Q & A Session

SAARC rabies webinar summary of participant questions and answers by the speakers/experts, Day 1, 2020/05/18

Note: If further clarifications are required, please directly contact the speakers/experts or refer the relevant publications.

Theme: Organizing a mass dog vaccination (MDV) campaign including use of oral rabies vaccines (ORV)

Canine mediated human rabies elimination from an Indian state: the example of Goa – Dr Andy Gibson (andy@missionrabies.com)

1. **Dog population management**
    a. How can you overcome challenges in dog population management using capture-neuter-vaccinate-release (CNVR)?

The evidence indicates that rabies is most efficiently eliminated through mass dog vaccination (MDV) alone and so this has been the foundation of our campaign in Goa. The data from our project has demonstrated that rabies was eliminated from the majority of regions in Goa without a CNVR component. Only in areas where rabies was persisting was CNVR implemented, where it may have contributed to slowing population turnover and therefore maintaining vaccination coverage.

There is still much disagreement on how MDV alone for rabies control and CNVR for population management should be implemented across municipalities, districts or states in India. Our experience in India is that dog nuisance, resulting from a perceived over-population, is often the primary public and political concern, with rabies coming lower on the priority list. Therefore, there is a demand for dog population management to be implemented at scale. Not only is the evidence for impact of CNVR lacking, but the technical, financial and logistical limitations mean that it would not be possible at the scale and speed required to eliminate rabies. What is clear is that low-coverage CNVR is unlikely to achieve the objective of either improved population management or rabies elimination. Therefore, it is necessary to differentiate priority regions where CNVR is applied intensively to improve dog population management and all the other regions where MDV is conducted to eliminate rabies on a wider scale.

We have found that although rabies may not be the top concern of many communities when it comes to dogs, unlike CNVR, MDV can be implemented quickly and cheaply on a large scale and is a fantastic first step in creating positive engagement and trust between the Government and the dog owning public, which is essential to longer term goals of dog population management (DPM).

b. Have you seen any drop in the number of stray dogs during the years which you have been working for rabies control?

The dog population in Goa appears to be stable, even in regions where CNVR is implemented. It seems that even where intensive DPM activities are conducted, the carrying capacity is generally stable and so although population turnover may reduce, the total number of dogs does not change dramatically.

c. How do you obtain data on dog population by different categories?

The Worldwide Veterinary Service (WVS) App enables the recording of information about every dog vaccinated. This includes information about ownership, confinement, age and sex.

2. Identification of vaccination zones

a. What is the process for determining vaccination zones?

Initially the vaccination zones were based on the village panchayat (council) administrative boundaries, with larger villages being manually subdivided. Goa has 402 village/municipal regions. During vaccination under team direction, the zones were further refined by campaign managers in the first cycle and then re-used in subsequent campaigns. This is quite a time-consuming job during early campaigns, and so we are working to automate the process of creating vaccination working zones.

b. Is there any application that helps to connect between the laptop & mobile phones regarding the specified vaccination zones?

The App used is called the WVS App and the methods have been published here:
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0200942

It is available for any organisation to use free of charge – please contact andy@missionrabies.com for further details.

3. Identification of vaccinated dogs

a. How did you get geotag location of all vaccinated dogs for geospatial data for analysis? Is microchip-based identification of dogs feasible? What method is used for identification after parenteral vaccination of stray dogs?

Please see response to the above question regarding the use of the WVS App and contact andy@missionrabies.com for further details.

Microchipping is not used routinely for the identification of dogs for a number of reasons, but primarily cost. The overall cost to catch, vaccinate and release a dog is in the region of 250 Rupees; however, the cost of a

microchip is around 150 Rs. Therefore, to microchip every dog would almost double the cost of the campaign.

We place collars on the dogs whenever possible. All dogs are marked on the head with a non-toxic paint which lasts for approximately 5 days. A nice video of the collaring method was produced by FAO and can be found here:

https://www.youtube.com/watch?v=ueJ0gDj6dY0&t=379s

4. For the mass vaccination program, would it not be more useful to move from east, north and southern borders towards sea - the natural barrier?
   The North and South Districts of the state are vaccinated by two separate vaccination squads who rotate through each of the six administrative regions (talukas) in each District. Each taluka is vaccinated over a period of 1 – 4 months depending on the size of the dog population; we have seen a taluka-wide reduction in canine rabies incidence following consecutive vaccination cycles and so it appears that the current order of vaccination has not hampered chances of elimination. In many cases the talukas are separated to some extent by rivers which may also help to contain the population. The initial order of rotation through the talukas was driven by practical considerations during early campaigns, however we will be re-formatting this gradually for the reasons suggested. It is certainly something to consider from the outset when planning district or state campaigns elsewhere.

5. **Post-vaccination monitoring**
   a. Are sero-protection levels useful to measure the protection levels for a specific population over specific periods after immunisation?

   We have conducted sero-prevalence studies in Goa to evaluate immunity within the population. This is also useful to confirm efficacy of the vaccine under field conditions where there are high temperatures for example. For the most part, however, vaccination coverage was evaluated through dog-sight surveys conducted the day after vaccination teams had moved to the next region. Data was recorded in the WVS App and in cases where the survey showed low coverage, teams were re-deployed to the region to conduct additional vaccination. https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-015-1320-2
   The most important indicator of adequate vaccination coverage, however, is a reduction in canine rabies incidence in that area. Several studies have demonstrated rabies elimination at estimated coverages as low as 40%, whilst in other areas repeated campaigns above 70% are needed. Establishing rabies investigations that geotag the location of the rabid dog generates critical data

for evaluating the efficacy of the vaccination campaign. As mentioned in the talk, we have built an app which helps to coordinate rabies case investigations. Please contact andy@missionrbaies.com if you are interested in using this tool.

6. Can you explain how the lateral flow (LFA) testing was used to strengthen rabies surveillance in the project area?
   LFA tests were used early in project before rabies testing capacity was available in Goa. Samples had to be transported for long distance by bus for testing in Bangalore. As we were sampling around 20 cases per month, this would involve sending samples in batches and so results were often not available until weeks after the investigation. The LFA test gave us an initial result at the time of post-mortem. These tests have been shown to have low sensitivity, (https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004776); however, specificity is good, meaning that a positive result could be acted upon as a positive case, but negative cases should still be considered potentially positive. Field data found that specificity of the tests was higher in dogs tested in Goa when compared with gold-standard diagnostics, possibly due to the higher viral burden in dogs presenting later in the course of disease. We found that having the LFAs available motivated field veterinarians to go through the process of taking samples to perform the test, even when there was little hope that they would ever hear the results back from the submission to the laboratory. https://www.mdpi.com/1999-4915/11/7/649
   These tests are not approved or endorsed by the OIE and should be used for research purposes only. Importantly, training of staff must emphasise that results of an LFA test must never be used to guide decisions on human post-exposure prophylaxis (PEP).

7. Can you outline the interface between dogs and wildlife with respect to rabies? Spill over of canine rabies virus to wildlife particularly at the interface of national park-village.
   It is possible that there are wildlife reservoirs alongside the primary canine reservoir; however, it will be challenging to determine this until canine rabies has been controlled. In areas of Africa where dogs and wildlife live in close proximity (https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0001796), it has been demonstrated that dogs are the drivers of transmission and once the virus is eliminated from the dog population, it does not persist in wildlife. We have tested one jackal positive for rabies in Goa, however it is unlikely that rabies is circulating in any wildlife population. The vast majority of people are infected

from a rabid dog and so to remove the risk of rabies from the human population it makes sense to eliminate it from dogs as a first priority and explore re-emergence from potential wildlife reservoirs in the process.

8. **Intersectoral collaboration**
    a. Could you please summarise how you collaborated with the human health sector in Goa?

The programme works closely with the State Epidemiologist in the Department of Health to coordinate awareness around rabies cases in dogs and people. The Department of Health took part in the Stepwise Approach towards Rabies Elimination (SARE) Workshop in 2018 and a collaborative human rabies case management and diagnosis was held in Goa Medical College in December 2017 as a collaboration between Government Goa, Mission Rabies and the National Institute of Mental Health and Neurosciences (NIMHANS). The Goa rabies surveillance officers also routinely coordinate with local Primary Health Centres (PHCs) to conduct Bite Case investigations for patients reporting with dog bites. .

    b. Do you work in collaboration with local veterinarians or local government to maximise vaccination coverage?

The local private and government veterinary sectors is engaged in the reporting of suspect rabies cases in their area. Local government vets are encouraged to take part in the vaccination campaign; however, with the current cyclical approach this is challenging as it may take 1-4 months to vaccinate a particular region of the state, and government vets have limited availability to take part in rabies activities. In the longer term we hope to find a way of conducting 'Pulse' campaigns across the whole state where the government and private sectors can divert their activities entirely to dog vaccination for an intensive 2 week period; however, this is not possible using current methods. Please see this paper for a more through discussion on these challenges: https://www.mdpi.com/2414-6366/5/1/47

9. It is great to see that there have been no rabies-associated human deaths in recent years in Goa. Is this attributable to a reduced incidence of canine rabies or increased coverage of post-exposure vaccination of people after dog bites? Can you please enlighten us on the post-bite vaccination situation there?

The medical sector has worked hard to increase availability and access to PEP during the course of the project. Additionally, the vaccination campaign and education initiatives will have increased awareness for the need of PEP following a dog bite. The decline in human deaths preceded the decline in canine rabies incidence, which is likely because of this; however, as was highlighted in Dr

Abela-Ridder's presentation, it would not be possible to maintain zero human rabies deaths indefinitely if the virus is present in the dog population.

Experiences of using oral rabies vaccines (ORV) in Thailand – Dr Karoon Chanachai (kchanachai@hotmail.com) & Ad Vos (ad.vos@orange.fr)

1. **Oral rabies vaccine (ORV) storage:**
    a. What is the shelf life of ORV?
    There is no general statement possible as it depends on the type of vaccine and the formulation used. In our case for the SPBN GASGAS vaccine strain, the shelf-life is 24 months (when stored correctly).
    b. Could you comment on maintaining cold chain for baits?
    Again this is of course product-specific, and we can only answer it for the vaccine we are presently evaluating. As it is a liquid replication-competent rabies virus vaccine, it is temperature-sensitive; in other words, when it is exposed to elevated temperatures, it rapidly loses its infectious potential which is required for inducing an immune response. Hence, long-term storage needs to be conducted by sub-zero temperatures (below -20°C). Once it is thawed, it will remain 'viable' for at least 7 days at refrigerator temperatures and for 5 days at 25°C, but with much higher temperatures it will denature rapidly.
    c. Regarding the thermostability issue for live vaccines, how can this be addressed in oral vaccines?
    The concept of ORV (dogs) as presently suggested is based on the hand-out and retrieve model. This means that vaccine baits are offered directly to dogs encountered and not placed in the environment as is done with wildlife where the animals must locate the distributed baits themselves. Hence, the baits are not exposed to outside temperatures for a long time. Long-term storage is under freezer conditions; during the actual campaign the baits are placed in a cool box and only exposed to the prevailing local temperatures during the short period that they are offered to dogs (within 5 minutes). If at a local level baits cannot be stored frozen prior to the campaign, they can be kept under refrigerator conditions for at least a week.
    Actually, the low thermostability of the vaccine virus has a big advantage. Field studies showed that the fate of vaccine bait (including blister) cannot always be ascertained. A few dogs take the bait and run away, hence it is not known if the dog swallowed the sachet or if the perforated sachet (usually a few drops of vaccine remain inside) is discarded. In the latter case, the blister will not be recollected and poses a potential risk for human contact. However, due to the thermo-

instability the vaccine inside these discarded sachets will rapidly be inactivated and lose its infective potential.

2. Marking vaccinated dogs:

a. Do you have any methods to verify repeat vaccinations in a population?
We decided to do oral vaccination during the parenteral vaccination campaign to avoid repeating with parenteral vaccination.
In an area where all stray dogs cannot be parenterally vaccinated, repeating with parenteral vaccination is not the issue. As shown in the presentation, multiple offerings to an individual dog are rare but cannot be completely circumvented as sometimes multiple dogs stay together, so one dog can consume multiple baits if it snatches the bait offered to another dog. In this case, an oral vaccination team member can assist to distract dominant dog to minimize this problem. The oral vaccination team should also complete stray dog vaccination at one time to avoid repeating vaccination as we cannot mark orally vaccinated stray dogs. Moreover, safety studies have shown that repeated doses and/or overdoses are not an issue.

b. What marking method is used with oral vaccines?
For wildlife we use tetracycline as a bait marker that we can detect later in the bones or teeth of the animals. This is unfortunately not feasible for dogs. The marking and identification issue remains partially unsolved for the moment. However, we should not forget that mass dog vaccination (MDV) is about herd immunity and not about the individual animal. Some concepts for a temporal optical marking are presently under investigation.

c. Is it possible to mark an ORV-vaccinated dog, e.g. using a biomarker?
See above comments in (a) and (b).

d. Regarding oral vaccination and the difficulty in marking parenterally-vaccinated dogs in a rural setting, what measures are in place to avoid re-vaccination? Is ORV performed in the area at the same time as parenteral vaccination?
In our pilot study, we considered this issue and try to ensure that oral vaccine is given to stray dogs who cannot be restrained for parenteral vaccination. We decided to do oral vaccination at the same period as the MDV campaign. The oral vaccination was not announced in advance to the community to create options for irresponsible owners. The MDV team was searching for groups of stray dogs while they were conducting the campaign. Then, the oral vaccination team did oral vaccination in

these identified groups of stray dogs. Cooperation with local people is very important.

Other possible strategies can also be done such as marking of parenterally vaccinated dogs and in the following days the area is systematically covered and all dogs not marked can be offered a bait (since these animals have not been vaccinated).

Several options can be done to avoid such a problem and selection can be based on cooperation of dog owners and other local contexts.

If people use the door-to-door approach, every dog encountered and those not accessible for parenteral vaccination can be offered a bait as well.

3. Comparison of rabies vaccines:

a. Which is more effective – ARV (parenteral) or ORV?

It is not about being more effective. The cornerstone of dog rabies control is mass dog vaccination campaigns using the traditional parenteral route. ORV is a complementary tool in areas where a large proportion of the dog population is free-roaming and cannot easily be restrained for vaccination. Under these circumstances, MDV cannot reach a vaccination coverage high enough to interrupt the chain of infection. Integrating ORV in these MDV campaigns could increase the vaccination coverage to such a level that rabies transmission among dogs is interrupted.

b. What is the cost-benefit analysis between conventional parenteral immunization and ORV?

A cost-benefit analysis in general is not possible as it depends on the local situation. Again, ORV is not an alternative to conventional parenteral vaccination, it is an add-on. In most countries with dog-mediated rabies, the vaccination coverage with parenteral vaccination is often too low to eliminate dog rabies locally. As ORV targets especially the free-roaming dogs it has both a quantitative (more dogs vaccinated) and a qualitative effect (especially important for rabies transmission in subpopulations of free-roaming dogs). Hence, this should not be about comparing both methods, ORV targets dogs that are normally not vaccinated because they cannot be restrained. So, you can compare for example ORV with Capture-Vaccinate-Release (CVR) campaigns where people try to catch and subsequently vaccinate dogs that cannot be vaccinated without special effort.

In Goa State, India, a cost-effectiveness study was conducted comparing CRV with ORV:

https://www.sciencedirect.com/science/article/pii/S2590136219300166

c. What is the cost of each dose of oral vaccine? What is the cost difference between oral and injectable rabies vaccines?
It is clear that a vaccine bait for oral vaccination of dogs against rabies is more expensive than an injectable vaccine from a multi-dose vial. However, just like with parenteral vaccines, there are huge price differences between for example countries. Import fees show huge differences, in some countries additional testing is required increasing the costs of the vaccine bait. Some countries prefer to use baits made from local material and do not need a bait matrix. The bait matrix does not only increase production costs but also storage and transportation costs as the vaccine bait takes up a lot more space than just a vaccine sachet. Costs can also vary depending on the formulation. Due to all these fluctuating factors it is not feasible to give a price for a vaccine bait just as it is not possible to give a general global applicable price for a parenteral vaccine dose.

4. ORV period of immunity

a. How many doses of ORV are needed each year *[to result in protective immunity]*?
A single dose (bait) is needed for most oral rabies vaccine candidates. It depends among other factors on the vaccine construct, so the duration of immunity cannot be claimed in general terms. As oral rabies virus vaccines are based on live replication-competent vaccine viruses, most will induce a very strong protective immune response that can last many years. In our serological study (phase 2), more than 80% of orally-vaccinated dogs had protective immunity at 1 year after vaccination - comparable with parenteral vaccination in the same study.

b. For how long does an orally vaccinated dog maintain a protective antibody titre? Have you performed any assessment of sero-protection?
Again, the duration of immunity (protection) depends on the vaccine construct. The one assessed by us in Thailand induces a protective immune response after the consumption of a single bait. The serology study conducted at the stray dog shelter showed that more than 80% of dogs still had protective antibodies one-year post vaccination. However, as all dogs showed a detectable immune response after vaccination, it can be assumed that even after the decline of the level of antibodies below the limit of detection the animals are still protected as a shift has occurred in immune response from circulating antibodies to the presence of memory cells that rapidly will produce antibodies when renewed exposure to the rabies virus will occur.

In the feasibility study, we did not test serological response because this needs very good planning and is time consuming. You need to test for antibody before and after vaccination. Capture and recapture of one stray dog is not easy. However, a serological study was done with stray dogs in a shelter as mentioned above.

5. Is there an international manufacturer for oral vaccine?
   There are several commercial manufacturers for oral rabies vaccines. However, all licensed (registered) oral rabies vaccines are used for certain wildlife species. At the moment, no product is specifically licensed for dogs. Oral vaccination is used in North America and Europe for the control of wildlife rabies. In these areas, dog rabies has been eliminated many years ago and therefore there is no market for ORV of dogs. You can find the currently available oral rabies vaccine products in the third report of WHO Expert Consultation on Rabies published in 2018 (https://apps.who.int/iris/handle/10665/272364).

6. **Safety concerns about ORV:**
   a. Have any adverse reactions been noticed? *[with ORV]*
      No adverse reaction was found in serological and feasibility studies
      However, this question cannot be answered in general for oral vaccination. It all depends on the vaccine type, the distribution method, the target species (dog or wildlife), etc. during the serology study in shelter dogs and the field study in Thailand no adverse events were reported in dogs and humans. A risk assessment (incl. adverse events) has been made for the vaccine strain we used in Thailand for ORV of dogs, see: https://pubmed.ncbi.nlm.nih.gov/31043646/
   b. What about safety concerns to the public while using live oral vaccines?
      See same reference as (a) above.

7. Is there an inactivated Oral Rabies Vaccine?
   No, presently all oral rabies vaccines are based on live replication-competent viruses. To induce a strong protective and long-lasting immune response the highly attenuated vaccines need to replicate at the site of entry (oral cavity). This replication is site-restricted and limited for a few days before the vaccine virus is cleared by the immune system

8. Can you please elaborate on the content of bait vaccine, its acceptability and efficacy?
   Many different types of vaccines, baits and sachets have been used for the different target species. So, there is no general recipe. Also, bait acceptance differs between species and the vaccine uptake (efficacy) depends among other factors on size, shape and texture of bait and sachet. The bait studies conducted in Thailand are described in the following publication: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6024691/

9. **ORV in wildlife:**
   a. How is oral rabies vaccine used in wild animals?
      In North America, Europe and several other countries like South Korea, Turkey and Israel, baits are distributed, predominantly by airplane, to control rabies in different wildlife reservoir species, such as red fox, raccoon, coyote, golden jackal and raccoon dog. A fixed number of baits per square km are distributed, mostly by homogeneously dropping the baits from the airplane along pre-determined flight lines.
   b. Is it feasible to use ORV in wildlife, specifically in foxes or wolves?
      ORV was actually 'invented' for red foxes and due to the great successes obtained it was also used for other reservoir species and recommended for dogs inaccessible for parenteral vaccination.
   c. What is the effectiveness for controlling cases in wildlife?
      If you have a safe and efficacious vaccine, a well-accepted bait with vaccine release in the oral cavity and a distribution system that optimizes bait uptake by the target population meanwhile reducing bait depletion by non-target species you have an excellent tool that can eliminate rabies from the reservoir species targeted. The European Union hopes to eliminate fox-mediated rabies from its Member States this year. Last year only a few cases (<10) of fox-mediated rabies were reported within the EU; all these cases were in the border regions with non-EU Member States. So, from the start of the first ORV campaigns when tens of thousands of cases were reported annually, now the disease has almost been eliminated from the fox population in Europe. The enormous success obtained with ORV lad to other 'fields of use'. For example, Japan is presently distributing vaccination baits to control the CSF outbreak in wild boar. So, oral vaccination of foxes against rabies has been a major breakthrough in wildlife disease management.
   d. Has it been trialled in Indian wildlife?
      No.
   e. Is there a method for ORV vaccine preparation e.g. ingredients?
      As mentioned before, the oral rabies vaccines are based on different

types so a general method cannot be given. However, the vaccine is just one part. You need also a sachet and a bait. Finally, you need to know how, when and where to offer the baits to the dogs. All three components (vaccine, bait and distribution system) are equally important.

How to do planning/costing for annual mass dog vaccination using an Excel-based tool? – Dr Ryan Wallace (euk5@cdc.gov)

10. 70% vaccination coverage:

a. Which categories of dogs are taken into the 70% protection levels (owned, strays, community-owned etc.)?
   i. The goal of dog vaccination is to observe an appreciable decline in cases in the months after vaccination, regardless of the coverage achieved. This means that programs should have some surveillance capacity by which to evaluate their vaccination programs.
   ii. Observational experience from rabies programs has shown that there is a wide degree of variation in "successful" vaccination coverages, which is largely dependent on the ecological factors of the dog population. Some areas have eliminated rabies with coverages around 50%. Other programs have needed much more intensive vaccination coverages, sometimes over 80%.
   iii. Models on rabies transmission largely agree that 70% vaccination coverage will eliminate rabies in the majority of settings. Observational experience from countries that have eliminated rabies supports these modelling conclusions.
   iv. 70% coverage refers only to the dogs that are part of the enzootic transmission cycle. If a dog is completely confined to an owner's house, and walked on a leash, and NEVER allowed to be out unsupervised, this dog likely does not play a meaningful role in rabies enzootic transmission. Dogs that are allowed to roam freely should be the primary target for vaccination. In many communities, these free roaming dogs are owned and well-cared for by families. Truly feral dogs, those that live with no human resources or interactions, are rare and unlikely to contribute to transmission.

b. When you talk of 70% coverage for vaccination, what is the geographical unit generally considered? Should that 70% coverage be at the community level or the national level, or is there any suitable geographic scale we need to consider?

i. Ideally, the vaccination program will cover as large of a geographic area as possible, regardless of political borders. This could even include vaccination programs that span international borders.
ii. In Latin America, the vaccination campaigns occur across the entire country over just several days. When there are resources to ensure adequate coverage (>70%) across these large geographic areas, this is the preferred vaccination method.
iii. The geographical unit for dog vaccination should consider the contiguous dog population, meaning the population of dogs (and their owners) that have regular communication with each other. Many times, this involves all communities that have no geographical separation, such as mountains or large bodies of water.
iv. Even mountains and rivers have not been able to STOP the spread of rabies, but they can slow the spread, allowing for operation of vaccination campaigns that are staggered or delayed by several months.
v. A process for identifying geographic units of vaccination was presented at the Rabies in the Americas conference in 2018, and can be shared if you contact the presenter, Ben Monroe (ihd2@cdc.gov) or Ryan Wallace (euk5@cdc.gov).

Other Questions (gongalg@who.int)

11. Rabies in other species:

a. How many vampire bats were positive in the study?

There are no vampire bats in Asian countries and there are only frugivorous and insectivorous bats in Asia. Bat lyssaviruses are different from classical rabies virus found in dog or carnivores. Only a few investigators reported presumable rabies virus (RABV) isolates of bat origin in India and Thailand.

Lyssavirus surveillance in bats was performed in Bangladesh during 2003 and 2004. No virus isolates were obtained. Three serum samples (all from *Pteropus giganteus*, n = 127) with a total of 288 serum samples, obtained from bats in 9 different taxa, neutralized lyssaviruses Aravan and Khujand. The infection occurs in bats in Bangladesh, but virus prevalence appears low.

(Citation: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291427/)

12. What will the impact be of COVID-19 on rabies cases in human and animal populations? Do you expect there to be a spike in cases?

    a. There is fear, anxiety and uncertainty as COVID-19 is a novel disease caused by the novel coronavirus SARS-CoV-2. There is an infodemic situation as all kinds of information (including fake news and disinformation on social media) have been circulated and rumours have travelled faster than COVID-19. As a result, century old quarantine, isolation, bans on air travel and lockdown measures have been introduced to prevent and control spread of COVID-19. There is a whole-of-government and whole-of-society approach in all countries as there are no risk-free countries due to the extensive air travel network around the world. All social, economic and cultural activities are on hold during the lockdown period which may continue further depending on the course of the pandemic. Even in the health sector, reprioritizing, reprogramming and repurposing have been done to deal with the COVID-19 crisis. There is a collateral damage for regular health programmes such as immunization, maternal and child health care, noncommunicable diseases, TB, malaria and HIV/AIDS and we will have to face non-Covid-19 issues in the coming days. Yes, we are expecting more incidences of human and animal rabies in the next 6-12 months due to closing of anti-rabies clinics, and disruption of vaccine supply, transport systems and dog vaccination campaigns. So, it is important for all of us to think and act on risk mitigation measures, i.e. how to address rabies in this unusual situation created by COVID-19 pandemic. The post-COVID era will be completely different and we have to change ourselves to adjust to a new order or environment, i.e. physical distancing, respiratory and hand hygiene, online services like webinars, cashless payment, contactless home delivery of food etc.

General questions (euk5@cdc.gov)

13. Post-bite action in people:

    a. If rabies virus enters inside the nerve cell after a rabid dog bite, is post-bite vaccination of the person helpful? Is PEP effective any time after the bite? If the virus enters the nerve cell, how does the vaccine work?

i. PEP is effective if it is completed at any time prior to symptom onset, which typically occurs days to weeks after the bite depending on location and severity of the exposure.

ii. WHO recommends completing a risk assessment for each suspected rabies exposure to determine if PEP should be provided immediately, or if it can be delayed in certain low-risk situations where the animal is available for observation and assessment. Note that severe bites, bites to the head, and bites to young children should always result in immediate PEP.

iii. WHO recommends PEP be given for any bite from a rabid dog, regardless of how long ago the bite occurred, as long as the bite victim is not showing signs of rabies.

iv. WHO has approved a one-week vaccination schedule in the case of intradermal vaccination (double dose on 0, 3 and 7 days), or a single dose on four visits in the case of intramuscular vaccination (0, 3, 7, and on 14 or 28 days).

v. The vaccine induces antibodies that can bind the virus. While nerve cells are immune-privileged, meaning the antibodies cannot enter, antibody can bind the rabies virus when the virus crosses post-synaptic junctions in the peripheral nerves.

vi. The pathogenesis of rabies and actions of antibody are not well known, but what is known is that rabies vaccine is effective if given any time prior to symptom onset, even if the virus has entered the peripheral nervous system.

vii. Once the virus enters the central nervous system (brain), PEP is not effective.

b. How do you determine the maximum period in which PEP can be effective? In the case of a delay of more than 48 hrs what would be the regimen?

i. In the case of exposure to an animal confirmed to be rabid, rabies vaccine should be provided regardless of the time since exposure, even if the exposure is reported years afterwards.

ii. The regimen is the same, regardless of the time that has passed since exposure.

c. What should we do immediately after a rabid dog bites us, if we do not have vaccine available near us?

i. The wound should be immediately washed with soap and running water for at least 10 minutes. Washing the wound thoroughly can significantly reduce the risk of developing rabies.

ii. The animal should be reported to an animal health official who can assess it for clinical signs consistent with rabies. If the dog is healthy, it can be placed under observation for 10 days. If the dog develops signs consistent with rabies or cannot be assessed, the need for PEP vaccine is very high and the bite victim should work with local leaders to get to a clinic with vaccine. If the dog shows any signs consistent with rabies, every effort should be made to get vaccine as soon as possible.

iii. Drone delivery of medications has become more popular. Rabies control programs should consider the applicability of drone delivery of rabies vaccine for remote, rabies-endemic villages.

iv. Pre-exposure vaccination of high-risk communities might be indicated in very rare situations. Consult with WHO or other rabies experts to determine when a population fits this criteria.

d. Does washing with soap prevents virus entry inside nerve ending?

i. Yes, soap is a surfactant that can disrupt the RNA virus' membrane and kill the virus prior to entry into the cells.

ii. Running water can flush out virus that has not yet bound to nerve cells.

14. Dog bite cases:

a. Is it meaningful to associate the number of dog bite cases with the dog population?

i. Dog bites are usually characterized as a rate of dog bites per human population; often this is presented as the number of dog bites per 100 people in the population. This value is important for monitoring declines in bite rates over time and for calculating expected human rabies cases in settings where surveillance is incapable of accurately detecting human deaths.

ii. Dog bite rates to people can vary based on cultural and economic status, but in most communities, 1–3% of the population experiences a bite from a dog every year.

iii. When characterizing dog bite rates, it is important to consider the source of data. Data obtained from bite clinics is almost always an under-representation of the true bite rate, as not every dog bite victim seeks medical care. Community surveys are the most accurate method for assessing the true rate of dog bites and reported healthcare seeking behaviors.

b. In my city, dog killing is used to control the dog population. Is it meaningful to associate dog bite cases from different towns in the city with the number of dogs killed?

i. Comparing dog bite rates per human population, over time, is one common way to evaluate rabies interventions. It is important to ensure that programs utilize consistent methods for estimating rates of dog bites, as differing methods can result in very different results. Even if the method is not accurate, it is more important to use consistent methods to compare changes over time.

ii. Indiscriminate culling of dogs is not a recommended action to control rabies, as it can have numerous negative impacts on rabies programs and instil distrust in the community. Culling of dogs has been associated with increased rabies presence if vaccinated dogs are killed, and can increase the spread of rabies if people take dogs out of the community in an effort to save them from the culling.

iii. An article on dog population management methods can be found here: https://pubmed.ncbi.nlm.nih.gov/28740850/

iv. The OIE guidance for dog population management can be found here: https://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_aw_stray_dog.htm

15. Do human and dog rabies vaccines have the same constituents?

a. While the stock viruses used to make human and animal rabies vaccines are sometimes the same, the manufacturing process and potency are very different and the validation studies to ensure the vaccines are effective are species-specific.

b. It is not advised to use vaccines off-label.

16. What can we do to ensure rabies is considered a notifiable disease in a country?

a. Two terms are crucial to understand when implementing surveillance for any disease, including rabies: reportability and notifiability.

b. **Reportable diseases** are those that must be reported from a community (i.e. local health, veterinarian, hospital) to a central, usually sub-national, authority.

c. **Notifiable diseases** are those that must be reported from sub-national authorities to the national authorities.

d. Reportability and notifiability of diseases are often legal requirements within a health system.

e. WHO recommends that rabies in humans and animals be notifiable nationally (WHO TRS, Page 112, "To promote awareness and vigilance and to ensure that rabies is recognized as a priority, human and animal rabies must be notifiable nationally.")

f. The OIE Terrestrial Code 8.14.11 recommends rabies be notifiable for recognition of an endorsed canine rabies control program: "documentation indicating that dog-mediated rabies is a notifiable disease and that the official control programme for dog-mediated rabies is applicable to the entire country;"

g. Processes for making a disease reportable and notifiable will differ between countries. Speak with health authorities to understand the process, and work with local, national, and regional experts to develop the legal framework.

17. What is the significance of rabies in cats?

a. No felids, anywhere in the world, are reservoirs for rabies virus. Cats are a common spill-over species, meaning they get the virus from the local reservoir species (often dogs). Cats can infect other animals as well as humans, but transmission is limited. Cats do not contribute in any meaningful way towards endemic rabies.

b. The reservoir species (primarily dogs) should be the target for any intervention, including vaccination.

c. If there are ample resources to vaccinate all of the necessary dogs, then cats could be vaccinated at the program's discretion. If there are not enough vaccines or resources to vaccinate the required amount of dogs, cats should not be vaccinated as part of a public vaccination campaign.

d. Bites from any mammal suspected to have rabies should be treated in the same manner.

i. Wash the wound.

ii. Contact an animal health official to assess the health of the animal.

iii. Seek medical care.

iv. Determine if PEP is necessary based on a risk assessment of the animal and with consideration to the bite severity.

List of references

The recorded video & all presentations from the webinars are on the OIE regional website: https://rr-asia.oie.int/en/events/saarc-rabies-webinar/

Evaluation of safety of ORV for dogs: https://www.nature.com/articles/s41598-019-42714-9

https://www.who.int/rabies/resources/who_trs_1012/en/

Serologic comparison between ORV and parenteral, in a field setting: https://www.sciencedirect.com/science/article/pii/S0264410X17313889?via%3Dihub

Cost benefit comparison: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6805755/

Cost effectiveness study on ORV and other methods can be found here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6805755/

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0200942

WHO risk assessment recommendations for PEP can be found at: https://apps.who.int/iris/bitstream/handle/10665/272364/9789241210218-eng.pdf?ua=1