**RABIES MANAGEMENT**

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**ABSTRACT**

Rabies is of great public health importance because it is almost universally fatal without timely intervention. Approximately over 60,000 people die from rabies each year. Canine rabies accounts for over 90% of human rabies cases worldwide and disproportionately affects the poorest population in Asia and Africa. The disability-adjusted life years due to rabies is estimated to be 1.9 million. The economic burden of rabies is US$ 6 billion globally. Rabies is often misdiagnosed due to limitation in ante-mortem diagnosis and the clinical signs often resemble encephalitis. Cost of rabies biologics is often a huge barrier to treatment for many in the developing countries. Canine rabies can be eliminated as demonstrated in North America and Western Europe. An integrative approach combining veterinary and human health services with commitment from local governments and support from international agencies is required for elimination to be successful and sustainable. In regions where canine rabies has been eliminated, continuing surveillance and maintaining adequate vaccine coverage are imperative to prevent re-emergence of canine rabies. In the U.S. where wildlife is the main reservoir for rabies, it is crucial to prevent spill over infection from wildlife into domestic animals. The Allegheny County Health Department in Western Pennsylvania processed 367 domestic animals during 2012, which accounts for more than half of all the animals submitted. The analysis to better understand the high number of domestic animals and to assess the reason for each domestic animal submission was done. The findings showed that key pieces of information that determine the need for rabies testing are often missing. An exposure date is often not reported and information on the vaccine status of the animal that is critical for monitoring vaccine failure is also lacking. Furthermore, the majority of the submission did not report the animal’s health status, which determines the need for quarantine and rabies testing. Accurate and complete information is essential for effective management and monitoring. Updating the existing submission form may increase the quality and the quantity of information collected for each submission.

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1. **Introduction**

Rabies is a zoonotic disease that is almost universally fatal once the rabies virus enters the nervous system. Exposure to rabies virus from dog bites accounts for over 90% of human rabies cases globally with the majority of the human deaths occur among the poorest population in Asia and Africa. Rabies is 100% preventable yet approximately 60,000 people die each year from canine rabies (1). The figure is likely underestimated due to poor surveillance, underreporting, misdiagnosis, and lack of coordination among human and veterinary services in many developing countries (2). Canine rabies has been eliminated from the United States, Canada, Western Europe, Japan, Malaysia, Australia, and a few Latin American countries. However, people in the developing countries continue to die from the disease even more than 120 years since Louis Pasteur developed the first rabies vaccine.

* 1. **The burden of rabies**

Canine rabies has been eliminated in North America and Western Europe. Wildlife such as raccoon in the United States and fox in Western Europe are the main rabies reservoirs. An estimated US$ 300 million are spent each year for rabies prevention and management in the United States (2). The cost of preventing rabies virus from re-emerging in Western Europe with oral vaccination campaign along the region bordering Eastern Europe is estimated to exceed US$6.5 million per year (2, 3). In Latin America, the Pan American Health Organization has made significant progress in eliminating canine rabies with an annual cost of US$ 40 million (4). There were 29 human rabies cases reported in 2006 in Latin America compared to 355 cases in 1982 (4).

Asia has the highest human deaths from rabies globally with an estimated 30,000 cases annually and the burden or rabies is estimated at 1.2 million disability-adjusted life years (DALYs) (2). There are more than 20,000 cases of human rabies or about 2 per 100,000 population in India alone (5, 6). The country has the highest incidence of human rabies cases in the world. It is most likely underestimated since rabies is not a reportable disease in India and there is a lack of infrastructure for rabies surveillance and reporting (7). India also has high incidence of animal bites at 17.4 per 1,000 populations and almost 92% were by dogs (7). China reported over 3,300 cases of human rabies in 2007 and an estimated 10 million rabies post-exposure prophylaxis treatments administered in 2010 (2). The true number is also unknown due to underreporting. Along with the highest incidence of human rabies case, Asia also has the highest cost associated with rabies post-exposure prophylaxis in the world, estimated at US$ 1.5 billion (2).

The most recent estimate of rabies death in Africa in 2010 was about 23,800 deaths. The burden of rabies in Africa approaches 609,000 DALYs. However, lack of data on rabies is a recurrent theme in Africa. It was reported that many animal bite victims die at home and those that are hospitalized are often misdiagnosed (8). The true incidence of rabies in Africa remains unknown and the official data is grossly underestimated by more than 100-fold (9).

Approximately 60,000 people die each year from canine rabies and more than 80% of deaths occur in rural areas. It represents 1.9 million DALYs (2). The World Health Organization (WHO) estimates the annual cost of rabies to be US$ 6 billion worldwide and the cost of rabies post-exposure prophylaxis to be US$ 1.6 billion (2). A lack of quality public health information on rabies is a common theme in developing countries. Therefore, rabies remains on the list of neglected disease due to the perception that it is a relatively insignificant human disease (9).

1. **Lyssaviruses classification**

Rabies is caused by single-stranded, negative-sense RNA viruses in the taxonomic order Mononegavirales. The order comprises of four families: Bornaviridae, Filoviridae, Paramyxoviridae, and Rhabdoviridae. These families are known for viruses that cause diseases in humans, other vertebrates, plants, and fish. Ebola virus and Marburg virus belong in the family Filoviridae. Nipah virus and respiratory syncytial virus are found in the family Paramyxoviridae. (10) The rabies virus, the prototype virus of genus Lyssavirus, is classified in the family Rhabdoviridae. It is the causative agent of the classical rabies disease and is responsible for the majority of all human rabies cases. Currently a total of eleven distinct lyssavirus species have been identified and 10 of which have been isolated from various bat species (11). They all appear to cause rabies encephalitis including European bat lysaviruses and Australian bat lyssavirus. Lyssaviruse particles are bullet shaped and measure about 75 nm by 200 nm in size. The RNA genome is 12 kb long and encodes five structural proteins (N, P, M, L, and G). The G glycoprotein is essential for pathogenesis because it mediates reception and fusion at cell surfaces. (10) The G glycoprotein has also been shown to induce virus-neutralizing antibody (12).

* 1. **Animal reservoirs**

Lyssaviruses are found on all continents except Antarctica and primarily infects mammals. Various species of Carnivora and Chiroptera serve as the primary host of rabies virus. In Europe, the red fox (*Vulpes vulpes*) is the main reservoir species for rabies virus (3). Raccoons, various bat species, skunks, coyotes, foxes, and Arctic foxes are the main reservoirs in North America. Certain species of Mongoose are considered the reservoir in parts of Africa, Asia and the Caribbean (10). Bats likely are the true primary hosts for lyssaviruses as the viruses have been detected in bats all around the world (2). However, despite various wildlife species that serve as the reservoir around the world, the domestic dog continues to be the major reservoir and vector in developing countries. Rabid dog bites are the major cause of human rabies death in canine rabies-endemic areas, mostly in Asia and Africa (1, 2). Approximately 40% of people who are bitten by suspect rabid animals are under the age of 15 years (13). Therefore, surveillance of canine rabies along with management of dog population and vaccination continue to be the main focus in controlling rabies in developing countries (14).

1. **Rabies Disease**
	1. **Pathogenesis**

Rabies virus is transmitted from an animal bite that inoculates the virus into wounds. Transmission has also been documented via mucous membranes contamination and corneal and organ transplantations (15). Upon entry into the wound, the virus replicates in the muscle tissue and reach the central nervous system via motor axons. It travels to the brain then enters other non-nervous tissues such as salivary glands and abdominal visceral organs (16). The virus may be shed in the saliva before, after, or at the same time as development of clinical signs (10). The typical incubation period lasts between 1 to 3 months; however, it can range from days to several years. The initial clinical signs of rabies may be flu like symptoms including general weakness, fever or headache. As the disease progresses, an infected person may either present with acute neurological syndromes with hyperactivity classified as furious rabies or paralytic syndromes classified as dumb rabies (2, 15). Common symptoms include hydrophobia, difficulty swallowing, hallucination, hypersalivation, and agitation. Once the infected person becomes symptomatic, the virus is already disseminated throughout the central nervous system and likely other organs too (17). Rabies patients often falls into a coma and die from cardiac failure.

* 1. **Diagnosis**

Although rabies is nearly always fatal without proper post-exposure prophylaxis and after the onset of clinical signs, ante-mortem diagnosis in human is important in initiating public health measures, controlling infection, avoiding unnecessary medical treatment and testing, and administering pre- or post-exposure prophylactic vaccines to family members and medical staff. Experimental treatment can also be initiated when appropriate as the recent documentation of a patient in Wisconsin who survived clinical rabies following a bat bite using the Milwaukee Protocol without post-exposure prophylaxis renews interest in exploring treatment protocols (18).

Diagnosis of rabies based on clinical signs is difficult especially with a lack of history of animal bite and when the patient presents with paralytic syndromes. Due to similarity in clinical signs, rabies is often misdiagnosed as encephalitis. According to the WHO guideline, a clinical case of rabies can be confirmed by detection of viral antigens, isolation of virus in cell culture or laboratory animals, presence of antibodies in cerebrospinal fluid or the serum of an unvaccinated person, and detection of viral nucleic acids using RT-PCR in samples such as brain tissue, nuchal skin, saliva, and concentrated urine (2). Demonstration of antibodies in CSF in the absence of previous vaccination is less useful for ante-mortem diagnosis. Immune response may vary among individuals and the negative predictive value of the serological tests is poor (19). Limitation in ante-mortem rabies diagnosis can lead to misdiagnosis and delay public health measures. Resistance to post-mortem autopsy and brain biopsy in suspect human cases due to religious and cultural factors in both developed and developing countries can further complicate rabies diagnosis (19).

The gold standard test for post-mortem rabies diagnosis in both human and animal is the fluorescent antibody test (FA). It is the most widely used test and one that is recommended by both the WHO and World Organization for Animal Health (OIE) (19). Brain tissue samples are stained with fluorescein isothiocyanate labelled polyclonal or monoclonal antibodies directed at lyssavirus antigens and observed under fluorescence microscope (10). The specificity and sensitivity of FA are nearly 99% in laboratories experienced in fluorescence microscopy (19). In addition, examination of medulla and brainstem tissues increases the chance of viral antigen detection (2). The usage of FA can be challenging and impossible in some developing countries with limited resources due to the need for expensive fluorescence microscope and skilled personnel in interpreting the test (20). Therefore, diagnostic tests that are low in cost, maintenance, yet still provide similar sensitivity and specificity are needed for management and surveillance of rabies in endemic regions. Newer diagnostic tests for rabies have been developed recently to be more user friendly and to reduce cost. One of the tests is Direct Rapid Immunohistochemical Test (dRIT) developed at the Centers for Disease Control and Prevention (CDC). The test does not require fluorescence microscope and has been shown to be 100% sensitive and specific compared to FA in a field test in Tanzania (19). Another test is the rapid immunodiagnostic test (RIDT), which detects rabies virus antigen from post-mortem sample using principle of immunochromatography and does not require laboratory equipment. A study was done using the RIDT under field conditions in Ethiopia on samples from rabies suspected dogs, cats, and cattle. Comparing to FA, the RIDT kit had 96.5% sensitivity and 100% specificity (20).

1. **Rabies prevention in humans**
	1. **Louis Pasteur**

In 1885, Louis Pasteur saved the life of a 9-year-old boy, Joseph Meister, who was bitten badly by a suspected rabid dog with daily injection of desiccated spinal tissue from rabid rabbits for 13 days (21). The boy survived and remained symptom free. It was the first rabies post-exposure prophylaxis (PEP) performed in human. Pasteur had previously demonstrated successfully that dogs could be protected from rabies infection when he inoculated them with the same desiccated spinal tissue of rabbits that were rabid. One year after Pasteur’s successful treatment of Joseph Meister, he reported successful PEP treatment on over 300 people with one failure, likely attributed to delay in treatment (21). The nervous tissue-derived rabies vaccine became widely used since then until the development of tissue culture-derived rabies virus in the mid 1950s.

* 1. **Rabies post-exposure prophylaxis**

The rabies post-exposure prophylaxis protocol has been modified and refined over the years to elicit less side effects and reactions since Pasteur’s first successful treatment. Avoiding viral exposure and initiating prompt PEP before the onset of clinical symptoms are the most effective ways to prevent human rabies. Failure of PEP to prevent rabies is rare. Reported cases of PEP failure are mostly in developing countries and can be attributed to factors such as delay in initiating PEP, poor quality rabies vaccine, lack of or inadequate wound cleaning, and lack of or improper administration of rabies immunoglobulin (2). Due to these factors, failure rate in developing countries is estimated to be 1 in 12,000, which is higher compared to failure rate of 1 in 80,000 in developed countries (22).

The PEP protocol begins with prompt and thorough wound cleansing using soap and water or antiseptics. It is followed by administration of rabies immunoglobulin if indicated and a series of rabies vaccination (human diploid cell vaccine or purified chick embryo cell vaccine). Wound flushing is an essential first step in reducing the amount of virus at the site of entry. Following local wound treatment; human rabies immune globulin (HRIG) should be initiated as soon as possible. The goal of HRIG is to immediately provide neutralizing antibodies at the bite wound before an infected patient’s immune system is able to produce antibodies after vaccination. Therefore, HRIG should be administered into and/or around the wound sites. The dose of HRIG is 20 IU/kg of body weight. If the entire dose cannot be given at the wound sites, the remaining amount should be given intramuscularly at a site away from the rabies vaccine injection site. HRIG should be given once and promptly after exposure and concurrently with the first rabies vaccine on day 0 (2). Rabies vaccination initiates an immune response with antibody production approximately 7 days after inoculation. Therefore, HRIG is only indicated up to seven days after the first rabies vaccine. Equine rabies immunoglobulin (ERIG) is available and can be used in place of HRIG. ERIG has the advantage of being less expensive than the human product. However, ERIG has shorter half-life in humans and the dose is higher at 40 IU/kg body weight (2). ERIG is often the product of choice in developing countries because the cost of treatment is often the main limiting factor. Cost can also affect the number of rabies vaccine injections and the route of administration in different regions of the world. The various regimens of post-exposure rabies vaccination can be categorized into intramuscular administration and intradermal administration. The Advisory Committee for Immunization Practices (ACIP) in the United States recommends a 4-dose vaccine schedule administered intramuscularly (23). For previously unvaccinated person, human rabies immune globulin (HRIG) should be injected around the exposure site then follow up with intramuscular injection of 1 mL of rabies vaccine on days 0, 3, 7, and 14. An additional vaccine should be given on day 28 for immunosuppressed patients. For previously vaccinated patients, HRIG is not needed and rabies vaccination is only required on days 0 and 3 (23). Rabies vaccine should be given intramuscularly in the deltoid muscle for adults and children aged > 2 years. Gluteal area is not a recommended vaccination site for rabies vaccine due to less reliable induction of immune response (23). The anterolateral thigh is recommended for children aged < 2 years (2). The higher cost of administering cell cultured-based rabies vaccine via intramuscular route can limit their use in developing countries where rabies is endemic. As a cost saving alternative, the WHO recommends and promotes wider use of intradermal PEP. The alternative route is equally safe, immunogenic, and cost effective (2). The protocol for intradermal administration consists of 0.1 mL of vaccine injected at two different intradermal sites on each of days 0, 3, 7, and 28. It was estimated that compared with intramuscular injection, the intradermal route reduce the volume of vaccine used and decrease the direct cost of vaccine by 60-80% (24).

There are no contraindications to post-exposure prophylaxis. Since rabies is fatal without PEP, treatment should be initiated promptly when appropriate in infants, pregnant women, children with HIV/AIDS, and other immunocompromised individuals. The safety of the cell-culture-based rabies vaccines has also been evaluated including a study of vaccine safety in pregnant women in Thailand (25). Minor reactions such as transient erythema, pain or swelling at the injection site occur in 35-45% of vaccinated people. In 5-15% of people who receive rabies vaccines, mild systemic reactions such as transient fever, headache, and gastrointestinal symptoms have been reported. The serious adverse reactions are rare and are mainly of neurologic and allergic nature (25).

**4.2.1 Rabies exposure categories**

To determine the need for initiating PEP and to maximize limited resources in rabies endemic countries, the WHO has established categories of exposure to help triage patients exposed to suspected or confirmed rabid animals (2). Category I exposures consist of touching or feeding potentially rabid animals, licks on intact skin, or contact of intact skin with suspected animal or human secretion and excretion. These are not considered rabies exposure and do not require PEP. Category II exposures consist of minor scratches and abrasion without bleeding, nibbling on uncovered skin, or licks on broken skin by suspected or confirmed rabid animals (2). The WHO recommends local wound treatment and series of rabies vaccination without the need for rabies immunoglobulin. However, in the United States, HRIG is still recommended for category II exposures because the nature and severity of the exposure is subjective; therefore, it is difficult to assess the risk with certainty. Category III exposures consist of single or multiple transdermal bites, contact of mucous membrane and broken skin with contaminated saliva from suspected rabid animals. It is considered the most serious exposure and requires urgent medical attention including local wound treatment, HRIG administration, and initiation of series of rabies vaccination (2).

**4.3 Rabies post-exposure prophylaxis in developing countries**

The WHO estimated that 20 million people receive PEP each year with a direct cost of US$ 1.6 billion (2). A full course of PEP is expensive especially for families of low socioeconomic status in the developing countries who are disproportionately affected by rabies. The cost of treatment is a huge financial burden and barrier to timely treatment. A full course of PEP can cost as much as 51 days’ wage for an average worker in Africa and 31 days’ wages in Asia (2). A study in India revealed that almost 80% of animal bite victims never receive any rabies vaccine (6). As many as 60% of animal bite victims resort to faith healing and herbal therapy (2, 6). Approximately less than 20% of those that sought treatment completed the full course of PEP (6). Furthermore, only 40% of animal bite victims washed the wounds properly and rabies immunoglobulin was only given in less than 2% of the cases (6, 7). Countries like Mongolia, Myanmar, Pakistan, Algeria, and Ethiopia still use nerve tissue vaccines that are not recommended by the WHO due to their low immunogenicity (2). Lack of public awareness, prohibitive cost of PEP, inadequate training of medical personnel, and limited access to proper medical care have all contributed to mismanagement and potentially fatal consequences.

**4.4 Rabies post-exposure prophylaxis in the United States**

Rabies post-exposure prophylaxis is relatively safe and extremely effective at preventing rabies in human when administered timely and appropriately. However, rabies vaccine and HRIG are expensive and have been associated with adverse events compared with other vaccines (26). The United States currently does not have a national reporting system for rabies vaccines. The vaccine manufactures have volunteered sales data in the past but it can be challenging to obtain routine and timely access. In addition, the sales data lacks information needed to make informed public health decision such as the rate of administration. The most recent analysis in 2009 base on surveys of state health department representatives estimated an approximately 23,415 courses of PEP administered annually, or 117,075 doses of vaccine (27). The rate of administration was estimated at 8.46 PEP per 100,000 populations. The estimated average PEP rate among U.S. population affected by raccoon rabies virus variant reservoir was 13.11 per 100,000 populations. However, it is most likely underestimated as public health surveillance systems only capture 50% of the total courses of PEP administered (28).

**4.4.1 National PEP surveillance program**

A national surveillance system for PEP in the United States is recommended and supported by public health officials, veterinarians, and state health departments (27, 28). The rabies vaccine supply in the United States is tenuous. Presently, there are only two vaccines licensed for use in the country. Imovax Rabies is a human diploid cell vaccine (HDCV) manufactured by Sanofi Pasteur. The other approved vaccine is a purified chick embryo cell vaccine (PCECV) named RabAvert produced by Novartis. A voluntary recall of HDCV in 2004 due to potential partial inactivation led to revaccination of persons starting PEP with the recalled lots (27). In 2007, Sanofi Pasteur halted production of HDCV temporarily followed by decrease in PCECV production by Novartis in 2008. A shortage of rabies vaccine could lead to vaccine being unavailable to a person exposed to rabid animals, rationing of vaccines, and difficulties in managing mass exposure. Historically, the rabies vaccine and HRIG were distributed through public health departments until 1980 when cell-culture vaccines became available (27). Since then, rabies vaccines and HRIG can be acquired and distributed through private sectors such as hospitals, emergency departments, and travel medicine clinics. The shift in access often leads to administration of PEP without consultations with public health officials who are most likely to be familiar with local rabies epidemiology, existing policies, and recommendation. One study showed that the majority of PEP was administered when existing recommendations for animal quarantine or laboratory testing were not followed (28). Public health consultation reduced PEP administration rate 5 to 7 fold compared with no consultation (29). Consultation also ensured that PEP was administered correctly according to protocol (29). Surveillance of PEP administration will allow assessment of the exposure circumstances that prompt PEP administration and whether public health recommendations are followed. In addition, development of a national stockpile of rabies vaccine to avoid future supply shortage requires an understanding of PEP use in the United States.

* 1. **Rabies pre-exposure prophylaxis**

Pre-exposure prophylaxis is recommended for anyone who is at risk of exposure to lyssaviruses. Pre-exposure vaccination protocol consists of 3 doses of rabies vaccines on days 0, 7, and 21 or 28. People such as researchers and laboratory staff working with lyssaviruses, veterinarians, animal control personnel, and zoologist should receive pre-exposure prophylaxis. Risk assessment should be done for travelers traveling to rabies endemic areas to determine the need for pre-exposure prophylaxis.

**4.5.1 Childhood immunization in developing countries**

Pre-exposure prophylaxis is indicated base on occupational risk. However, some rabies endemic countries have proposed incorporating rabies pre-exposure prophylaxis into routine childhood immunization schedule for children at high risk of exposure to rabies virus. According to the WHO, about 40% of all animal bits occur in children under the age of 15 (30). Victims of dog bits often do not receive timely and proper post-exposure prophylaxis treatment. In addition, pre-exposure prophylaxis eliminates the need for HRIG in the event of an exposure since HRIG is costly and not always available in developing countries. A controlled, randomized trial performed in 240 Vietnamese infants showed that purified Vero-cell rabies vaccine when given intradermally at the same time as diphtheria, tetanus, whole-cell pertussis and inactivated poliomyelitis vaccines at 2, 3 and 4 months of age was safe with only mild, local reaction reported (31). The infants achieved the WHO acceptable protective antibody titers of > or = 0.5 IU/mL at 5 months of age. However, the debate for inclusion of rabies vaccine into childhood vaccination schedule is on going (32). Each country will need to evaluate risks, financial resources, infrastructure, and logistic capacity to determine area of focus for rabies control programs.

1. **Rabies in animals**

**5.1 Rabies surveillance in the United States**

An understanding of rabies epidemiology is crucial for eliminating animal rabies and for making recommendation regarding potential rabies exposure. Canine rabies virus variant has been eliminated in the United States since the 1970s (33). It was one of the major public health successes achieved through dog mass vaccination, licensing, stray dog control, and public education during the 1940s (2). The CDC formally declared the United States free of canine rabies virus variant associated with dog-to-dog transmission in 2007. However, spillover to wildlife population was detected as early as 1970 (34). Wildlife now accounts for more than 90% of all rabies positive animals reported in the U.S. Several circulating wildlife rabies virus variants are now well established in different terrestrial animal reservoirs with distinct geographic boundaries (35). Raccoon rabies is enzootic in all of the U.S. eastern coastal states in addition to Alabama, Ohio, Pennsylvania, Tennessee, Vermont, and West Virginia (35). There are three different skunk rabies virus variant enzootic in California, north central, and south central United States. Arctic and red foxes are the reservoir species for rabies virus in Alaska. Gray foxes in Arizona and Texas harbors two different rabies virus variants. Mongoose is the wildlife rabies reservoir species in Puerto Rico. Surveillance is crucial in preventing and controlling rabies in wildlife species. Human and animal rabies have been notifiable conditions since 1944 (35). Rabies positive animals detected from human or domestic animal exposure are reported to the CDC Poxvirus and Rabies Branch. In addition, the United States Department of Agriculture (USDA) conducts targeted and enhanced active surveillance using direct rapid immunohistochemistry test. The animals submitted under the enhanced rabies surveillance are sampled from road kills, animals found dead, euthanized animals from trapping sites with recent confirmed rabid animals, and animals exhibiting abnormal behaviors (36). Rabies surveillance results in the U.S. are published annually in the Journal of American Veterinary Medical Association. The most recent surveillance data showed that a total of 6,162 rabid animals were reported from 49 states and Puerto Rico in 2012 (33). It is a 2.1% increase from the 6,031 rabid animals reported in 2011. Out of all the reported rabid animals, 92% were wildlife with raccoon being the primary contributor. There were 1,953 (31.7%) raccoons, 1,680 bats (27.3%), 1,539 skunks (25.0%), 340 foxes (5.5%), 257 cats (4.2%), 115 cattle (1.9%), 84 dogs (1.4%), and 41 mongooses (0.67%). There are no distinct geographical boundaries for bats. Rabid bats were reported in all 48 contiguous states. No rabid bats were found in Alaska, Hawaii, and, Puerto Rico (35).

Countries and borders do not limit movement of wildlife and infectious diseases. As a result, rabies surveillance data from the two closest neighbors, Canada and Mexico, are published along with the US data annually to closely monitor potential movement of the disease. During 2012, Canada reported 142 laboratory confirmed cases of rabies. As is the case in United States, wildlife accounted for the majority of the rabid animals (n=119 [83.8%]). The wildlife tested positive for rabies in Canada during 2012 included skunks, bats, arctic foxes, and red foxes (33). Unlike the United States, Canada has not had rabid raccoons reported since 2008. The canine rabies virus variant has not been eliminated in Mexico. The country reported 12 laboratory confirmed canines rabies involving the canine rabies virus variant. The majority of the cases reported occurred in southeast Mexico where there is a large population of stray dogs and low canine vaccine coverage rates (33).

**5.2 Bats and rabies**

Bats are the primary reservoirs of lyssaviruses on all continents. The prototype rabies viruses have only been found in bats indigenous to the New World. Bat rabies was likely present in America well before colonization by European base on historical records (10). However, rabies in bats was not definitively diagnosed in the United States until early 1950s with the first documented human death from a bat bite (10). Since the elimination of canine rabies virus variant in North America, the bat variant rabies virus, especially those associated with silver-haired and eastern pipistrelle bats, has become the main cause of rabies in humans. Bats are nocturnal and prefer to hunt at night. Therefore, healthy bats normally have minimum contact with humans. Rabies infection rate in bats has been estimated to range from 4% to 15% (10). Bats that are aggressive, active during the day, or found on the ground could be ill, injured, or rabid. Some rabid bats may also appear disoriented, lose the ability to fly, and exhibit erratic behaviors such as attaching to the hands or heads of humans (10). Encounter with humans also increased due to urbanization and shared living spaces between bats and humans.

There were a total of 56 indigenously acquired cases of bat variant rabies in humans documented from 1950 through 2007 in the United States and Canada (22). A bat bite was reported by 39% of the cases and 16% reported direct contact with a bat without a bite. No direct contact with a bat was reported by 11% of the case patients who only found bats in their home. Of all the cases, 34% reported no history of bat exposure of any kind. Bats are small creatures and their bites may be less than one millimeter in diameter. As a result, many human case patients often could not recall encounter with bats. Men accounted for 76% of all the cases and 40% of the cases were between 10 to 29 years of age. The majority of the cases (72%) had < 10 weeks of incubation period with the median incubation period of 7 weeks. California (8 cases) and Texas (7 cases) had the highest number of positive cases. Diagnosis of rabies was not made until postmortem in 11% of the cases. Therefore, it is likely that human rabies in the United States could be under diagnosed in cases without autopsy or suspected exposure history. The overall incidence rate of bat rabies in humans since 1950 was 3.9 cases per billion person-years in United States and 4.4 cases per billion person-years in Canada (22).

**5.3 Rabies in domestic dogs and cats in the United States**

 A total of 519 domestic animals including cats, dogs, cattle, horses, and other farm animals accounted for 8.4% of all rabid animals reported during 2012 (33). It represents an increase of 4.6% compared to 2011. Virginia, Pennsylvania, North Carolina, Texas, Georgia, and Puerto Rico reported more than half of the rabid domestic animals during 2012. With 257 positive cases (49.9%), rabid cats accounted for most of the domestic animals reported followed by 115 cattle (22.2%). There were 84 rabid dogs reported which accounted 16.2% of all raid domestic animals (33). With the canine rabies virus variant eliminated in the United States, most of the rabid domestic animals were infected with the raccoon rabies virus variant, south central skunk variant, and the north central skunk variant after coming into contact with wildlife (33). The expansion of urbanization continues to force wildlife to come into contact with people and their pets. It was estimated that approximately 86% of post-exposure prophylaxis administered in the emergency departments were for exposure to potentially rabid dogs and cats even though dogs and cats only account for less than 10% of animal rabies each year (37). This is mainly due to the estimated 4.7 million dog bites in the United States each year with more than 300,000 patients treated in emergency rooms annually for dog bite related injuries (38). It not only highlights the close relationship people have with their pets but also the importance of continual surveillance, rabies vaccination of domestic animals, and the critical role of animal control personnel as well as local animal shelters in managing strays and unwanted cats and dogs.

Since domestic animals can serve as a link for rabies virus between wildlife and humans, vaccination of dogs and cats continue to be an extremely effective public health measure in preventing rabies in humans. However, vaccination does not offer 100% protection and rabies has been documented in vaccinated animals. Vaccine failure can be attributed to manufacturing problem, improper vaccine storage and handling, inadequate host immune response, or a particularly virulent virus variant (39). Consequently, it is important to document rabies vaccine status of rabid domestic animals to identify any potential vaccine failure associated with a specific vaccine lot number or a certain rabies virus variant enzootic in the United States. A recent study estimated that approximately 4.9% of rabid dogs and 2.6% of rabid cats had a history of rabies vaccination (39). Of the rabid dogs and rabid cats with vaccination history, 14.3% were considered currently vaccinated. Furthermore, rabies virus variant was only identified in 76.9% of rabid dogs and 9.0% of rabid cats with vaccination history. During 2012, rabies vaccination status was reported for 58.3% of all rabid dogs (33). There was no known rabies vaccination history for 36.9% of rabid dogs and 16.7% reported unknown vaccination history. For rabid cats, only 18.6% of the positive cases reported rabies vaccination status. It would be challenging to monitor trends in vaccination failure without relevant data on vaccination status. Additionally, many states do not keep or regularly monitor these data (39). Although canine rabies virus variant has been eliminated in the United States, lyssavirus can potentially reestablish among the canine population from wildlife spillover infection or importation of canine rabies virus from rabies endemic countries. Consequently, vaccination of domestic animals, rabies surveillance, and monitoring of potential vaccine failures continue to be vital public health measures.

**5.3.1 Importation of dogs**

It was estimated that more than 287,000 dogs were imported into the United States in 2006 (40). Approximately 25% of these dogs were unvaccinated including puppies under 3 months old that are not legally required to be vaccinated. The number of imported dogs appears to have doubled from 2003 to 2006 due in large part to expansion of international commercial puppy trade. Humane organizations also import rescue dogs to the United States for adoption from rabies endemic countries. The importation of dogs both legally and illegally represents an increased risk for reintroduction of canine rabies virus variant from rabies endemic countries. Rabies virus infected dogs may appear healthy due to the longer incubation period of 4 to 8 weeks in dogs. Rules and requirements can be confusing because multiple agencies like the Animal and Plant Health Inspection Service and the CDC oversee the regulation on dog importation (40). There are also exemptions in place that allow importation of unvaccinated dogs, which often require an importer to sign a confinement agreement. However, a recent survey showed that less than 35% of state agencies in the United States actually perform any type of follow-up to ensure compliance when a confinement agreement is issued (4). There are two documented cases of canine rabies virus infection in unvaccinated puppies imported from rabies endemic countries that developed clinical signs after arriving in the United States between 2004 and 2007 (40). The cost of laboratory testing, identifying potential animal and human contacts, and post exposure prophylaxis for human contacts can be high in each case (41). The CDC recently increased the minimum age of imported dogs to 4 months of age to ensure puppies are vaccinated at least 30 days before arrival in the United States with the exception of importing dogs from a rabies-free country. Constant vigilance, border control, and stringent requirements for animal importation can prevent reintroduction of canine rabies virus.

1. **Management of rabies in animals**

**6.1 Wildlife**

**6.1.1 Oral rabies vaccination**

With the elimination of canine rabies virus variant, wildlife in North America and Western Europe serve as the main reservoir for rabies virus. Rabies management program that rely mainly on oral rabies vaccination (ORV) has been successful in eliminating rabies in red foxes (*Vulpes vulpes*) since 1980 in Western Europe (3). Canada also successfully eliminated arctic fox rabies virus variant in red foxes in southern Ontario using ORV (36). However, the arctic fox rabies virus persists in southwestern Ontario from spillover infection into skunk. Moreover, the currently available ORV has been ineffective for use in skunk. Oral rabies vaccination program in the United States started in the early 1990s with the goal of preventing raccoon rabies variant from spreading westward (42). The United States Department of Agriculture, Animal and Plant Health Inspection Service, Wildlife Services program successfully initiated and eliminated canine rabies in coyotes (*Canis latrans*) in Texas from 1995 to 2007 (42). A National Rabies Management Program (NRMP) was established in 1998 within the Wildlife Services to target raccoon rabies in 15 eastern states, gray fox rabies in west Texas, and reemergence of canine rabies from Mexico (42). The NRMP and the signing of the North American Rabies Management Plan (NARMP) by Canada, Mexico, the United States, and the Navajo Nation in 2008 represent a collaborative and interagency approach in addressing rabies in North America. Various disciplines and authorities such as public health, agriculture, and wildlife management agencies are needed to coordinate, plan, and implement ORV program across numerous jurisdictions. International partnership achieved through NARMP also allow for sharing of rabies animal data, research, and surveillance in border areas between the three countries. A series of ORV zones, including the border in the northeast between the United States and Canada and border areas between Texas and Mexico, have been strategically established to prevent spread of raccoon rabies. Approximately 8.7 million baits containing live Vaccinia virus vector were distributed in 2010 via aerial and ground distribution over an area of 190,387 km2 (42).

The USDA conducts the enhanced rabies surveillance using direct rapid immunohistochemistry as part of the ORV program along the ORV zone and approximately 80 km into the areas suspected to be free of raccoon rabies. The animal data is then mapped using geographic information system so near real-time decisions can be made to adjust ORV zones or utilize other management method like trap-vaccinate-release (TVR) (36). On average, only 30% of raccoon population within the ORV zones has positive antibody response to vaccination. The response is low compared to the annual 61% average reported for gray fox and 63% for coyotes with the same oral rabies vaccines and baiting strategy (36). Because of the lower population immunity observed in raccoons with ORV, other management actions such as TVR and point infection control tactic, which integrates population reduction, TVR, and ORV around the location of a confirmed rabid animal, have been applied as contingency. Even though raccoon rabies has not spread since the implementation of ORV program, the low level of immunity in raccoon is of concern. There is a real risk for spillover infection of raccoon rabies virus into skunks in eastern United States because ORV has not been shown to induce immunity in skunks. It highlights the need for continual research and advances in new oral vaccines.

The costs of individual oral rabies vaccine bait range from $1.00 to $1.25 in the United States. The cumulative cost of the ORV program with the goal of eliminating raccoon rabies in Appalachian Ridge has totaled more than $57 million between 1997 and 2007 (43). The ORV program that eliminated canine rabies virus variant in coyote in Texas had a total cost of $28 million. A benefit-cost analysis of the program from 1995 through 2006 estimated savings ranged from $89 millions to $346 millions in cost associated with PEP treatment and testing of animals for the canine variant rabies virus with the benefit-cost ratio ranged from 3.38 to 13.12 (44). The ORV program has proven to be effective at eliminating rabies virus from wildlife reservoirs like coyotes in Texas, red fox in Western Europe, and raccoon in Canada. Though expensive, the ORV program has also been shown to be cost efficient.

**6.1.2 Control of rabies in bats**

*Carnivora* and *Chiroptera* are the major reservoir hosts for lyssaviruses. Even though annual human deaths associated with rabies is low in the United States at 2 to 3 deaths per year, bat associated rabies virus variant is responsible for most of the cases. However, eliminating lyssaviruses in bats is not possible. Bats help maintain a healthy ecosystem with seed dispersal and pollination. They are also important for agriculture by preying on night flying insects that can damage crops. Many bats species are now endangered and are protected by regulations. Urbanization continues to increase direct contact between bats and humans. Public education is one of the best measures for preventing human rabies associated with bat rabies virus variant. Preventing bats from establishing colonies in homes and commercial buildings as well as humane removal of existing colonies can decrease exposure risk. Surveillance of rabies prevalence, distribution, and diversity among wild bat population will also aid in control efforts.

**6.2 Quarantine and observation of suspected domestic animals**

Making appropriate recommendation for potential rabies virus exposure requires an understanding of local rabies epidemiology. Public health officials often have to counsel health care professional or the general public with limited information. Exposure history can be lacking or inconsistent. Suspected rabid animal may be missing or have incomplete background history. The Compendium of Animal Rabies Prevention and Control published by the National Association of State Public Health Veterinarians sets the standard for management of rabies in animals (45). According to the Compendium, a healthy dog, cat, or ferret that bites a human, regardless of vaccination status, should be quarantined and observed for 10 days. If clinical signs suspicious of rabies develop during confinement, the animal should be euthanized and tested. The 10-day quarantine period of domestic animals is a reliable way to assess the risk of rabies virus transmission from a domestic animal. However, it is not reliable in assessing wildlife and should not be used in cases of wildlife exposure. Any stray domestic animal and wildlife that bites a person should be euthanized immediately and submitted for rabies testing (45).

**6.3 Domestic dogs**

Among other emerging infectious diseases, rabies has one of the highest case fatality rates. Globally, the domestic dog remains the major species responsible for more than 90% of all cases of human rabies, especially the poorest populations in Asia and Africa. Effective tools for prevention and post-exposure prophylaxis have been used in North America and Western Europe to eliminate canine rabies with Latin America currently making great progress towards its elimination (2).

**6.3.1 Rabies control in domestic dogs**

Vaccination and population management are two main methods for rabies control in dogs. Mass culling, regardless of vaccination status of individual dogs, as a tool to control rabies has been shown to be ineffective and inhumane as there is no evidence that transmission is density dependent (46). However, it is still being carried out in several countries like China as a way for government to visibly respond to public concern about rabies. In 2006, China culled 50,000 dogs as a way to manage rabies (5). It was unsuccessful as rabies continues to persist in China with over 3,300 cases of human rabies the following year (5). Humane management of dog population through responsible ownership, basic veterinary care, and availability of sterilization services can help achieve the goal of maintaining vaccine coverage and reducing aggressive behavior and roaming. However, the role and the significance of humane management program alone or in combination with vaccination program have not been fully evaluated. Vaccination remains the most effective method for controlling rabies.

Canine mass parenteral vaccination should be held annually and must ensure at least 70% vaccination coverage to achieve herd immunity (2). All dogs regardless of age, weight, and health status should be vaccinated. Dog population must be estimated to calculate the resources required. In addition, local dog keeping practices should be considered not only to encourage more turnouts but also help in designing educational campaign regarding rabies and veterinary care. Accessing dogs for vaccination can be difficult in developing countries especially in rural areas. Most dogs in the community that appear to be strays are actually owned (47). Therefore, a combination of three approaches have been used and shown to be effective. The most time consuming approach is for vaccinators to go from house to house. The other two approaches include placing designated vaccination posts in popular sites within a community and temporary vaccination posts manned by mobile teams (2). Registration and marking of vaccinated dogs is important to evaluate the vaccination coverage and for annual follow-up vaccination. Dog collars are common and ubiquitous in developed countries. However, they are rare in rural areas and use of colored collars as temporary marking has been shown to be useful and more importantly motivate owners to take their dogs for vaccination (47). The WHO does not recommend routine serological monitoring after mass vaccination campaign if vaccination teams have been trained in proper administration technique, cold chain has been maintained, and the type of vaccine used is approved to confer protection for 2 years or more with a single injection. Recent advances in areas of oral rabies virus vaccine provide a potential alternative method for vaccinating dogs (48). Oral vaccination of dogs in developing countries can improve coverage in areas with difficult access. However, cost-effectiveness of dog oral vaccination in reaching 70% coverage has not been evaluated.

**6.3.2 Global partnerships**

Despite the availability of effective vaccine for dogs, rabies continues to be a significant problem in developing countries. Lack of political will and finance has contributed to the persistence of canine rabies in many countries. A “One Health” approach bringing together experts in animal and human health is required for eliminating canine rabies. However, there is a lack of collaboration between veterinary and human health services in many rabies endemic countries. In 2007, the Global Alliance for Rabies Control (GARC), a global nongovernmental organization, was founded to specifically focus on rabies prevention and eliminates human deaths from rabies, especially those from canine rabies(47). GARC aims to bring together different stakeholders including local communities, rabies experts, international health organizations, and pharmaceuticals. In 2008, GARC assembled experts from the Pan American Health Organization, Food and Agriculture Organization of the United Nations, the World Organization for Animal Health (OIE), the WHO rabies collaborating centers, research scientists, representatives from the Bill and Melinda Gates Foundation, the UBS Optimus Foundation, and representatives from industry to establish an initiative called Partners for Rabies Prevention (PRP). The PRP identified several key components for eliminating canine rabies (47). They are human rabies prevention, animal rabies control, education, advocacy and communication, funding, diagnostic, surveillance, and reporting. The PRP has been a prominent advocate for global rabies management base on the “One Health” approach that develop interdisciplinary partnerships to address health holistically. The Bohol Rabies Prevention and Elimination Project (BRPEP) in the Philippines was one of the first PRP initiatives that successfully managed rabies virus infection in humans and dogs.

**6.3.3 Partners for Rabies Prevention Initiatives**

Canine rabies is endemic in the Philippines with an average of 250 reported human deaths per year (49). The country has committed to eliminate human and dog rabies by the year 2020 with the enactment of the Philippine National Rabies Program (PNRA) in 2007. The province of Bohol in Philippines is the tenth largest island of the Philippines with a population of 1.13 million. It was estimated that only 2.8% of the total dog population were vaccinated against rabies in Bohol in 2006. It consistently ranked among the top ten provinces in the country with the most human rabies cases at a rate of 0.77 per 100,000 populations (49). Children less than 15 years of age accounted for 25% of the reported human rabies cases. The provincial government in Bohol conducted the first mass dog vaccination program in 2001 utilizing only the existing veterinary service at the time and failed when vaccination coverage dropped back to 2% the following year (49). The PRP, with a commitment from the provincial government, helped to launch the Bohol Rabies Prevention and Elimination Project (BRPEP) in 2007 with an ultimate goal of eliminating canine rabies virus in dogs and to ensure sustainability (47). The program brought together experts from agriculture, public health, veterinary, education, environment, and local government. The program recruited over 15,000 staff and community volunteers to facilitate vaccination, improve turnout in mass dog vaccination campaigns, and increase awareness. The dog population was initially managed by elimination of stray dogs, unclaimed dogs, and dogs voluntarily surrendered by owners. By the third year of the program in 2010, improved veterinary care such as neutering, spaying, and humane euthanasia procedures were performed by a mobile veterinary clinic (49). Rabies prevention modules were integrated into all elementary schools in Bohol to educate children on the proper way to approach dogs and that dogs can transmit rabies virus. A community wide educational campaign was also conducted to increase awareness and local support through media, posters, flyers, and hosting of seminars at churches. Surveillance was instituted to monitor vaccination status and movement of doges into and out of Bohol. Reporting of human and animal cases of rabies to provincial and national agencies was strengthened with improved laboratory diagnosis. Treatment centers specialized in dog bite related injures and administration of post-exposure prophylaxis were expanded with the government subsidizing the cost of rabies vaccines and HRIG to improve access and affordability. In addition, training of doctors and nurses in dog bite management and PEP were done for all primary care hospitals in Bohol to ensure timely diagnosis and proper PEP administration in accordance with the WHO recommendation. The legal framework for the program was in place with the enactment of PNRA at the national, provincial, and municipal level to improve compliance. One of the key features of the program that ensured its sustainability was the introduction of a small dog registration fee that was invested back into the program every year. The program has been a great success and exemplified the importance of collaboration between human and veterinary services and a nationally coordinated response in combating zoonotic diseases like rabies. The annual human rabies deaths had decreased from 0.77 to zero per 100,000 from 2007 to 2009. The mass vaccination campaign in 2007 registered and vaccinated 40% of dog population with the goal of 70% vaccine coverage achieved in 2008. The total cost of the program implementation was US$ 450,000 between 2007 and 2010 with a total of US$ 105,740 dog registration fees collected. Since the average program cost to vaccinate a dog was US$ 1.62, the registration generated enough revenue to sustain the program the following year. The success of BRPEP has led to availability in funding and similar initiatives in Indonesia, Africa, and other parts of the Philippines with the help of PRP (49).

One of the PRP’s major achievements is the Blueprint for Rabies Prevention (47). This free, web based information and practical guide offers developing countries a blueprint for designing, implementing, funding, and sustaining a rabies prevention program in their own countries. The website has also been translated into 5 different languages to ensure accessibility. The creation of World Rabies Day by GARC, observed on September 28th annually, is another PRP major initiative that aims to raise awareness and unit the global movement to end human rabies (47).

1. **Rabies in Allegheny County**

Pennsylvania ranked second in the country for the highest number of rabid raccoons reported during 2012 with 237 (12.1%) positive cases (33). Virginia ranked first with 272 (13.9%) cases of rabid raccoon. In addition, Pennsylvania reported the highest number of rabid cats with 41 cases (15.6%) during 2012 followed by Virginia with 28 cases (10.9%). In 2014, Pennsylvania reported 37 cases of rabid cats between January 1st and October 31st. Western Pennsylvania is situated in the raccoon oral rabies vaccination zone. Therefore, rabies surveillance is crucial in eliminating raccoon rabies in this strategically important area. With a population of more than 1.2 million, Allegheny County is the most populous county in Western Pennsylvania. The Allegheny County Health Department (ACHD) manages animal bite reports and advises the public and health professionals on post-exposure prophylaxis. The Public Health Laboratory at the ACHD performs direct fluorescent antibody testing on approximately 600 animals per year. Animals are submitted to the Laboratory from the public, veterinary hospitals, animal shelters, and local animal control agencies.

**7.1 Wildlife**

The Compendium of Animal Rabies Prevention and Control recommends testing of wildlife involved in human exposure to be base on the species, the local epidemiology of rabies, and the animals’ history. Unlike dogs and cats, the shedding period for rabies virus is unknown in most species and monitoring for signs of rabies infection is unreliable in wildlife (45). Therefore, rabies testing should be done if the suspected animals are available, especially for the major rabies reservoir species in Pennsylvania. During 2012, the ACHD Public Health Laboratory processed 658 animals. Less than half (44%) of the animals tested were wildlife (Table 1). Raccoons and bats were the most common wildlife submitted. There were 8 positive cases of rabid raccoons out of 89 raccoons tested. A total of 151 bats were tested and 10 were positive for rabies. There were 2 foxes that tested positive for rabies. Raccoons and bats are the two reservoir species that pose the highest risk for rabies infection in Allegheny County.

**Table 1. Animals tested at the ACHD Public Health Laboratory in 2012**

|  |  |  |
| --- | --- | --- |
|  | **Tested** | **Positive for rabies** |
| **Domestic animals** | **367 (56%)** | **0 (0%)** |
| **Wildlife** | **291 (44%)** | **20 (7%)\*** |

\*Positives: 10 bats, 8 raccoons, and 2 foxes

**7.2 Domestic animals**

In 2012, the ACHD Public Health Laboratory tested 367 domestic animals. None of the domestic animals tested positive for rabies. Even though wildlife accounts for the majority of the rabid animals in Pennsylvania, the ACHD Public Health Laboratory processed more domestic animals than wildlife. This is likely due to the close relationship people have with domestic animals and the high number of dog bite related injuries. According to the Compendium of Animal Rabies Prevention and Control, the shedding period of rabies virus in an infected dog and cat ranges from a few days before animals become symptomatic, during clinical symptoms, and to a few days before death. Therefore, a healthy dog or cat that bites a person should be confined and observed daily for 10 days from the time of exposure regardless of rabies vaccination status. However, the confinement may not be possible due to a variety of factors including limited resource, decision to euthanize by pet owners, and unavailability of suspected animals. To better understand the high number of domestic animal tested in Allegheny County and the reason for each animal submission, data including animal health status, exposure history, ownership information, and vaccination status from each animal submitted during the year 2012 were collected from rabies submission forms.

**7.2.1 Methods**

Data on all the animals submitted to the ACHD Public Health Laboratory for rabies testing during 2012 were analyzed. Rabies submission forms were used to collect data regarding animal types, exposure information, vaccine status, animal health status, ownership information, and rabies test result. The submission forms were not available in electronic format; therefore, data were entered into an excel spreadsheet manually and analyzed.

**7.2.2 Results**

The ACHD Public Health Laboratory processed and tested 367 domestic animals during 2012. Dogs and cats accounted for the majority of the domestic animals (Figure 2). Submission information was analyzed to determine whether an exposure was confirmed (Figure 2). 84.7% (n= 311) of all the domestic animal submissions indicated the animal exposed a person and 8.2% of the submitted animals did not. The rest of the submissions either had unknown exposure history or the exposure information was not specified. Of the submissions (n=311) with a confirmed exposure, 79.7% indicated the exposure occurred through bite (Figure 3). The majority (86.6%) of all the domestic animal submissions, regardless of exposure status, did not report the animal’s health status (Figure 4). Only 12.5% of all the domestic animal submissions reported that the animal exhibited neurological symptoms prior to death. The majority of the animals died by euthanasia (Figure 5). The data showed that over half of all the domestic animals (56.8%) tested at the ACHD had an owner listed (Figure 6). Shelter animals accounted for only 27.3% of all the domestic animals tested. The rest of the domestic animals (15.6%) tested were either strays or didn’t have an owner specified. Shelter animals often appear to be the majority of the submitted animals because most of the animals received at the ACHD came from animal shelters. However, further analysis showed that in addition to submitting shelter animals, Western Pennsylvania Humane Society (WPHS) and Animal Rescue League (ARL) euthanized and delivered almost half of the owned animals to the ACHD Public Health Laboratory (Figure 7). Based on the information from the rabies submission forms, 5 out of the total 208 owned animals were submitted for testing due to bite exposure while the animals were in the process of being euthanized. The rest of the submissions did not provide further case history. The information regarding the status of rabies vaccination is also lacking. Only 10 out of a total of 367 submissions reported the animal’s vaccine status. Furthermore, none of the submissions reported the date of exposure, which in combination with the animal’s health status and vaccine history are imperative in making appropriate recommendation as well as determining the need for rabies testing.

 Of the 367 domestic animals tested during the year 2012, 48.8% were dogs and 51% were cats.

**Figure 1. Types of domestic animal tested at the ACHD Public Health Laboratory**

84.7% of the total domestic animal submissions reported human exposure to domestic animals. 5.2% of the submissions did not provide exposure information. 1.9% reported that it was not known whether a human was exposed.

**Figure 2. Human exposure to domestic animals**

Out of the 311 confirmed exposures, 79.7% reported animal bite exposure, 5.5% reported physical contact only with the animals, and 8.1% reported human exposure but did not specify the type of exposure.

**Figure 3. Types of animal exposure reported**

Out of a total of 367 domestic animals submitted for testing, regardless of exposure status, only 12.5% reported that animals exhibited neurological symptoms. The majority of the submissions did not provide information regarding the animal’s health condition.

**Figure 4. Animal health status reported on submission forms**

The majority of all the domestic animals submitted were euthanized.

**Figure 5. Domestic animals’ means of death**

Over half of all the domestic animals tested at the ACHD during the year 2012 had an owner listed on the submission form.

**Figure 6. Domestic animal ownership information**

WPHS and ARL delivered approximately 49% of the domestic animals with an owner listed. 38.5% of the domestic animals with an owner listed were delivered by private veterinary hospitals.

**Figure 7. Sources of animals with an owner listed**

**7.2.3 Discussion**

The analysis of all the domestic animal submissions to the ACHD Public Health Laboratory revealed three important findings related to information that would be crucial for monitoring and managing rabies. First, more than 80% of all the domestic animals submitted during 2012 lacked information on the health status of the animal. Health status of the animal at the time of exposure is an important factor that determines the need for the 10-day quarantine. In addition, manifestation of clinical symptoms that resemble rabies infection during the observation period is an indication for rabies testing. Second, vaccination status was only reported for 10 out of a total of 367 domestic animals tested at the ACHD Public Health Laboratory during 2012. The low reporting can be attributed to the lack of questionnaire on vaccination history on the current rabies submission form. Rabies can still occur in vaccinated dogs and cats. Therefore, documentation of vaccine status is essential for monitoring vaccine failure, vaccine manufacturing problems, improper vaccine storage, and emergence of a more virulent strain of virus. Third, none of the domestic animal submissions included the date of exposure. The question on date of exposure is also not included on the current rabies submission form. Testing for rabies is not indicated in an animal that is healthy 10 days after the exposure incident. Therefore, this information is crucial in determining the appropriateness of rabies testing. Accurate and complete information is essential for effective management and monitoring. Updating the existing submission form to include vaccine history, health status, animal identification information, and date of exposure may increase the quality and the quantity of information collected for each submission.

**8.0 Conclusion**

Rabies disease is associated with significant health and economic burden. The cost of rabies is estimated to exceed US$ 6 billion worldwide including US$ 1.6 billion spent on rabies PEP alone (2). More than 60,000 people die from rabies each year, mostly in developing countries. Canine rabies is associated with the majority of the disease burden especially in Asia and Africa. Unlike previously eradicated smallpox and rinderpest that infect only humans and animals, respectively, eliminating canine rabies requires a One Health approach that integrates various sectors. A sustainable solution to combat canine rabies that combines government support, linkage of veterinary and human health services, community involvement, and support from international agencies have been demonstrated to be successful in several pilot projects in Southeast Asia and Africa. In addition to the obvious benefits in preventing human deaths and maintaining a healthy dog population that live in close contact with people, elimination of canine rabies is also economically attractive in that it is more cost effective to vaccinate dogs against rabies long term than administering PEP to victims. In countries where canine rabies has been eliminated, continuing surveillance and maintaining adequate vaccine coverage in the dog population are imperative to prevent re-emergence of canine rabies. The tools and the strategies are available to eliminate canine rabies. Global elimination can be achieved only with commitments from the governments and the global community

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