Government Response to the Discovery of a Rabies Virus Reservoir Species on a Previously Designated Rabies-Free Island, Taiwan, 1999–2014

S.-S. Chang¹, H.-J. Tsai², F.-Y. Chang³, T.-S. Lee⁴, K.-C. Huang⁵, K.-Y. Fang⁶, R. M. Wallace⁷, S. Inoue⁸ and C.-Y. Fei⁹

¹ Bureau of Animal and Plant Health Inspection and Quarantine, Council of Agriculture, Taipei, Taiwan
² Animal Health Research Institute, Council of Agriculture, Taipei, Taiwan
³ Taiwan Centers for Disease Control, Ministry of Health and Welfare, Taipei, Taiwan
⁴ Forestry Bureau, Council of Agriculture, Taipei, Taiwan
⁵ Department of Animal Industry, Council of Agriculture, Taipei, Taiwan
⁶ Endemic Species Research Institute, Council of Agriculture, Taipei, Taiwan
⁷ United States Centers for Disease Control and Prevention, CDC, Atlanta, GA, USA
⁸ National Institute of Infectious Diseases, Tokyo, Japan
⁹ School of Veterinary Medicine, National Taiwan University, Taipei, Taiwan

Impacts

• On 17 July 2013, the Taiwan government confirmed the diagnosis of rabies virus in wild Taiwan ferret-badgers, the first recognition of endemic rabies transmission since 1961.
• The distribution of rabies virus can be categorized into two distinct geographic clades: the Main Epizootic Area and East Epizootic Area. The two areas are separated by the Central Mountain Range, suggesting that the clades have evolved separately over numerous years.
• Humans are at risk mainly through exposure to the virus from dogs and cats that have been infected by rabid ferret-badgers. As part of a large-scale government response, mass vaccination of dogs and cats was conducted to provide an immunological barrier.

Keywords:
Public health; rabies; dog; epidemiology; infectious disease; risk assessment

Summary

Taiwan had been considered rabies free since 1961. In 2013, Taiwan confirmed the detection of rabies virus in wild Taiwan ferret-badgers. Up to December 2014, there have been 423 rabies-confirmed ferret-badgers and three cases of spillover infection into non-reservoir hosts. Genetic analysis indicates that TFBV is distinct from all other known rabies virus variants. To date, ferret-badger rabies is known to occur only in China and Taiwan. The temporal dynamics of rabid ferret-badgers in Taiwan suggests that the epizootic appears to have subsided to enzootic levels as of December 2014. According to the current epidemiologic data, there is only one TFBV strain in Taiwan. TFBV is still sequestered to the mountainous regions. Humans are at risk mainly through exposure to the virus from infected domestic meso-carnivores, mainly dogs and cats. Dogs and cats should be vaccinated to establish an immunological barrier to stop the spread of the disease from mountainous regions to domestic meso-carnivores.

Rabies in Taiwan

Rabies virus (RABV) is the most significant virus in terms of human health impact among all members of the genus Lyssavirus and is the causative agent of rabies in human and animals. On 17 July 2013, Taiwan confirmed RABV in wild Taiwan ferret-badgers (OIE 2013), which marked the first appearance of rabies in Taiwan since WHO declared
Taiwan rabies free in 1961 (WHO 1966). Subsequent retrospective testing and prospective surveillance activities detected a total of 423 rabid ferret-badgers from 2010 to 2015 (Table 1). RABV was detected in very few other species during this testing period, providing epidemiologic evidence that the ferret-badger is the sole reservoir species for this virus in Taiwan. RABV circulation has been reported in the Chinese ferret-badger since as early as 1995. However, genetically, the RABV variant that is enzootic to the Taiwan ferret-badger is distinct from all other known rabies virus variants (Chiou et al., 2013). The temporal dynamics of the Taiwan ferret-badger rabies virus variant (TFBV) in Taiwan, from July 2013 to December 2014, suggests that the epizootic has subsided to enzootic levels (Fig. 1). The TFBV can be categorized into two clades, forming the Main Epizootic Area and the East Epizootic Area. The two epizootic areas are geographically separated by the Central Mountain Range and Kaoping River. These epizootic areas are also geographically separated from the northern one-third of Taiwan by the Daan River. Despite hundreds of samples tested, to date, no rabid animals have been detected north of the Daan River. To date, there have been three cases of spillover infection from the Taiwan ferret-badger virus (TFBV) into non-reservoir hosts (OIE 2014), and no human rabies deaths have been associated with the TFBV epizootic.

Due to the threat of canine rabies from surrounding enzootic countries, Taiwan has instituted elevated rabies control policies since 1999, when the Bureau of Animal and Plant Health Inspection and Quarantine (BAPHIQ) implemented an active surveillance programme for the detection of canine rabies. Furthermore, in 2008, BAPHIQ instituted passive and active surveillance programmes for the detection of rabies in bats and in 2013 additional programmes for detection of zoonotic diseases in wild meso-carnivores (Table 1). On 16 July 2013, several months after the disease surveillance programme of meso-carnivores had been implemented, researchers diagnosed rabies virus infection in three Taiwan ferret-badgers (Chiou et al., 2013). BAPHIQ reported these findings to the OIE on 17 July 2013 (OIE 2013). Laboratory tests were performed by the Taiwan National Animal Health Research Institute (AHRI)

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<td>4/47</td>
<td>271/1409</td>
<td>146/452</td>
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</table>

| Pet animals      |                |           |      |      |      |      |      |      |      |       |
| Dog              |                | 0/693     | 0/1478 | 0/1480 | 0/1134 | 0/1196 | 0/860 | 1/1553 | 0/948 | 1/9342 |
| Cat              |                | —         | 0/5    | —     | —     | —     | 0/12 | 0/12  | 0/129 |       |
| Ferret           |                | —         | 0/3    | —     | —     | —     | 0/3  | —     | 0/3   |       |
| Subtotal         |                | 0/693     | 0/1478 | 0/1485 | 0/1134 | 0/1196 | 0/860 | 1/1668 | 0/960 | 1/9474 |
| Total            |                | 0/693     | 0/1605 | 0/1545 | 2/1197 | 2/1235 | 4/907 | 272/3077 | 146/1412 | 426/11671 |

Note: The number of rabid animals and animals tested is recorded as ‘number positive/number tested’.

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or commissioned universities, using the method in Chapter 2.1.13. of OIE Terrestrial Manual of Diagnostic Tests and Vaccines for Terrestrial Animals.

**Government Actions Taken in Response to Sylvatic Rabies Epizootic**

On 24 July 2013, a temporary, preventive inter-ministerial incident command system (ICS) was established to combine the efforts of both human and agricultural institutions. The ICS is a systematic tool used for the command, control and coordination of emergency response. On 1 August 2013, a Central Epidemic Command Center (CECC) for rabies prevention was established, in which the Vice Premier served as commander in chief. The Minister of the Council of Agriculture (COA) as well as the Minister of the Ministry of Health and Welfare (MOHW) jointly served as commanders. CECC regularly invited relevant ministries to review preventive measures against rabies in order to coordinate the measures of prevention and epidemic control. The contingency actions are described as follows.

**International consultation of experts and scholars**

Local and international experts and scholars were invited to attend two conferences: ‘Domestic Experts Joint Advisory Council on People and Livestock Health Inspection’ and the ‘Domestic Rabies Prevention Measures Seminar’ held on 14 August and 26 August 2013, respectively. Medical professionals, veterinarians, epidemiologists, wildlife scholars and representatives of international and domestic government agencies discussed the status and inspection policy concerning animal rabies issues, in order to reach a consensus and facilitate the implementation of follow-up epidemic prevention measures. Local and international experts and scholars, including experts from the Centers for Disease Control and Prevention (U.S. CDC), conducted site visits to the Animal Health Research Institute, and Endemic Species Research Institute of the COA and several endemic areas from 12 August to 21 August of 2013. Furthermore, experts from the United States, France, Japan, Mainland China and the Philippines were invited to attend an international conference held on 30 and 31 August 2013 to discuss many significant issues, such as the role of wild animals in the spread of rabies, epidemic prevention and social challenges of rabies, as well as the knowledge concerning differential diagnosis, pathology and pathogenicity of rabies and other viral encephalitis. These consultations and conferences helped greatly to guide the Taiwan response and in the development of national recommendations for rabies control. Major issues discussed included the following:

1. At the time of the outbreak, Taiwan did not have enough human vaccines in stock to fit the exigent needs.
2. Dog and cat vaccination rates were alarmingly low and not enough animal vaccine was available in country.
3. Consensus was reached that current rabies diagnostic capacity was not powerful enough in manpower, facilities and materials to timely and reliably meet demand in this outbreak situation.
4. Little information was known about the reservoir species, the ferret-badger. Important information for understanding the epidemiology of this outbreak was missing, including the populations of medium-sized carnivores, habitat and ecological factors of the Taiwan ferret-badger, and the prevalence of rabies in other wildlife populations.

![Fig. 1. The temporal dynamics of rabid Taiwan ferret-badgers; Taiwan, July 2013–December 2014 (n = 413).](image-url)
5 Experts debated on the infectiousness of this rabies virus variant, with a contingent believing that the low reports of cross-species transmission events could indicate that this variant was not as virulent, while the majority of experts believed that this variant was no different in virulence than any other known rabies virus.

6 Disparate opinions on management of strays with animal protection groups.

7 Experts debated on methods for rapidly increasing the vaccination rate for rabies in dogs and cats.

Strengthening epidemic surveillance

The BAPHIQ and the Taiwan Centers for Diseases Control (CDC) established rabies information hotlines to serve people and animal owners separately. The BAPHIQ offered toll-free telephone to serve animal owners, and the CDC offered toll-free telephone to serve inquiries concerning human rabies exposures.

BAPHIQ and CDC developed three methods of animal rabies surveillance. Retrospective studies to identify and test archived ferret-badger samples were conducted. Active surveillance programmes were immediately implemented to detect rabies in found-dead terrestrial mammals. These activities included roadside surveillance and active submission of found-dead ferret-badgers in national parks. Finally, in an effort to ensure that the TFBV had not shifted back into the Taiwan dog population, surveillance programmes were instituted to identify and test rabies suspect dogs. Fluorescent antibody testing of brain tissue was used to confirm rabies infection, although occasionally positive diagnosis was based solely on the presence of Negri bodies in histological sections of brain tissue that had been formalin-fixed. The numbers of rabid animals and the number of animals to be tested were recorded as ‘number positive/number tested’ in Table 1.

Rabies prevention communication

Two health promotion campaigns were developed to improve public awareness of rabies and the importance of domestic pet and human vaccination. The first was the ‘2 don’t & 1 do’: Do not abandon pets; Do not contact wild animals; and Do vaccinate your pets. The second was the ‘R-W-S-O principle’: Remember what animal bit you (to tell doctor); Wash with plenty of water; Send patients to the hospital; Observe animals in quarantine for 10 days. CDC and BAPHIQ created rabies websites to provide epidemic notifications for people and animal owners separately. Additionally, many health programmes for rabies prevention were broadcasted through various media channels: TV, radio, etc., consisting of the following:

1 Holding regularly scheduled press conferences;
2 Offering daily press releases;
3 Providing rabies-related information through seminars and workshops;
4 Disseminating information on television and radio stations broadcast in 14 aboriginal languages;
5 Holding advocacy campaigns in all levels of schools through the Ministry of Education;
6 Registering and vaccinating every dogs adopted and raised in all levels of schools;
7 Forestry Bureau, COA and Ministry of Interior campaign reminding people to avoid bringing pets into forest recreation areas and national parks through public announcements;
8 Making timely advocacies to village leaders through reports and city council meetings.

Coordination of rabies vaccines and immunoglobulin stockpiles

Legislation has required that dogs and cats be vaccinated against rabies since 1961. However, after numerous years being considered rabies free, public knowledge of the benefits of vaccination and enforcement of the legislation were lacking. This resulted in a pre-outbreak estimated vaccination coverage in dogs and cats of lower than 40%. In accordance with the rabies control plan, upon recognition of the ferret-badger as a rabies reservoir species in Taiwan, approximately 2 500 000 doses of animal vaccines, 85 000 doses of human vaccine, 2870 bottles of anti-rabies immunoglobulin and 2000 bottles of horse anti-rabies serum were procured. Domestic animal population surveys had been routinely conducted since 2001 and served as the basis for calculation of necessary vaccine doses and infrastructural needs for vaccine distribution (Chen et al., 2013; Tung et al., 2010). Local animal health inspection authorities built stations for dog and cat vaccination in cities, villages, towns, campuses and aboriginal locations. National vaccination campaigns were planned using data from a 2011 national population estimate for dogs and cats for the basis of determining population distributions. Utilizing these 2011 measured estimates, it was estimated that the 2013 vaccination campaigns reached 97% of cats and dogs in enzootic villages. The vaccination rate in non-epizootic areas was 62%, while the overall vaccination rate nationwide was 66%. The COA procured and distributed free vaccines to animal protection groups to promote dog and cat vaccinations. The COA also provided vaccines for governmental shelters to have shelter animals fully vaccinated. All first line people in animal health inspection, wildlife conservation, dog management, impounding and other related institutes were priority targets for pre-exposure rabies vaccination. Persons who were potentially exposed to rabid animals were assessed by medical
professionals to determine whether rabies PEP was necessary. Taiwan CDC provided free rabies vaccination for any individuals who were determined to have had a likely rabies exposure.

Strengthen the management of dogs and cats

Institutes of animal welfare and disease control in local governments implemented policies to improve health inspections and comprehensive rabies vaccinations in animal shelters. Health monitoring systems, disease quarantine and isolation measures for the shelter animals were also strengthened at the local government level. As a result, the capacity of animal shelters and impoundment facilities increased by nearly 43% from the capacity of a total of 7071 dogs/cats to 10 110 dogs/cats, in order to accommodate an influx of animals abandoned or surrendered due to the fear of pet owners. Local governments offered incentives for animal adoption and extended working hours to lower the pet abandonment tide, in order to decrease the risk of rabies epidemic in case the ferret-badger rabies spillover into stray dogs. Microchips were provided freely for pet registration especially in high-risk enzootic areas. Total pet registrations increased by 160 000 during January–November of 2013, with the cumulative number of dog and cat registrations reaching 1 240 000 nationally. To prevent cross-species transmission from ferret-badgers into domestic animals, pets were prohibited from entering forest recreation areas from 1 August 2013 to 31 July 2015. Additionally, coastguard officers strictly monitored smuggling activities at sea, coasts, estuaries and non-trading ports and strengthened quarantine and anti-smuggling activities in international airports and sea ports.

Results from Three Surveillance Programmes Developed in Response to the Recognition of Rabies in Taiwan

Retrospective studies identified 16 unique ferret-badgers samples with adequate brain tissue for rabies testing. Samples were collected between July 2010 and June 2013 from found-dead or injured ferret-badgers submitted to an animal rescue facility. Of these 16 archived specimens, 10 were confirmed positive by DFA and PCR for the TFBV. The earliest case had died on 17 July 2010, which as of the date of this publication remains the earliest recorded ferret-badger rabies case in Taiwan. Up to 31 December 2014, 423 rabid ferret-badgers and three spillover infections were diagnosed (Table 1). The three cases of TFBV spillover infection included: one Suncus murinus with confirmed diagnosis on 30 July 2013, one 6-week-old puppy, which was bitten by a rabid ferret-badger and was confirmed diagnosis on 10 September 2013 and one Paguma larvata with confirmed diagnosis on 29 December 2014 (BAPHIQ 2014) (Table 1). Epidemiological data in Table 1 indicate that the ferret-badger is the sole recognized rabies reservoir species in Taiwan.

Prospective surveillance activities began immediately following the diagnosis of rabies, in July 2013, and consisted of passive surveillance reporting of abnormally acting animals as well as active surveillance of found-dead terrestrial mammals on roadsides and within national parks. The epidemiologic curve for rabid ferret-badgers, from July 2013 to December 2014, is shown in Fig. 1. The number of cases peaked in August in the Main Epizootic Area \( (n = 64) \) and in October in the East Epizootic Area \( (n = 35) \). The temporal dynamics of this epizootic suggest that, as of December 2014, the epizootic has subsided to enzootic levels in Taiwan.

The epidemic distribution of the 423 diagnosed rabid ferret-badgers in Taiwan from July 2010 to December 2014 is shown in Fig. 2, which shows that cases were primarily detected from 9 cities/counties. The TFBV can be categorized into two clades by the characteristics of genome sequence, referred to as the Main Epizootic Area and the East Epizootic Area. The Main Epizootic Area comprises Taichung City (49 cases), Nantou County (69 cases), Yunlin County (26 cases), Tainan City (22 cases), Chiayi County (14 cases), Kaohsiung City (15 cases). The East Epizootic Area comprises Taitung County (18 cases), Taitung County (197 cases) and Pingtung County (13 cases). The two epizootic areas are geographically separated by the Central Mountain Range and Kaoping River as indicated in Fig. 2. These two areas are also separated from the northern third of Taiwan by the Daan River. An important epidemiological phenomenon is that no rabid cases in the whole Taiwan Island have been diagnosed on the north side of the Daan River. To date, no human rabies deaths have been associated with the TFBV epidemic.

Discussion

The TFBV was recognized through the well-timed establishment of a wildlife disease active surveillance system. Molecular evolutionary genetic analysis shows that the TFBV is a member of the canine rabies virus lineage, with low genetic similarity to other Asian rabies virus variants, but high similarity within samples from Taiwan. Time to common ancestor estimates suggests that the TFBV most likely branched off from its canine predecessor and became a genetically distinct virus variant between 1900 and 1922. It suggests that the TFBV was likely cryptically circulating within Taiwan ferret-badger population for many decades (Chiou et al., 2013).

Recognition of ill or dead ferret-badgers increased drastically in 2013, and testing capacity was increased to allow...
Testing of hundreds of suspect cases. The epizootic pattern of temporal dynamics of rabid ferret-badgers (Fig. 1) suggests that the outbreak was recognized shortly after its origin; however, due to a dearth of historical samples, it is difficult to describe the epidemiology of this disease prior to recognition by public health officials. It also suggests that the epizootic has subsided to enzootic levels in Taiwan (Childs et al., 2000). According to the current epidemiologic data, the TFBV is still sequestered to the mountainous regions. The epidemic distribution of TFBV has been categorized into the Main Epidemic Area and the East Epidemic Area by the characteristics of genome sequence (to be published), which are geographically separated by the Central Mountain Range and Kaoping River (Fig. 2). The concept that the Central Mountain Range can be a barrier of interactions of terrestrial mammals has been noted in the Formosan wood mouse and other species (Hsu et al., 2001).

The European Commission report of rabies indicates that physical barriers such as rivers, mountains or anthropomorphic structures may deter the progress of expansion of rabies epizootics (European Commission 2002). The geographical barrier created by the Daan River is a possible cause of the current rabies-free situation in the northern third of Taiwan. However, rabies viruses have been shown to cross water barriers and this may not be a long-term preventive barrier. Therefore, if preventive measures are not undertaken to limit the spread of the TFBV, it is possible that the TFBV could extend throughout the entire island in the future. Other preventive strategies comprise amending the contingency plan, sustaining passive surveillance, estimating the population dynamics and distribution of ferret-badgers for the assessment of effective control policies. To complement control measures in the reservoir species, rabies control activities must include effective surveillance as the primary tool for various surveillance, as well as high vaccination rate of dogs and cats. In total, the government of Taiwan spent more than $4 500 000 USD for procurement of human and animal vaccine and to support the contingency actions listed in this report. This cost, however, does not include the monetary costs incurred by pet owners, non-vaccine medical costs for bite victims or salaries for personnel involved in the response.

Future Plan

Taiwan would like to one day be reclassified as a rabies-free area. Wildlife rabies reservoirs have been controlled and the virus eliminated from the reservoir species through intensive programmes in Europe and North America. BAPHIQ and AHRI are evaluating the potential success of programmes such as oral rabies vaccination through hand baiting as well as aerial distribution vaccine in Taiwan. However, bait palatability, vaccine efficacy and delivery systems for ferret-badgers are still unresolved issues that must be addressed before oral rabies vaccination can be realized in Taiwan. Programmes developed to combat the epizootic are continuing to operate as of 2015.

References