REVIEW ARTICLE

AN OVERVIEW OF RABIES OUTBREAKS IN MALAYSIA, ORDINANCES AND LAWS

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ABSTRACT. Rabies is a serious global threat causing an estimated 60,000 human deaths and is responsible for more than 15 million post-exposure prophylaxis in our world population every year. Malaysia was historically known to have rabies since 1884 but records were only found dating from 1924, of numerical records of incidences. Rabies was successfully eradicated in Malaysia in 1999. However, multiple outbreaks in the states of Perlis, Kedah and Penang occurred in July 2015 which was resolved by November 2015. An isolated case of rabies was identified in Perak in June 2017. Sarawak had the first case of rabies declared by the Health Ministry on 1st July, 2017. Perlis had another outbreak on 13th June, 2018. Disease control measures such as stray dog population control, vaccination in response to the outbreak, public awareness, surveillance within a 10 km radius and within the infected zone, movement control within the country, quarantine, containment of infected zone and official disposal of carcasses were carried out in response to the outbreaks. Besides that, the continuous sampling for rabies diagnosis highlights the efficacy of an outbreak containment. Therefore, diagnosing rabies effectively and accurately is important in controlling the disease and subsequently, to regain rabies free status in Malaysia. With this objective, rabies diagnosis has been carried out by the National Reference Laboratory, Veterinary Research Institute (VRI), Ipoh and State Veterinary Diagnostic Laboratory, Kota Samarahan, Sarawak.

Keyword: rabies, outbreak, control measures, diagnosis, Malaysia

INTRODUCTION

Rabies virus, belonging to the *Rhabdoviridae* family, is known to be one of the most ancient pathogen that commanded fear in mankind (Nyoman *et al.,* 2015; Tuvshintulga *et al.,* 2015; Yu *et al.,* 2014). There are seven genotype of rabies viruses present world-wide, namely Genotype 1 – rabies virus (worldwide, not Australia) and other rabies related viruses (RRV), Genotype 2 – Lagos bat virus (Africa), Genotype 3 – Mokola virus (Africa), Genotype 4 – Duvenhage virus (South Africa), Genotype 5 – European bat

Lyssavirus EBLV1, Genotype 6 – European bat Lyssavirus EBLV2 and Genotype 7 – Australian bat lyssavirus ABLV (pteropid and insectivorous bat) (Wakeley *et al.,* 2005).

Rabies is known to cause rapid ascending central nervous system infection and severe encephalitis in affected mammals, claiming an estimated 60,000 human lives annually worldwide, with 95% of human rabies attributed to dog bites (Yu *et al.,* 2014). People from the poorest of economic status, of vulnerable categories (children below 15 years of age, elderly, immune-compromised, heavily exposed) or from remote areas, are at higher risk of infection (WHO, 2019). Clinical onset of the disease has varied ranges of incubation period across different species of mammals, with the most common between one week to five weeks. An infected mammal has probably an estimated seven days to live once clinical signs have developed. There is only an estimated 4% survival rate among rabies victims, making it a major global public health concern as the cure rates are scarce and frequently unsuccessful (WHO, 2019). However, both human and animal rabies can be prevented through consistent pre-exposure or prophylactic vaccination.

Up to year 1999, rabies had only occurred in Peninsular Malaysia, involving 1,241 animal cases (99.6% of which were dogs) and 24 human cases (OIE GS, 2013). There have been numerous publications on the overall occurrence of rabies up to 1999, when Malaysia was declared rabies free. The focus of this paper is on the reccurrence of the disease from 2015 onwards.

Rabies in Malaysia

The first recorded case of rabies was in Kedah in 1925 (Narayanan, 1928) of a rabid dog in neighbouring Perlis. Most cases were reported in the northern states of Peninsular Malaysia which share a common border with Thailand where the disease prevalence was high.

In 1945 during WW II, the Allied Forces were implicated in a major outbreak that occurred in Province Wellesley (now known as Seberang Perai) and Perak (1945) through the introduction of affected dogs along the common trunk road cutting through various states in Peninsular Malaysia (Ganesan *et al.,* 1993; Wells, 1957). Between the years 1946 to 1951, an annual average of 112 confirmed canine cases were detected (Wells, 1957).

A major epidemic occurred southwards of the peninsula in 1952, involving Selangor (Lim, 1998) and Kuala Lumpur which prompted the formulation of a National Rabies Control Programme involving the vaccination of all dogs and rigorous destruction of stray dogs (Wells, 1957). The outbreak was successfully brought under control by April 1954, and the country was then declared free from rabies (Lim, 1998).

As a consequence of the 1952 rabies epidemic, an immune belt was established in 1955 in the states at the border of Malaysia and Thailand. Since then, sporadic cases were reported in the states of Perlis and Kedah with isolated incidences in Selangor and Province Wellesley (Ganesan *et al.,* 1993).

In 1995, two canine cases were detected in Terengganu through a routine follow-up investigation on human dog-bite cases. The possible source of the

disease was then traced to seafaring dogs on detained Thai fishing vessels berthed at the Chendering Fishing Port in Kuala Terengganu awaiting the court's decision for trespassing onto Malaysian waters (Loke *et al.,* 1998; Townsend, *et al.,* 2013). By the end of January 1997, further detection of 10 animal cases (8 dogs and 2 cattle) in 1996 was followed by another 6 cases detected in Terengganu (1 case), Kedah (4 cases), and Perlis (1 case) (Lim, 1998). The last record in Kedah was of a human case in 1998 and a canine case in 1999. After a prolonged hiatus of disease occurrence, Malaysia was declared free from rabies by the World Animal Health Organisation (OIE) in July 2013 (Ganesan *et al.,* 1993; Lim, 1998; OIE GS, 2013).

The 2015 outbreak began with the first reported canine case at Kaki Bukit, Perlis on 27th July; followed by Balik Pulau, Penang on 9th September and Kota Setar, Kedah on 12th September (WAHIS Interface, 2015). All three states simultaneously had confirmed canine cases which were later declared resolved by 18th September, 2015 (WAHIS Interface, 2015). Fortunately, these episodes were not accompanied by human cases. There was a total of 11 canine cases in the outbreak. The strain affecting Perlis and Kedah was traced to the SEA lineage [Combodia/Thailand/ Laos] (VRI, 2015), carried by free-roaming dogs observed moving across the border between both countries in the vicinity of Kaki Bukit, Perlis and Songkhla, Thailand. However, immediate intensive cross-agency responses of the three states brought the disease under control by the end of 2015.

The East Malaysian state of Sarawak, on the island of Borneo, recorded its first wave of rabies outbreak beginning July 2017 in the Serian division involving 3 human (children) cases from Kampung Paon Rimu and Kampung Lebor. Sarawak was historically free from rabies with no vaccination practiced and was declared free of the disease prior to the outbreak. The source was traced to the freely roaming dogs observed moving across the border between both countries in the vicinity of Serian, Sarawak and West Kalimantan. Phylogenetic analysis of the virus confirmed the Indonesian origin of the disease (VRI, 2017).

By 31st December, 2018, 332 (EpiS, 2019) confirmed rabies cases were identified from 911 brain samples of dogs (847) and cats (78) by VRI, Ipoh. 59 areas from eleven divisions: Serian (22 areas), Sri Aman (4 areas), Kuching (7 areas), Samarahan (3 areas), Sarikei (4 areas), Betong (3 areas), Sibu (2 areas), Kapit (1 area), Miri (6 areas), Mukah (4 areas) and Bintulu (3 areas) were declared as infected zones. Limbang (next to the state of Sabah) was the only rabies-free division (DVS, 2019). A total of 88,969 dogs and 8,503 cats were given the first dose of rabies vaccine, while 11,630 dogs and 38 cats were given the second dose (DVS, 2019). 13,944 dogs and 226 cats were destroyed across the eleven divisions. 72,506 members of the public participated in the awareness programmes carried out throughout Sarawak (DVS, 2019). 16 human cases were recorded, claiming 15 lives and leaving 1 survivor (child) with severe neurological complications (MOH, 2018) (Figure 1).

17 months later after the first human case in July 2017, despite rigorous disease control efforts, canine cases in Sarawak persisted indicating that rabies was still present within its canine population. Canine

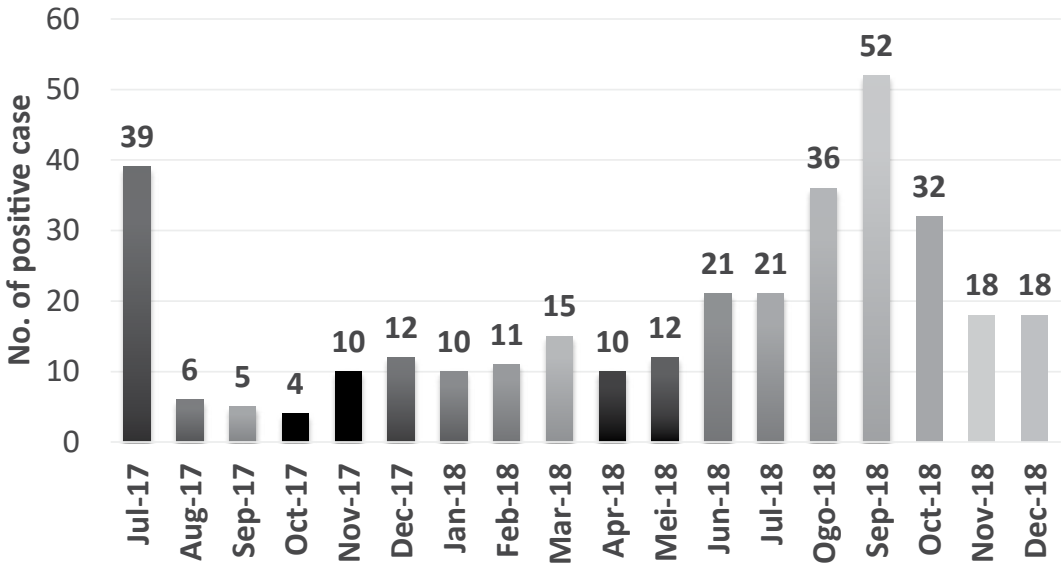

Figure 1. Rabies epidemic curve in Sarawak, Malaysia.

cases increased in the months leading up to March 2018, followed by a slight drop between March and May 2018, with a sudden spike in June with increase of cases thereon. Another spike of cases in September (52 canine cases) and a sudden decrease in October (32 canine cases) was seen, followed a sudden reduction in November and December 2018.

The peninsula of Malaysia had also experienced an outbreak in 2017. Although an isolated case, it triggered an alarm in the Perak state because there had not been any case since 1951). It was a dog bite case involving 2 children aged 11 and 12 years old in a fishing village at Kuala Sepetang, Taiping. The dog, which inflicted the bite, died on 13th July. Rabies was positively identified on 14th July from samples of the dog (WAHIS Interface, 2017). Phylogenetic analysis of the virus confirmed the Indonesian origin of the disease (VRI, 2017). A regional-level declaration of rabies outbreak was instituted – triggering disease control measures via mass vaccination and control of strays. 369 animals of various species were vaccinated and 100 stray dogs were destroyed within a kilometer radius from the foci, which was then also supported by multiple public awareness programmes jointly carried out by the state and federal departments of veterinary services (EpiS, 2019).

Perlis relived another rabies episode with a confirmed case on 7th June, 2018 (30 months after being declared rabies-free). It was a human bite case inflicted by a stray dog in Kangar with confirmation of the virus on 13th June, 2018 (WAHIS Interface, 2018a). Another similar case was detected from Beseri, Perlis, also from a bite case, with confirmation on 3rd November, 2018 (WAHIS Interface, 2018b). Only 2 samples have been confirmed positive from the 159 brain samples submitted to VRI, Ipoh. In

mitigation, 1,864 animals of multiple species were vaccinated and 217 stray dogs were destroyed within the buffer zone (EpiS, 2019). Awareness programmes in Perlis were informally carried out on top of awareness about the disease through routine rabies campaigns.

Incidences in Perlis, Kedah, Penang and Perak draws attention to the possibility of introducing rabies into any part of Peninsular Malaysia via various entry points, by land, sea or air. The continuous outbreaks in Sarawak trigger alarms as an early warning to Sabah and Brunei to strengthen prevention measures at their porous borders.

Rabies preventive measures

A. Immune belt areas

As the prevalence of rabies in Peninsular Malaysia is concentrated in the states bordering Thailand, an immune belt established in 1955 (OIE GS, 2013), spanning the entire state of Perlis, the districts of Kubang Pasu, Padang Terap, Sik, Baling, Kota Setar and Pendang in the state of Kedah, the whole of northern part of Perak state and the districts of Tanah Merah, Pasir Mas, and Tumpat in the state of Kelantan. The state of Sarawak deliberated and agreed upon the establishment of an immune belt in a meeting on Control of Rabies and Creation of Rabies Immune Belt in January 2018, set at 650 km in length (CRCRIB, 2018). The immune belt stretches from Teluk Melano in Sematan District (Kuching Division) to Lubok Antu (Sri Aman division) (CRCRIB, 2018). Sabah has yet to establish any preventative measures despite rabies being enzootic in both Sarawak and Kalimantan, Indonesia.

The functions of the immune belt include having the designated areas acting as buffer zones to allow permanent intensive disease control measures to be continuously and diligently carried out. Some of these measures include activities such as:

Licensing

Licensing is compulsory for all owned dogs within an immune-belt. The Department of Veterinary Services is empowered via legislative authority to register and license all owned dogs within the immune belt area (DVS, 2011).

Vaccination

Rabies vaccination is compulsory and is required for license applications. Vaccination is annually with vaccines approved by the Department of Veterinary Services.

Destruction of stray dogs

Any unlicensed and stray dogs will be destroyed through approved humane methods within the immune belt as part of a permanent and continuous exercise. The aim is to reduce persistence of infective hosts within the canine population.

Public awareness and disease education

Members of the public are periodically educated about the disease, health risks and hazards, do's and don'ts and methods of detection, via control programmes

through inter-agency awareness campaigns. The education process is carried out via conventional media (i.e. press release, radio, television, brochures and posters) and social media in the state. Cross-agency and involvement of other entities, for example, collaborations with the information departments, district offices and community and village leaders, would make an effective publicity campaign.

B. Non-immune belt areas

In the non-immune belt areas where the probable occurrence of rabies is low, the DVS is authorised to closely monitor the situation by following the procedures outlined by legislation Act A1452: Animals Amendment Act 2013 (CLR, 2013) and by collaborating with the local governments (municipal councils) to enable proactive rabies control in Malaysia.

All dog owners are subjected to obtain licensing under the purview of either their local district veterinary office or local municipals according to local by-laws. Examples of stray population control which have been carried out were: good waste management practices at sites where strays have a predilection (e.g. food courts or stalls, markets and dumpsites), and neutering campaigns to reduce uncontrolled breeding.

Legislation (Section 15, Animal Welfare Act 2015) is in force to restrict commercial breeding and sales of pet animals under license by the DVS. Responsible pet ownership is encouraged via the implementation of the Pet Passport System that stores the identification and health records of an animal in a microchip. Penalties are imposed on persons involved in abandonment of owned animals at public areas via the Animal Welfare Act 2015 (CLR, 2013; SSL, 2015; CLR Sarawak, 1999).

Animal movement controls are also part of the preventative measures and executed via the following:

a) Restriction of dogs moving out of the immune belt areas. Movement is permitted within the month following an anti-rabies vaccination.
b) Any dog or cat brought into the country is to be accompanied by an import permit and health certificate issued by the relevant competent veterinary authority of the exporting country. The animal is then subjected to quarantine procedures according to relevant federal or state import regulations under the DVS.

Disease surveillance and monitoring is via timely detection of animals showing suspected clinical signs of rabies, recording history of recently dead companion animals and following-up dog-bite cases. Any dog bite case is to be notified to the DVS by the local health authorities. For bite cases involving pet animals, the identified animal is detained and quarantined for observation by the DVS for fourteen days (DVS, 2011; CLR, 2013). Should the animal show suspected clinical signs of rabies, brain samples are to be taken and submitted to the Veterinary Research Institute (VRI), Ipoh for laboratory confirmation. As for bite cases involving stray dogs, the identified dog is to be immediately and humanely euthanised and sampled for rabies confirmation. If the stray dog is not identified, 5 brain samples of stray dogs will be collected by DVS at 5 km radius of the

bite case. The samples will be sent to VRI for analysis.

Control Procedures for outbreak

The main objective of any disease outbreak control is to halt and prevent the spread of the infection into areas of possible naïve animal population at risk of becoming infective hosts. Speed, efficiency, clarity and effective communication are essential in the control of communicable zoonotic diseases especially rabies.

A. Setting up of the Operations Room

Upon diagnostic confirmation of rabies, the Minister with the assigned responsibility on animal health will issue a gazette of an area to be declared as a rabies infected area according to Section 39, Act A1452, Animals Amendment Act 2013 (Peninsular Malaysia) or Section 46, Animal Enactment 2015 (Sabah) and Section 37, Chapter 32 Veterinary Public Health Ordinance 1999 (Sarawak), at the advice of the Director-General of the DVS. The veterinary directors of the relevant states will be duly notified about the laboratory results by the Director-General.

Upon primary confirmation of a positive case, operations centres will be set-up at the district, state and federal levels with their assigned responsibilities.

The district level is responsible for the day-to-day operations at the infected area. The state animal health coordinator and the district veterinary officer are responsible for the execution of field control and eradication operations, personnel adherence of instructions, legislations and procedures, and staff safety protection, as well as the recording of essential relevant outbreak data and operations which is to be relayed to the State Operations Centre (DVS, 2011).

The State Operations Centre is responsible for the compilation of data from the District Operations Room, collation and coordination of personnel and resources, supply management of vaccines, biologics and equipment, ensure personnel adherence to instructions and procedures, and coordination of public awareness campaigns (DVS, 2011).

At the federal level, two operation rooms will be set up i.e. at Federal Department of Veterinary Services Headquarters in Putrajaya, and at the Veterinary Research Institute (VRI).

The Headquarters Operations Room is responsible for coordination of the control schedule, administrative arrangement of field personnel and experts to be sent to the affected state, ensuring sufficient supply of vaccines and biologics, coordination of awareness campaigns at the national level, compilation of reports and analysis of data relayed by the State Operations Centre (including detection of new foci), and daily reporting to relevant stakeholders and mass media (DVS, 2011).

The VRI Operations Room is responsible for monitoring the national disease situation due to its function as a rabies diagnostic centre, monitoring surveillance and clinical sampling by the relevant states, and daily laboratory reporting to the Headquarters Operations Room.

B. Procurement of Animal and Human Rabies Prophylactic Vaccines

The Federal DVS, in the event of an outbreak, is responsible for the supply and delivery management of animal rabies vaccines to affected sites as well as management of pre-exposure protective prophylactic vaccination of front-line personnel exposed to heightened risks in contracting the disease.

C. Zoning

In the event of an outbreak, the affected areas will be divided into three areas which shall be gazetted in accordance with Section 39, Act A1452, Animals Amendment Act 2013 (Peninsular Malaysia) or Section 46, Animal Enactment 2015 (Sabah) and Section 37, Chapter 32 Veterinary Public Health Ordinance 1999 (Sarawak). Each area will be treated with its own respective control protocol (DVS, 2011):

Infected area (1 km radius from foci)

- Quarantine order will be enforced and all movement of dogs and cats are halted.
- The State Veterinary Director may issue orders for necessary confinement measures of owned dogs (e.g. confined in controlled spaces, chaining, compulsory collaring, muzzling of dogs upon entering public areas).
- Quarantine notices will be issued to the infected premise(s).
- Targeted culling of stray dogs.
- Heightened active and passive surveillance.

Control area (10 km radius from infected area)

- Restricted dogs and cats movement unless explicitly permitted by the State Veterinary Director.
- Rigorous vaccination of companion canine population.
- Targeted culling of stray dogs.
- Heightened active and passive surveillance.
- Public education and awareness through persistent campaigns.

Surveillance area
(10 km radius from infected area)

- Restricted animal movements unless explicitly permitted by the State Veterinary Director
- Rigorous vaccination of companion canine population
- Targeted culling of stray animals
- Heightened active and passive surveillance.
- Public education and awareness through persistent campaigns.

Destruction of Suspected Animals

Targeted culling and control of free roamers or stray dogs will be required, to control infective hosts within the canine population at risk (CLR, 2013). The procedure is in accordance with Section 40, Animals (Amendment) Act 2013 as part of rabies control. Targeted culling and destruction is in areas within 10 km radius from the

infected foci. The area of destruction will be evaluated from time to time so that the outbreak can be controlled at the earliest possible time (DVS, 2011).

Laboratory Confirmation of Brain Samples

All brain samples from suspected and surveillance cases will be referred to the national reference laboratory, that is, the Veterinary Research Institute (VRI), Ipoh or in the case of Sarawak, samples will be submitted to State Veterinary Diagnostic Laboratory.

Direct fluorescence antibody test (dFAT), as recommended by both WHO and OIE, is the confirmatory test for the presence of rabies virus antigen (OIE, 2018). It is used directly on a brain impression smear and cell culture or in brain tissue of mice that have been inoculated for diagnosis. Impression smears are prepared from a composite sample of brain tissue (Meslin *et al.,* 1996), that includes the brain stem, cerebellum, cerebrum and hippocampus. The dFAT is highly sensitive and specific (between 96% and 99%) and gives reliable results on fresh specimens in less than 2 hours (OIE, 2018). The sensitivity of dFAT is dependent on the specimen, the degree of autolysis and the sample type.

Autolysed samples will be subjected to RT-PCR for the detection of rabies virus antigen.

Virus isolation using rabies tissue culture infection test (RTCIT) will be used to detect viable (replicating) rabies virus from specimens of an outbreak involving a new infected zone in order to initiate virus sequencing and phylogenetic tree analysis to facilitate the investigation of molecular epidemiology of the outbreak.

Prophylactic Vaccination of Dogs and Cats

Rigorous mass prophylactic vaccination of dogs and cats will be carried out within relevant strategic areas with the aid of authorised veterinary personnel mobilised by the Federal DVS. Private companion animal practitioners in the affected areas will also be required to vaccinate animals against rabies (DVS, 2011). Mass vaccinations may be concurrent with on-site licensing of companion dogs for public ease (DVS, 2011).

Public Awareness and Educational Campaigns

Awareness campaigns will be carried out to sensitise members of the public towards the disease, its intensity and severity, required steps in the event of an animal bite and the essential need to immunise their companion animals against rabies (DVS, 2011). Mass media such as newspapers (including vernacular papers), radio and television, as well as social media platforms shall be used for public education. Disease awareness pamphlets and notices on referring all dog-bite cases will be distributed to the district or general hospitals, clinics and to general practitioners within the affected state. Schools will be targeted for information dissemination especially among the high-risk group of school-going children.

Animal movement control

Movement of companion animals (especially dogs and cats) will be halted within

the outbreak area according to Section 39, Animals (Amendment) Act 2013, in Peninsular Malaysia and Labuan; Section 46, Animal Enactment 2015 in Sabah; and Section 37, Chapter 32 Veterinary Public Health Ordinance 1999 in Sarawak.

CONCLUSION

Continuous active surveillance is crucial for the early detection of rabies. Immediate fresh sample submission will expedite the detection of the disease, subsequent immediate control measures to be applied effectively will allow speedy post-exposure prophylaxis treatment of human victims. Disease response preparedness in the face of possible disease outbreaks and information sharing of rabies cases across neighboring countries are vital in strategic control and implementation of preventative measures for a successful outcome. Mass prophylactic vaccination of dogs which are at risk and sustained by annual boosters is the best long-term control measure to reduce and eradicate rabies in Malaysia.

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