated animals.

Nonvaccinated mongooses displayed clinical signs of rabies 16 days after infection (mean, 21 days; range, 16–25 days). Signs included increased aggression (100%), abnormal vocalization (60%), ataxia (60%), and hypersalivation (60%).

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TABLE 1. Detection of rabies virus neutralizing antibody titers (IU/milliliter) in small Asian mongoose (*Herpestes javanicus*) following vaccination with SPBNGA-S oral vaccine.[a]

Group	Day 7	Day 14	Day 21	Day 28	Day 7 postchallenge	At euthanasia
Control						
A	<0.05	<0.05	<0.05	<0.05	<0.05	50.40
B	<0.05	<0.05	<0.05	<0.05	<0.05	2.00
C	<0.05	<0.05	<0.05	<0.05	<0.05	6.40
D	<0.05	<0.05	<0.05	<0.05	<0.05	0.07
E	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
Vaccinate						
F	0.11	1.48	9.56	27.17	255.60	30.77
G	0.05	0.22	2.00	9.56	255.60	23.59
H	<0.05	0.43	1.74	2.96	64.00	11.28
I	<0.05	6.09	10.43	52.17	68.00	16.02
J	0.05	0.74	1.83	3.83	48.00	6.15
Control GMT[b]	<0.05	<0.05	<0.05	<0.05	<0.05	0.85
95% CI[c]	—	—	—	—	—	(0.01–22.3)
Vaccinate GMT	0.01	0.91	3.64	10.90	106.42	15.18
95% CI	(0–0.09)	(0.30–2.78)	(1.62–8.17)	(3.7–32.15)	(52.3–216.6)	(8.7–26.4)

[a] At day 0, all animals had <0.05 IU/ml rabies virus neutralizing titers.

[b] Geometric mean titer.

[c] Confidence interval.

All control animals developed clinical signs of rabies and were euthanized. Diagnosis was confirmed by DFA on fixed brainstem impressions. Vaccinated animals remained healthy, and were euthanized 100 days following challenge. DFA testing did not detect any viral antigen.

The results of this preliminary proof of concept indicate that the SPBNGA-S rabies virus vaccine is immunogenic, effective against severe challenge with rabies virus, and superior to V-RG for the vaccination of mongoose. In addition, the lack of any overt adverse reactions following vaccine administration suggests that it is safe at the given dose in captive mongooses. Additional studies will be necessary to fully test the safety of the vaccine under other conditions, discover the optimal dose for protection, and determine the duration of its immunity. In addition, to enhance studies on the SPBNGA-S vaccine, research will be needed to determine the ideal bait for mongoose as well as the efficacy of vaccine incorporation into the bait. As laboratory studies continue, field studies should consider suitable island sites for a clinical study of the utility of oral vaccination in mongoose rabies control.

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