ORAL VACCINATION CAMPAIGNS OF DOGS AGAINST RABIES

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1 INTRODUCTION.

Effective control of terrestrial wildlife rabies seemed almost impossible in Europe until the development of oral vaccination. Nowadays, oral vaccination of foxes (Vulpes vulpes) by distributing vaccine baits is the method of choice in rabies control in most European countries. Consequently, large areas are now rabies-free and here baits are no longer distributed or the distribution of baits is limited to border regions in order to prevent re-infection. Hence, this successful method has also been suggested for dog rabies control. Especially, in countries where a large segment of the dog population is not accessible for vaccination by the traditional parenteral route. Next to a safe and efficacious vaccine virus and attractive bait, a bait distribution system is required that assures bait availability to the target species, the domestic dog (Canis familiaris), meanwhile minimizing bait accessibility to non-target species, including humans. The latter constraint is essential, because of the safety concerns associated with the presently available oral rabies vaccine viruses. All licensed products are live viruses, live-modified or recombinants, therefore certain safety risks are associated with their use. Dogs live in close proximity of humans, thus unintentional direct or indirect human contact with the vaccine virus cannot be completely ruled out.

The following three bait distribution systems have been suggested:
- distribution of baits at selected sites,
- distribution of baits at a central location,
- and distribution of baits during a house-to-house campaign (WHO, 1993).

These different strategies are aimed at different segments of the dog population. In this paper, all three baiting systems will be reviewed and the major advantages and disadvantages discussed.

2 DISTRIBUTION OF BAITS AT SELECTED SITES.

Baits are distributed at selected sites and the dogs have to locate the baits themselves. The target population are therefore free-roaming dogs, irrespective of their vaccination and ownership status. This system is similar to oral vaccination of wildlife. A major disadvantage is the fact that not only the target population can locate and consume the baits, but other animals as well. To estimate bait degradation by non-target species, baits were distributed at selected sites in different urban areas of Istanbul, in Turkey. A total of 400 Köfte-baits (minced meat mixed with bread crumbs) were distributed and possible bait-uptake was investigated by direct observation. The baits were placed during day and night and observed, on average, for two hours. 53% of the baits were consumed by dogs. Birds, especially hooded crows (Corvus frugilegus), were the most important bait competitors during daytime; 26% of the baits were removed by birds. Cats (Felis catus) consumed 13% of the baits distributed. The fate of 8% of the baits could not be assessed; especially during the evening and night it was sometimes impossible to determine which animal species located the bait. Astonishingly, only once a man was seen to kick a bait aside with his shoes. It was never observed that a human picked up a bait or a discarded vaccine container. However, it is clear that this distribution system is associated with a potential high number of human contacts, especially children playing (Vos and Sanli, 1998).

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Although more than 50% of the baits were consumed by dogs, it doesn’t mean that also more than 50% of the target population of free-roaming dogs has been vaccinated. To assess the vaccination coverage by distributing baits at selected sites, free-roaming dogs were caught, bled and tagged in two areas of Istanbul; Sarigazi and Ferhatpasa. Most of these dogs were ownerless. Subsequently, baits were distributed at selected sites and one month later, tagged dogs were recaptured and a second blood sample was collected (Gleixner et al., 1998; Vos, unpublished data). The results are summarized in Table 42. In this study the seroconversion rate (>0.5 IU/ml) was selected as an indicator of the vaccination coverage. Vaccination coverage is sometimes also determined by detection of a biomarker incorporated in the bait, like tetracycline or rhodamine-B. However, this will only determine bait-uptake and not the actual vaccination coverage. The latter is often lower than the observed bait-uptake. For example, dogs remove the vaccine container from the bait or swallow the vaccine container without puncturing it with their teeth. Hence, the vaccine virus is not released in the oral cavity. Also, dogs may puncture the vaccine container but most of the vaccine is spilled on the ground.

Table 42: vaccination coverage of the free-roaming dog population after distribution of baits at selected sites in two municipalities, Sarigazi and Ferhatpasa (Istanbul, Turkey).

<table>
<thead>
<tr>
<th>Sarigazi</th>
<th>Ferhatpasa</th>
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</thead>
<tbody>
<tr>
<td>Number of dogs tagged</td>
<td>22</td>
</tr>
<tr>
<td>Bait density (bait/km²)</td>
<td>43</td>
</tr>
<tr>
<td>Bait disappearance rate (%)</td>
<td>64.7</td>
</tr>
<tr>
<td>Seroconversion rate (%)</td>
<td>4.5</td>
</tr>
</tbody>
</table>

The results were disappointing, only a very small percentage of the target population was vaccinated. A similar study conducted in Tunisia confirmed these results (Matter et al., 1998).

To reach high vaccination coverage at least hundreds, if not thousands, of baits per km² would have to be distributed. The associated costs would be unacceptably high and of course the high number of baits would also increase the potential risks associated with unintended human contacts with the vaccine virus considerably. Thus, this method is not very suitable in terms of cost-effectiveness and safety. Only in certain situations this method can be useful, e.g. to reach true feral dogs. For this purpose, baits could be distributed at areas like dump sites where these animals gather regularly.

3 DISTRIBUTION OF BAITS AT A CENTRAL LOCATION.

Baits can also be distributed to dogs at a central vaccination location. The baits can be offered directly to the dogs, or they can be handed over to the dog owners who will take the baits back home and give it to their dog(s). Oral vaccination of dogs at a central location is aimed at owned dogs that can be handled by their owners. Therefore, it seems more appropriate to vaccinate these dogs by the traditional parenteral route. Mass parenteral vaccination campaigns at a central location have shown to be very effective. In Turkey, this approach was especially effective in rural villages. Here, there are no or few true ownerless dogs and most dogs can be restrained without problems by their owners. A well organized campaign can result in very high vaccination coverage. However, in urban areas the situation is likely to be completely different. Many dogs can not be handled by their owners, so these dogs will not show up at the vaccination centre. Simultaneously with the trial to determine the vaccination coverage of free-roaming dogs by distributing baits at selected sites in Sarigazi, Istanbul, a vaccination campaign at a central located veterinary clinic was organized. The dogs were vaccinated free of charge during a three-day period. To promote this campaign different methods were used, e.g. banners, posters, radio announcements, driving around with a megaphone. A survey conducted directly afterwards revealed that 206 owned dogs were present in this area. Only 45 dogs (21.8%) showed up for vaccination at the clinic during the campaign. 18% of the owned dog population had been vaccinated against rabies during the previous 12 months. So, after this campaign only 39.8% of the owned dogs were vaccinated against rabies. This figure is most likely not sufficient to control dog rabies. Coleman and Dye (1996) mentioned a vaccination coverage of 70% to prevent a dog rabies outbreak. The distribution of baits to dog owners at a central location must be discouraged, although it has been suggested that this distribution system could achieve high vaccination coverage (Matter et al., 1995). A study in Tunisia showed that by using this method 1.7% of the human population had unintended contact with the vaccine virus (Ben Youssuf et al., 1998). In view of the previously mentioned risks associated with the use of live virus vaccines, this is unacceptable.
4 DISTRIBUTION OF BAITS DURING A HOUSE-TO-HOUSE CAMPAIGN.

The last suggested method is by going house-to-house and vaccinate all dogs encountered.

The selected area is systematically covered and every dog encountered is approached. To achieve better results, it is suggested that the vaccination team is accompanied by locals. This to ensure community acceptance. People are often reluctant to cooperate and distrust vaccination teams as a result of, for example, dog removal campaigns. Local children are often more than willing to help. They often know all dogs, if they are owned or not, where the owners live and where the ownerless dogs can be found. It was even observed that children were able to handle many ownerless dogs without difficulties. These animals could be handed over to the vaccinators, and these animals could subsequently be vaccinated by the parenteral route. In case of a dog with an owner who could be located within a reasonable period of time and could restrain the animal, the dog was vaccinated by the parenteral route and the owner became a vaccination certificate. If the dog did not have an owner, or the owner was afraid to handle the animal, a bait was offered. The bait was thrown to the animal by one of the vaccinators and later on the empty discarded capsule was picked up by a member of the vaccination team. An enormous advantage of this method is that the risk of unintentional human exposure to the vaccine virus is almost eliminated.

This above described system was also tested in Sarigazi (after the campaign at the central located clinic) and Ferhatpasa, Istanbul - Turkey. The house-to-house campaign was combined with a survey to estimate the number of owned dogs in these areas. The results of these campaigns are summarized in Table 43.

Table 43: vaccination coverage of the owned dog population in Sarigazi and Ferhatpasa, Istanbul – Turkey.

<table>
<thead>
<tr>
<th>Vaccination coverage (%)*</th>
<th>Sarigazi</th>
<th>Ferhatpasa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to campaign</td>
<td>18.0</td>
<td>15.5</td>
</tr>
<tr>
<td>Campaign at clinic</td>
<td>21.8</td>
<td>-</td>
</tr>
<tr>
<td>House-to-house campaign</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral</td>
<td>22.8</td>
<td>40.5</td>
</tr>
<tr>
<td>Oral</td>
<td>21.2</td>
<td>18.1</td>
</tr>
<tr>
<td>Total</td>
<td>83.8</td>
<td>74.1</td>
</tr>
</tbody>
</table>

* - percentage of dogs vaccinated by the oral or parenteral route

During these house-to-house campaigns, no blood samples were collected to examine seroconversion. So, the vaccination coverage achieved by oral vaccination is based on the number of dogs that accepted bait, and subsequently punctured the vaccine container. Dogs that swallowed or discarded the vaccine container without being punctured were not included. In Sarigazi, an additional 44% of the owned dog population could be vaccinated, of which 21.2% were inaccessible for parenteral vaccination but could be offered bait successfully. From the results obtained, it becomes clear that the dogs vaccinated at the clinic in Sarigazi could easily have been vaccinated during the house-to-house campaign. In both areas, vaccination coverage of more than 70% was achieved. So, by going house-to-house and include oral vaccination for all dogs not accessible for vaccination by the traditional parenteral route, the overall vaccination coverage was raised to levels that are assumed to be sufficient to stop the spread of rabies. The remaining dogs not vaccinated were too young (less than 3 months old), or could not be located. As a result of the very high population turn-over, it may be necessary to organize a vaccination campaign twice a year, in order to maintain high vaccination coverage. However, oral vaccination does not only have a quantitative effect by increasing the overall number of dogs vaccinated, it also has a qualitative effect by immunizing dogs that play an important role in the maintenance and spread of rabies; the free-roaming owned and ownerless dogs. During a mass vaccination campaign in Kusadasi, a coastal town in Turkey, 8.2% and 43.3% of the restricted (owned) and free-roaming (owned and ownerless) dogs, respectively, could not be vaccinated by the parenteral route and were subsequently offered bait. The advantages of oral vaccination become even more pronounced when looking at the ownership status. 12.3% of the vaccinated owned dogs could not be vaccinated by the parenteral route and were given bait. However, 74.1% of the vaccinated ownerless dogs could only be reached by offering them vaccine bait (Güzel et al., 1998). An even more extreme situation was observed in the coastal village of Mindoro, the Philippines. Here, none of the 216 owned dogs had previously been vaccinated against rabies. All, except one dog, were free-roaming and no ownerless dogs were present in Mindoro. During the vaccination campaign, only 17 dogs (8%) could be restrained by the vaccinators and 19% were considered not eligible for vaccination (less than 3
The data presented here clearly show the feasibility of oral vaccination of dogs as a promising additional tool in dog rabies control. Oral vaccination does not only increase the total number of dogs vaccinated, but can be used to immunize especially those animals that play an important role in the maintenance and transmission of this virus disease; the free-roaming dogs. However, in order to optimise vaccination campaigns, including oral vaccination, the selected system must be adapted to the local situation. For example, in certain areas a well organized mass parenteral vaccination campaign at a central location can reach enough dogs to halt or prevent a rabies outbreak. Hence, oral vaccination of dogs is not required. Also parenteral vaccination campaigns by going house-to-house have shown to be effective. Unfortunately, in areas with a high number of free-roaming dogs, owned or ownerless, that are not accessible for vaccination by the parenteral route, the obtained vaccination coverage, by using the latter method only, is often not sufficient for effective rabies control. In Turkey, this was often the case in urban and semi-urban areas (Vos and Aylan, 1999). In other countries, like the Philippines, also in rural areas only few dogs were accessible for parenteral vaccination. In these areas, oral vaccination of dogs could increase the vaccination coverage considerably. The potential advantages of oral vaccination of dogs has been studied in many different countries; Tunisia, Turkey, Sri Lanka, the Philippines, Zimbabwe and the Republic of South Africa (Perry et al., 1988; Matter et al., 1995, Güzel et al., 1998; Bishop et al., 1999; Perera et al., 2000; Estrada et al., 2001b).

5 DISCUSSION.

However, it seems that all these and other studies were not able to convince authorities to incorporate oral vaccination of dogs in their (national) rabies control programme. Two major reasons for the reluctance to use this promising new tool can be identified; financial constraints and safety concerns. In most countries with dog-mediated rabies, the financial resources for rabies control are limited and the available funds are predominantly used for human treatment. This is by all means understandable; however one should not forget that it does not solve the rabies problem. To eradicate rabies, including human rabies, the most cost-effective method is by controlling the disease in the main vector species; the domestic dog. To lower the acceptance threshold for oral vaccination, the price of vaccine bait should be as low as possible and not surpass that of a single dose for parenteral vaccination. Presently, the price of manufactured vaccine baits is much higher. To circumvent this problem, for example, baits prepared from local available cheap material can be used (Estrada et al., 2001a). Thus, only the capsule filled with vaccine virus must be imported, reducing costs considerably.

Also, the safety issue associated with the present available oral rabies vaccines seems to be an almost insurmountable barrier. It is clear that for oral vaccination of dogs more stringent safety precautions are required than for oral vaccination of wildlife. However, the safety issue should not be overrated. In Europe, more than 150 million vaccine baits have been distributed since 1978. So far, not a single serious incident of human exposure to any of the vaccine viruses used has been reported. Furthermore, the suggested bait delivery system by going house-to-house and re-collection of all discarded vaccine containers will greatly reduce any possible unintended human exposure to the vaccine virus. Many studies with potential safer vaccine candidates have been investigated, including more attenuated live rabies viruses (Visser et al., 2001; Dietschold et al., 2001), replication-defective recombinants (Wandeler et al., 2001; Vos et al., 2001), DNA-vaccines (Tordo et al., 2000), transgenic plants (Loza-Rubio et al., 2000). However, most of these candidates are not capable of inducing a protective immune response after a single oral administration. Hence, it will most likely take many years before a suitable candidate will be available, meanwhile every year thousands of people are dying of rabies after being bitten by a rabid dog. On the one hand we have the live-savings potential of oral vaccination of dogs and on the other hand we have possible adverse effects; reduced human deaths and number of PET versus human exposure to the vaccine virus. Evaluating this moral dilemma we must be aware that the perception of risks and benefits are tremendously different in developing and developed countries.

In Europe, with only a few (imported) human rabies cases annually, oral vaccination of wildlife is widely accepted and developed into the preferred method to control and eradicate rabies. The ratio to
withhold this method for countries where hundreds, if not thousands, of people die from rabies every year seems, at least, puzzling. Especially, considering that the suggested vaccine virus candidates for oral vaccination of dogs have been used extensively in Europe without any reported human incident. Of course, the safety risks associated with oral vaccination of dogs should not be ignored, but by applying the suggested baiting strategy unintended human contacts with the vaccine virus can almost be eliminated. Oral vaccination of dogs against rabies therefore deserves the (increased) active support and advocacy of (international) organizations involved in rabies control.

6 CONCLUSIONS.

Parenteral vaccination of dogs remains the cornerstone of dog rabies control. However, when a large segment of the dog population is not accessible for parenteral vaccination, oral vaccination can increase the vaccination coverage of the dog population considerably.

A house-to-house campaign is the most efficient and safest method to distribute oral rabies vaccine baits. The risk of unintentional direct human contact with the vaccine virus are minimized and almost non-existent. Therefore, oral vaccination of dogs as a supplementary tool to parenteral vaccination should be encouraged, especially in view of the present impasse in dog rabies control as observed in many countries.

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7 REFERENCES


