

**Technical Consultation on Oral Rabies Vaccines –
A complementary tool for vaccination in animals
10 November 4 PM Tokyo time**

Introduction

Since May 2020, Sri Lanka has reported cases of rabies in jackals, dogs, cattle and two human deaths in the Kalutara district in western part of Sri Lanka. Following a request made by the authorities in Sri Lanka, the OIE Regional Representation organised a technical consultation meeting on 10th November 2020 in which OIE experts from the Friedrich-Loeffler Institute (OIE reference laboratory for rabies), Germany were invited to share their expertise in dealing with such wildlife rabies cases as well as introduce the oral rabies vaccines. Participants from Sri Lanka included representatives from the Public Health Veterinary Services, Department of Animal Production and Health, Department of Wildlife Conservation, Ministry of Health, WHO Sri Lanka, University of Peradeniya and other key stakeholders. A total of 37 participants attended the consultation meeting including participants from OIE RRAP, OIE SRR, FAO Regional office for Asia and the Pacific and WHO South East Asia Regional Office.

Topics	Speaker/Moderator	Time (GMT+9)	Duration
Introduction	OIE RRAP Tokyo	4 pm	5 min
Situational analysis of rabies in Sri Lanka with focus on current episode of cases at the human-animal-wildlife interface	Dr Dilshan Wijeratne and Dr Tharaka Prasad	4:05 pm	15 min
Oral Rabies Vaccines – Background in terms of historical development, technical specifications, current production situation, research updates	Dr Conrad Freuling, Friedrich-Loeffler Institut	4:40 pm	10 min
The concept of oral rabies vaccination and basic principles	Drs Conrad Freuling, Thomas Müller, Friedrich-Loeffler Institut	5:10 pm	10 min
Experiences in the use of ORVs as a tool for control of rabies in wildlife in Europe	Dr Thomas Müller, Friedrich-Loeffler Institut	5:40	10 min
Discussions and Q & A		6:00 pm	30 min
Way forward		6:20 pm	10 min
Total		6:30 pm	120 min

Situational analysis of rabies in Sri Lanka with focus on current episode of cases at the human-animal-wildlife interface

- Since May 2020, Sri Lanka has reported cases of rabies in jackals, dogs, cattle and two human deaths in the Kalutara district in western province of Sri Lanka.
- Most of the animal rabies cases and jackal bites were reported from Millaniya, Madurawala, Horana, and Ingiriya MOH areas of the Kalutara district.
- Jackals are involved in the current outbreak with 18 out of 19 total jackals testing positive for rabies.

- Jackals are the only wild canine species in Sri Lanka and their current population data is unknown. They are under wild animal species and protected by FFPO in Sri Lanka. Home gardens with monocrops are good environment for jackals. They are not visible until late evening and early morning.
- Dog vaccination coverage in the affected areas from 2009 to 2018: 56,335 | 42,327 | 42,391 | 36,582 | 41,453 | 71,473 | 79,170 | 62,949 | 61,584.
- In Sri Lanka, 30% of the owned dogs roam freely during daytime. The national campaign is to focus on dog vaccination.
- So far, no viral sequencing is done from the samples. WHO Sri Lanka is coordinating sending samples to Pasteur Institute in France.

Activities Carried out by authorities in Sri Lanka to control the situation

Multi-sectoral rapid response team was established soon after the verification of this unusual wild-animal rabies situation to take timely actions to control the epidemic. Mass Dog (domestic and free-roaming) vaccination program to enhance the herd immunity by giving special focus to the high risk areas (below table).

MOH area	PHI Areas affected	Human Population	Estimated dog population	Number dogs vaccinated (01/05/20 - 31/10/20)	Percentage
Horana*	7	117720	14715	6814	46%
Ingiriya*	3	57704	7213	4212	58%
Madurawala	3	37384	4673	4315	92%
Millaniya	3	37008	4626	6073	85%
Total	16	249816	31227	21414	
<p>*MDV program in above areas were temporarily stopped due to COVID-19 situation In addition over 3900 cats were vaccinated in above areas Source: RDHS Kalutara & PHVS Database</p>					

Conducted special Ring Vaccination programs to vaccinate dogs in 2km radius areas for animal rabies positivity cases.

Contact tracing: Field level mechanism was developed to identify individuals with suspicious animal exposures and referred them to hospitals for Anti-Rabies Post-Exposure Treatment.

Case-based management mechanism in hospitals OPDs for patients presented with suspicious animal exposures:

- All patients presented to hospitals with suspicious animal exposures received due prioritised attention and were assessed by Medical Doctor according to the National Anti-Rabies PET guidelines and where necessary instructions were obtained from the Consultant Vaccinologist at MRI.

Conducting public awareness through a wide range of awareness programs. Special Dog sterilization programs carried out in identified high risk areas.

Strengthening surveillance through enhancing sending samples to laboratories (*PHVS has provided training on sample collection and transportation and have established a mechanism*

to send samples of domestic animals to laboratories, Hotline was opened by Wildlife sector for public to report on wild animal incursions)

Public awareness was done to minimise sending livestock to barren lands for grazing and ways of observing/ isolating livestock and other domestic animals with suspicious exposure.

Background on Oral Rabies Vaccines (ORVs)

- Several variants of attenuated oral rabies vaccines are now available (up to 3rd generation). They have undergone passaging, plaque purification/ clonal selection, Mab selection, and genetically modified (reverse genetic).
- Modified live rabies virus vaccines are the only possible way to immunize wildlife (including Jackals). Jackals are known to be responsive to ORV.

Concept of ORVs

- Key pillars for success of using ORVs include selection of vaccine strain, vaccine baits, vaccination strategy, bait delivery and distribution system.
- Basic principles include: biology of target species (distribution, density, home range, mating season, interaction with other reservoir species), suitable bait attractant, bait density to be applied, mode of bait distribution, timing of vaccination campaigns/temperature stability of vaccine, bait competitors, size of vaccinated area
- aerial bait distribution → with georeferencing by the dropping device, but quite expensive because uses helicopter

European experience in the use of ORVs to control rabies in wildlife

- In Europe, fox-mediated rabies might have been a result from sustained rabies spill-over from domestic dogs. This was assumed to have occurred and has spread from 1940 to 1990s. Culling, trapping, poisoning, and destruction of fox cubs were conducted to reduce rabies incidence but were proven to be very ineffective. The fox population. Oral vaccination of wildlife to induce immune barrier within the species and concept was invented in the US and applied to Europe eventually.
- The oral rabies vaccination has undergone significant technical milestones and political milestones.
- ORV strategy for foxes are also effective for racoon dogs.
- ORV programs from 1978 has been implemented in 30 countries of Europe, and out of them, 15 are declared as rabies free.
- It is important to understand that wildlife rabies cannot be eradicated, and elimination is only feasible for certain reservoir species only such as foxes and even jackals. According experience, it is best to concentrate on one species in one certain area at a time.
- Challenges: vaccinations will be a long, stony road and will take decades, need for sustained political and financial support, development of alternative, more potent or species-specific oral rabies vaccines, and more applied research is needed.

Key outputs

- An understanding of the current situation of rabies cases in animals including jackals in the affected area.
- An understanding of the control measures implemented by the authorities in Sri Lanka.

- An understanding of the farming practices and environmental factors in the affected area including information about ecology of jackals and other wildlife in the area.
- A good understanding about the historical perspectives, the concepts and principles, and European experiences in the use of oral rabies vaccines for elimination of wildlife rabies in Europe.
- A platform for discussion and networking between the participants for further follow up.

Next steps

- Need to enhance dog rabies surveillance in the outbreak area as well as other parts of Sri Lanka. The use of rapid diagnostic kits (lateral flow assays) for rabies surveillance on the ground could be considered to mount rapid response. In the long run, it might be advisable to set up diagnostic capacity using direct fluorescent antibody tests in the provincial laboratories to enhance animal rabies surveillance in the field.
- Need to collect and send brain samples for laboratory confirmation at MRI Colombo and refer for molecular phylogenetic studies to determine the virus strain.
- Step-up strategic dog vaccination at the wildlife-human habitat corridors to build up immunity (sort of immune barrier).
- Enhance multisectoral coordination amongst the key stakeholders in Sri Lanka to have coordinated and effective interventions.

Q & A Session

Situational analysis of rabies in Sri Lanka with focus on current episode of cases at the human-animal-wildlife interface

1. Current situation of the rabies situation in Sri Lanka

1.1 What percentage is dog-mediated and wild-life mediated rabies in Sri Lanka, and what actions were recommended by the participants?

- *Dog-mediated rabies contributes to over 95% of the rabies situation in Sri Lanka, and the rest of the rabies are coming from felines and wildlife. It was suggested to achieve herd immunity among stray dogs in the area first, and to put human and physical resources to vaccinate the dog population in these particular area within short period of time. Once the domestic dog population are immune, they will act as natural biological barriers for wildlife rabies.*

2. Domestic-wildlife-domestic animals spill-over phenomenon

2.1. Why the sudden increase in wildlife rabies?

- *It is a common phenomenon to see an upsurge in wildlife rabies cases once dog mediated rabies cases are controlled as this is often camouflaged by the high incidences in domestic animals. Turkey for example has seen rabies cases spill-over from domestic dogs to foxes. After they have successfully controlled dog rabies, the situation reversed, and rabies cases are now seen spilling-back from foxes to domestic dogs. Israel has shown the same trend from fox-mediated rabies cases spilling-over to jackals, and today, jackals are the more*

prominent rabies carriers of rabies. Similarly, in Sri Lanka, there could possibly be a sustained spill-over from dogs to Jackals and now spill-back into dogs.

- *After successful mass dog vaccination in dogs, it is observed that the rabies virus is preserved by nature into wildlife. The only way to control this is through oral rabies vaccination (ORV) as experienced by Europe.*

2.2. Is it possible to control wild animal rabies without controlling dog rabies?

- *In principle it is possible to control wild animal rabies without controlling the dog rabies. In areas with an established sylvatic cycle (i.e. jackal mediated rabies) usually cases in livestock show up. So, livestock vaccination could be envisaged to prevent losses. However, this will not control the disease in jackals. The same inactivated vaccines used in dogs can be used in livestock.*
- *Oral rabies vaccination is usually used as complementary measure. Current oral rabies vaccine strains are just registered for wildlife. But some trials from Asia looks promising (Thailand and India). They need to now try for registration for use in dogs. Also, acceptance of the method is also important by countries.*

Oral Rabies Vaccines

1. Concept of ORV

1.1. Does it matter which strain or baits are used for ORV in terms of efficacy?

- *The bait/vaccines used in Europe have been extensively tested and have passed all safety and efficacy requirements. In Europe, 1st generation vaccines have even been used for wildlife, but with the high population densities in Sri Lanka, 3rd generation vaccines should be used.*
- *It is also important to note that baits are not species-specific. There is a need to account for population density of both target and competitor species when considering bait density.*

2. The European Experience

2.1. How did Europe initially control fox-mediated rabies cases and how did it progress?

- *Fox-mediated rabies might have been a result from sustained rabies spill-over from domestic dogs. This was assumed to have occurred and spread from 1940 to 1990s. Culling, trapping, poisoning, and destruction of fox cubs were conducted to reduce rabies incidence but were proven to be very ineffective to the growing fox population.*
- *They have also used tetracyclines as biomarkers in the beginning and checked the serology by blood sampling of hunted animals.*
- *The oral vaccination of wildlife was conceptualized to induce an immune barrier within the domestic and wild species. It was a concept initially invented in the US and then applied to Europe eventually. It has undergone significant technical and political milestones to achieve this current status.*
- *Through the implementation of the vaccination, they have notice that the ORV strategy for foxes are also effective for racoon dogs.*
- *ORV programs from 1978 has been implemented in 30 countries of Europe, and out of them, 15 are declared as rabies free.*

2.2. Can wildlife rabies be eradicated?

- *It is important to understand that wildlife rabies cannot be eradicated, and elimination is only feasible for certain reservoir species only such as foxes and even jackals. According to the European experience, it is best to concentrate on one species in one certain area at a time.*

2.3. What are the challenges that a country might encounter in ORV implementation?

- *Several challenges are to be overcome by the country. Vaccinations will be a long, stony road and will take decades. There is a need for a sustained political and financial support. The development of alternative, more potent or species-specific oral rabies vaccines are recommended, and more applied research is needed.*

3. Possible Risks

3.1. What is the risk of introducing a new strain to the environment by ORV?

- *The risk is virtually Zero! There is no shedding of vaccine virus. There is, for a certain period of time, residual input virus still in the oral cavity of the animal.*

3.2. Jackals have no boundaries and mix with people and animals in agricultural land. Is there any risk via non-target species?

- *The requirements mentioned are all met by the available vaccines/baits in the market. So, there is no risk for non-target species including humans. The use of the vaccine should not pose a problem as it is ok with other animal populations. They may also develop immunity.*
- *There is no need to retract baits from the field. The only measure is awareness campaigns so that people, especially children will not touch the baits. The World Health Organization (WHO) recommend PEP in cases of contact with vaccines, just as another precautionary measure. There is a need to raise awareness in the community that baits should not be touched to avoid losing attractiveness and also its availability to jackals.*

3.3. Some of the ORV are vaccinia-based recombinant vector virus, some using "replicative" poxvirus vector. Is it the same thing you were using in Europe and are there additional safety measures we need to apply for humans in contact with these baits (because of poxvirus)?

- *This type of vaccine is not really used in Europe. According to reports, only 2 adverse events in humans where people got poxvirus, and there is negligible risk.*

3.4. Is there any risk for the vaccine to mutate?

- *Every vaccine has gone through passaging and checked for reversion to virulence. The vaccines baits will not pose a problem to humans and other animals taking up the baits might even be vaccinated. The public must be aware they should not touch the baits.*

4. Cost and Operations

4.1. Must we also be concerned with the cost of the entire ORV operation?

- *Yes, costs are an issue. But also, timing. The earlier one starts, the smaller the affected area gets and the cheaper it becomes. It is probably good to plan with a Cost/Benefit aspect rather than only the cost itself as Sri Lanka is spending a huge amount of money already on PEP too (on top of dog sterilization and dog vaccination). In the experience of Europe, they were able to eliminate fox-mediated rabies in one large area within 5 to 6 years of implementation.*

4.2. How do we know how much area to cover for ORV?

- *It is important to consider the size of the population of jackals. Draw a circle of 50 km around any rabies case to define the minimum vaccination area. If the area for vaccination is too small, the rabies infection might spread further. So it is better to start with larger area to be successful.*

4.3. The affected area in Sri Lanka has many other wildlife species other than Jackals. What can be done to ensure that the oral vaccines reach jackals?

- *Usually, as a first step, it is important to monitor bait disappearances by using camera*

traps at certain Points. This will provide information about the percent baits taken by the target species as well as bait competitors.

4.4. How long can we expect to apply the ORV program until it is successful?

- *Program period might take many years according to the European experience. Political commitment and continuous funding are needed to sustain the program.*

List of References

- Lyssavirus in Indian Flying Foxes - https://wwwnc.cdc.gov/eid/article/22/8/15-1986_article
- (<https://www.oie.int/en/standard-setting/terrestrial-manual/access-online/>)