History of Rabies Control in Taiwan and China

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Abstract

Rabies is one of the top ten causes of death from infectious diseases in the world; it is also an ancient global zoonosis. The first case of rabies was recorded in 2300 BC. In China, the earliest report of rabies was recorded in "Zhuo Zhuan", written during the Spring and Autumn Period and the Warring States Period in 556 BC. China has the second highest number of rabies deaths in the world, just behind India, with 90% of the deaths occurring in farmers, students, and children. Most deaths are caused by dogs, followed by cats and other animals. Rabies virus isolated from humans and animals are all of genotype 1. Rabies caused 782 deaths in Taiwan during 1948 - 1959. In 2002, 2012, and 2013, there was an imported human rabies case each year. In 1956, Taiwan began rabies control by vaccinating dogs. Along with the control of domestic and stray dogs, rabies was successfully eradicated in 1961. However, in July 2013, following the detection of rabies in ferret-badgers, a house shrew and a dog also tested positive for rabies virus. On August 1, 2013, the Rabies Control Central Epidemic Command Center was established. Through inter-ministerial collaboration, increased health education, vaccination of dogs and cats, and the use of pre- and postexposure prophylaxis in humans, there have been no human infections reported. The response phase is now largely completed. Follow up actions are also being planned. History has shown that as long as the people are united in disease prevention, rabies may become a historic term in Taiwan once again.

Key words: rabies, rabies virus, ferret-badger

History of rabies in China

Rabies is an ancient global disease. The first recorded case of rabies is reported in the Eshnunna Code in Mesopotamia in 2300 BC [1]. At that time, if rabies occurs, dog owners would be notified to put the dog under strict custody. If the dog attacks and causes infection and death, the owner would be heavily fined. Rabies was rampant during the middle ages. It was found in dogs and wild animals in Europe during the1500's. The disease was brought to the Americas by immigrants during the middle of the 18th century. Rabies in Africa may be traced to 1772, when the British brought in the disease, which slowly spread to the entire

African continent. Rabies is more prevalent in northern and eastern Africa. Currently, rabies is one of the top ten causes of death from infectious disease in the world. Each year, an estimated 55,000 people die from rabies, of which, 31,000 occurred in southeast Asia, 24,000 in Africa. This is more than the deaths caused by Japanese encephalitis, dengue fever, and yellow fever combined.

Rabies has been circulating in China for a long time. The earliest report of rabies was recorded in the ancient text of "Zhuo Zhuan", written during the Spring and Autumn Period and the Warring States Period. It was written "in November of the 11th year of Xianggong (556 BC), a person was chasing a rabid dog". This indicated that rabies has been around in China for 2500 years. Later on, Han and Jin dynasty history texts also recorded the danger posed to humans by rabid dogs, and rabid dogs were driven out. Old medical texts, including books from the Jin, Tang, and Song dynasties all have texts on diagnosis, treating, and preventing rabies. The earliest medical text, the "52 Prescriptions" included treatment for "bites by rabid dogs" and "bites by dogs", indicating that even then, the distinctions were made between bites by rabid dogs and non-rabid dogs [2-4].

During 1911 - 1949, rabies was rampant in all provinces. With incomplete recording of cases, there were approximately 5,000 cases a year, with a mortality rate of 1.2/100,000 persons. After 1949, there were cases reported in accordance with the Communicable Disease Control Act, which listed rabies as a category II reportable disease. In 1956, there were 24 provinces reporting 1,942 cases, resulting in the first epidemic peak. During 1980 - 1989, there were 55,367 deaths caused by rabies, resulting in the second epidemic peak. This was an increase of 266% compared to the 1970's. On average, there were 5,500 deaths each year. Mortality rate was the highest among all infectious diseases in China. During the late 1990's, rabies rose once again. During 2000 - 2006, there were 13,104 cases reported. Compared to 519 cases reported in 2000, having 3,279 cases reported in 2006 represents a 513.8% rise. The only places with no rabies reported were Tibet and Qinghai province. Provinces with the most severe epidemic, in descending order, were Hunan, Guangxi, Guizhou, Guangdong, Jiangxi, Jiangsu, Hubei, Anhui, and Henan. These 9 provinces reported 89.3% of the cases. In 1996, there were 98 counties reporting rabies; by 2007, there were 910 counties in 195 regions, located in 23 provinces, reporting rabies. Overall, the number of rabies cases in China rose quickly, spreading from provinces with high incidence. Since the 1980's, China's rabies deaths has been the second highest in the world. There were 4,000 - 8,000 rabies deaths reported annually, just behind India,

which has approximately 20,000 deaths each year. In recent years, the number of dogs has been estimated to be close to 200 million. Because 95% of the human rabies cases is associated with exposure to dogs, this runaway situation must be reversed, or rabies control will become more difficult. In addition, because of the complex geographical and ecological environment, controlling rabies will also have to rely on effective immunization and surveillance of the disease in wild animals [2-4].

History of rabies in Taiwan

Rabies was first reported in Taiwan in 1903, when the Capitol Church News (now Taiwan Church News) printed an article on "crazy dogs", describing rabies. This indicated that Taiwan had rabies, but most people did not understand its seriousness or have the knowledge of the disease [5]. During colonial Japanese rule, literature also documented rabies. Since 1900, there were at least 11 cases, occurring in southern and northern Taiwan. Starting in 1930, the Japanese began to control rabies by producing inactivated vaccine for canine use at the then Danshuei Manufacturing Institute for Animal Antisera, instituting strict dog registration, and poisoning stray dogs; human rabies vaccines were produced by then Research Institute of Tropical Medicine for the prevention and treatment for rabies. Human rabies cases decreased gradually, eventually disappearing completely. According to literature, before 1948, there were decades when Taiwan had no rabies. However, after the end of World War II, there were frequent traffic between the ports in Taiwan, Shanghai, Hongkong, and Hainan, where rabies were present. On June 17, 1948, the first case of rabies was diagnosed by Dr. Tsung-Yi Lin of the Taiwan University Hospital. In the "Health Statistics, 1984" published by the Department of Health, it was also recorded that rabies in Taiwan, at the time, came from Shanghai. The record stated that during 1948 – 1958, there were no infectious disease specialist, and most dog bites were treated by surgeons. Other than catching and observing dogs and cats that bit humans, patients did not receive immunoglobulin or human rabies vaccine following exposure, and animal catchers also did not receive pre-exposure vaccination. Therefore, there were 782 deaths in Taiwan. The highest number of deaths occurred in 1951, when 238 deaths were reported, followed by 1952, with 102 deaths. In 1956, the Joint Commission on Rural Reconstruction and the Taiwan Provincial Health Department instituted rabies control measures including vaccinating dogs with vaccines imported from the United States and culling stray dogs to control animal reservoir. These policies successfully controlled rabies. The last human death from rabies occurred in 1958. The dog brain sent from Bali in Taipei County on January 13, 1961 became the last case of rabies in animals. After that, no more animal rabies was reported, and Taiwan proclaimed to have eradicated rabies. Since the last human rabies case occurred in 1959, there were cases of imported human rabies case from China occurring in both 2002 and 2012. In 2013, a case was imported from the Philippines. All three cases died. The Domestic Animal Hospital of the National Taiwan University College of Agriculture (now National Taiwan University Veterinary Hospital) was established on June 15, 1955. The hospital actively provided free chick-embryo live attenuated rabies vaccines to dogs. In addition, Professor Rong-biao Liu, Dean of Veterinary Medicine, instructed chief of laboratory, Dr. Si-Kwang Liu, to provide testing for all suspected rabies specimens sent in by veterinary hospitals, health stations, or individuals. They contributed to the rabies eradication in Taiwan. The first case was sent in on July 18, 1958. On December 21 of that same year, a dog brain sent in by the health bureau in Chiayi became the first confirmed rabies case, and the first rabies case in animals.

The Bureau of Animal and Plant Inspection and Quarantine of the Council of Agriculture has contracted National Taiwan University to conduct surveillance of wild animals since 2011. In 2013, rabies was added to the disease under surveillance. In 2013, National Taiwan University received dead ferret-badgers. Autopsy of the animals showed severe encephalopathy, but repeated testing for etiologies causing encephalopathy, including canine distemper and measles, failed to identify the cause of death. The University used RT-PCR to test for rabies in June 2013 which turned out positive, and reported the finding to the Bureau of Animal and Plant Inspection and Quarantine on June 24. On June 26, the specimens were sent to the Animal Health Research Institute, Council of Agriculture, for confirmation. After the Council of Agriculture convened a meeting of rabies experts on July 16, which confirmed the diagnosis of rabies, the incident was reported to the World Organization of Animal Health (OIE) on July 17. May 23, 2012, the date the first rabid ferret-badger was found, became the onset date of the current epidemic [7]. Comparison of the rabies epidemics in different eras is listed in table 1.

	1941–1961	2002–2013
Method of importation	Imported from Shanghai in 1948.	 Unknown source of infection in ferret-badgers. 3 human cases were all imported from abroad.
Confirmed infections	Humans, dogs, and apes. (Anecdotal report of disease in cattle, goats, and pigs, but no literature documentation). Transmission in urban cycle.	Other than a house shrew and a dog bitten by ferret-badger, all animals with confirmed disease were ferret-badgers. Ferret-badger and house shrew infection considered sylvatic cycle transmission.
Cases	 1947: spread by rabid dog brought in from Shanghai. 1958: last rabies human case died. 1959: last dog case died. 	 2002, 2012, 2013: 3 human cases imported from abroad. 2013: ferret-badgers, house shrew, dog confirmed to be infected. The 7 persons bitten by rabid ferret-badgers all received rabies vaccination and immunoglobulin; none had become ill.
Control measures	 Rabies vaccines imported from the United States. Stray dogs culled. Other coordinated policies. 	 Increase awareness and increase rabies vaccine coverage among dogs and cats. Stockpile supplies prior to July 2013, because Taiwan was considered rabies-free, approximately 200 doses of human rabies vaccine were stockpiled for travel clinic use. After rabies was reported in Taiwan, there was an emergency procurement of rabies vaccine. Post-exposure prophylaxis for humans bitten by high risk animals and pre-exposure prophylaxis for personnel working in animal disease control.
Virus strain	Unknown (Speculated to be genotype 1).	 Genotype 1 isolated from ferret-badgers, house shrew, and dog. Genotype 1 found in the 3 imported human cases.
Treatment of animals bites	 No infectious disease specialists were available at the time; most patients were treated by surgeons. Observation of dogs and cats that bit humans. No post-exposure prophylaxis; sedatives and supportive treatment given. 	 Treatment in accordance with guidelines published by the Centers for Disease Control, Taiwan. Clean wound with water and soap, followed by disinfection using iodine-containing solutions. Post-exposure prophylaxis: provide human rabies immunoglobulin and rabies vaccines.
Mortality rate	100%	Deaths in ferret-badgers, house shrew, and dog. No locally-acquired human fatal case reported. All imported cases died.
Note	To prevent rabies, since 1930 (during Japanese colonial rule), inactivated canine vaccines have been produced by the then Danshuei Manufacturing Institute for Animal Antisera. Human vaccines for treatment and prevention were produced by the then Research Institute of Tropical Medicine. At that time, dog registration and poisoning of stray dogs were instituted and rabies was thus controlled (Annal of animal disease control in Taiwan, 1988, published by the Department of Agriculture and Forestry, Taiwan).	

Rabies control in China

Statistics show that farmers (65%), students (16%), and children (8%) make up 90% of the rabies cases. Among them, 92.5% of the infected live in rural areas, which indicate that residents in the countryside are at high risk of disease. Furthermore, rabies occurrence is also increased in summer and autumn, when both humans and animals have increased outdoor activities. Main reasons for increased incidence include:

- Increased number of dogs and cats with decreased vaccine coverage: dogs are the main source of infection. Farming communities use dogs to guard their homes and frequently do not leash the dogs. Farming communities in the south have high pet density, up to 15-20 dogs per 100 persons, and 5-10 cats per 100 persons. Vaccine coverage among dogs only 10-20%, and nearly no vaccination among cats, the low vaccine coverage could not establish effective immune shield.
- After being bitten by dogs or cats, because of the limited knowledge and financial support, many people do not receive wound management or post-exposure prophylaxis with rabies immunoglobulin and vaccine.
- 3. Lack of knowledge on preventing rabies: surveys show that only 50% of the residents in farming communities know that rabies has a 100% mortality rate; 30% know that wounds must be treated after animal bites. Only 65% of the people sought medical attention after bite. In addition, healthcare personnel also need to have strengthened capabilities on wound treatments.
- 4. Poor vaccine quality and management [2-4].

Epidemiological studies in China show that 95% of rabies cases were bitten by dogs, 3% by cats, and 2% by other animals. In some areas, this proportion has changed. For example, in Zhejiang, during 1994 - 2004, there were 114 rabies cases, of which, 108 (75%) were caused by dogs, 31 (21.5%) were caused by ferret-badgers, and 5 (3.5%) by cats; and in Hangzhou and Huzhou, ferret-badgers caused 77.3% (17/22) and 60% (12/22) of the rabies cases, respectively. Other than dogs and cats which can be infected with rabies, the disease has also been found in pigs, cattle, goats, horses, and deer. Regarding rabies in wild animals, after the first human rabies case caused by ferret-badgers was reported in 1994 in Huzhou, Zhejiang, the epidemic continued for 3 years. Hangzhou also continued to have cases. Most people reported being bitten in the hands. Dogs, cats, and pigs in the area were also bitten by ferret-badgers. During 2008 - 2009, Wuyuan, Jiangxi, also reported 6 human rabies cases caused by ferret-badgers. Therefore, ferret-badgers became the only wild animal proven to be an independent reservoir for rabies in China. Cases of rabies have also been reported in wild animals including rats, foxes, yellow weasels, wolves, and badgers. These are most likely spillover infections, and do not play a significant role in the overall epidemiology and control of rabies. Only one bat in Tonghua, Jilin has been found to cause rabies death after biting a human. Rabies virus isolated from humans and animals all belong to genotype 1. Virus nucleoprotein from the isolated viruses shared 86.6% - 99.9% similarity. China uses genotype 1 vaccines strain. The effectiveness of the different vaccine strains used in China is similar to the rest of the world, and is effective in preventing rabies infections [3,4,9].

China has prohibited the use of nerve tissue vaccines (NTV) since 1991. In 2006, cell cultured vaccines were completely replaced NTV. According to the 2009 China Department of Health statistics, approximately 12 - 15 million doses of rabies vaccines were given each year, making China the country with the most human rabies vaccines provided in the world. Rabies control agency is collaborating with the international societies with a goal to eradicate rabies in China by 2025. Recently published "Mid- to long- term animal disease eradication plan for 2012 - 2020" has set target date 2020 for rabies control. The plan identified 12 provinces (cities, and regions) with rabies epidemics for strengthened rabies control, including Hebei, Shanxi, Jiangxi, Shandong, Hubei, Hunan, Guangdong, Guangxi, Chongqing, Sichuan, and Guizhou. Rabies is now reported mainly in the southeast. Inter ministerial collaboration is an important characteristic China's rabies control program. For example, the Ministry of Health, Ministry of Agriculture, Ministry of Public Security, and the Bureau of Food and Drug Monitoring and Control jointly published the "Memorandum for strengthened rabies control and prevention" in 2003.

Rabies control in Taiwan

Literatures have documented numerous rabies control measures implemented in the 1930's. There was no rabies reported until June 17, 1948. The case was reported by the National University Hospital doctor, Tsung-yi Lin, who identified the first case of rabies in Taiwan. In 1956, the Joint Commission on Rural Reconstruction and the Taiwan Provincial Health Department instituted rabies control measure including vaccinating dogs with vaccines imported from the United States and culling stray dogs to control animal reservoir. These measures successfully controlled the rabies epidemic. In 1961, the government pronounced that rabies was eradicated. At that time, there were no effective methods such as pre- or post- exposure prophylaxis for the control of human rabies infection. In both 2002 and 2012, a case of human rabies was imported from China. Then in 2013, a case was imported from the Philippines. None of the cases received post-exposure prophylaxis, and died after disease onset, despite best medical management [7,8].

In July 2013, after the incident of rabid ferret-badger was discovered, in order to protect the health of the citizens and avoid panic among the public, the Executive Yuan established the "Central Epidemic Command Center" in response to rabies outbreak, in accordance with item 1 in the Communicable Disease Control Act. Deputy Premier Chi-Kuo Mao was appointed as the Commander General, Chief of the Council of Agriculture, Bao-Ji Chen, and Ministry of Health and Welfare Minister, Wen-Ta Chiu

were appointed co-commanders. Inter-ministerial collaboration accelerated rabies response. After the establishment of the Central Epidemic Command Center, the first meeting was convened. All ministries began action to prevent rabies, to protect the health of the people. In the first meeting on August 1, chaired by Commander General Mao, he assigned the responsibilities among different ministries, and instructed all ministries to use the most strict criteria in response, implement control measures, closely monitor the epidemic, and, depending on the severity of the epidemic, to communicate with the public [7,8].

To prevent the spread of rabies, health education for residents living in rural and mountainous areas must be increased, dogs and cats should be vaccinated against rabies regularly, pets should not be abandoned. International literature indicates that abandoning pets increases the population of stray animals. These animals may stray into the territory of wild animals, become infected, and bring diseases back into the city. This will in turn worsen the epidemic. To prevent pets from coming into contact with wild animals, it s recommended to avoid taking dogs or other susceptible animals to go hiking. The prevention measures are as following:

- (1). All dogs and cats should be vaccinated against rabies and do not abandon pets. If vaccine coverage reaches 70% among dogs and cats, it can effectively prevent 96.8% of rabies in animals. Literatures also point out that abandoning pets increases the population of stray animals. These animals may stray into the territory of wild animals, become infected, and bring diseases back into the city. This will in turn worsen the epidemic.
- (2). Avoid all contacts with wild animals, including hunting, eating, or keeping them as pets.
- (3). Immunity in humans: some persons are at high risk of being infected by rabies because of their work or occupation, including veterinarians and those who work with wild animals. These people should receive rabies immunization [7-9].

The Central Epidemic Command Center continues to remind people to practice "2 don'ts and 1 do". That is, please don't contact, hunt, or keep wild animals as pets; don't abandon pets, but vaccinate pets regularly; and do report to animal disease control authorities when finds animals with abnormal behavior, such as the animal has stopped eating or drinking, has become anxious, has more urinary frequency, is afraid of the light, or has become aggressive (reporting hotline: 0800-761-590). For more information on rabies, please visit the rabies pages <u>www.cdc.gov.tw</u> at the Taiwan CDC webpage at, or call the public inquiry hotline, 1922 or 0800-001922. For information on animal's rabies, please go to the website for the Council of Agriculture (<u>www.baphiq.gov.tw</u>), or call the Council of Agriculture hotline at 0800-761-590. If one comes across dead animals, please do not touch the animal, but call the Bureau of a Animal and Plant Inspection and Quarantine hotline at 0800-761-590, or call the local animal disease control center.

If one is scratched or bitten by animals, please remember the following steps: remember, rinse, go, and observe.

- (1). Remember: please keep calm, and remember the characteristics of the animal.
- (2). Rinse: rinse the wound with copious amount of water and wash with soap; then disinfect the wound with iodine-containing solution.
- (3). Go: go to the hospital to be evaluated for possible need for post-exposure prophylaxis.
- (4). Observe: if possible, observe the animal for 10 days and see if the animal develop symptoms consistent with rabies. If animal has rabies, symptoms will usually appear in 5 8 days. If the animal is very aggressive, please do not venture to catch the animal.

If one receives correct treatment before symptom onset, the likelihood of becoming ill decreases dramatically. The prodromal symptom of rabies is not specific. Patients may have fever, nausea, vomiting, or have pain or numbness at bitten site. One should use soap to clean the wound following animal bites and see a doctor be evaluated for the possible need for post-exposure prophylaxis. Post-exposure prophylaxis includes active immunization with rabies vaccine and passive immunization with rabies immunoglobulin. Immunoglobulin infiltrated at the wound provides passive immunization and neutralizes viruses in the wound. Active immigration through the use of vaccines induces the body to develop anti-rabies antibodies. Both types of immunization can effectively decrease the viral load in the body [7,8].

Conclusion

Many emerging and reemerging disease in animals and humans, including many zoonoses, had major influences on human history. Literatures have shown that 38%-57% of non-immunized human die from rabies after being bitten by rabid dogs. This did not result in significant decrease of human population. However, humans are still fearful of rabies because of the frightful symptoms and inevitable death caused by rabies. Mortality following rabies disease onset is very high, but the disease is 100% preventable. The preparedness and response plan to rabies reemergence is mostly completed. The work to be accomplished could not be done immediately. But, history has proven that as long as the people are united in disease prevention, rabies may be eradicated from Taiwan once again.

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