### Master of Public Health Field Experience Report

## RABIES, A GLOBAL THREAT: TAKING A LEAD ON EDUCATION & VACCINE INITITATIVES

by

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submitted in partial fulfillment of the requirements for the degree

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#### **Summary**

Rabies is the most deadly disease on earth and has a 99.9% human fatality rate. Rabies kills 61,000 humans annually and results in an economic burden of \$124 billion USD annually. Each day 3.3 million people live with the risk of rabies. It is estimated that 95% of human rabies cases are a result of coming in contact with an infected canines, majority of these cases being children 15 years and younger. It is estimated that 1 person every 8 minutes dies of rabies. Rabies is a highly neurotropic disease which attacks the brain and central nervous system. Once clinical symptoms are presented, death is invariably the outcome as no cure exists for rabies. Rabies is 100% preventable in humans by proper wound management and proper administration of prophylaxis. Rabies can be adequately controlled in animal populations by contraception and animal rabies vaccine efforts. Whilst it is known that rabies can be prevented in humans and controlled in animal populations, further scientific efforts are still warranted to fully understand this deadly virus so that a cure can one day be discovered. Limitations for a solid global foundation for the prevention and control of rabies consist of lacking national immunization programs for canines and the lack of political commitment. As human and animal populations continue to grow, so does the cost and burden of this horrific disease. Education and animal vaccine initiatives play an instrumental role in combating rabies. As we coexist with wildlife it is important to utilize and promote available resources in preventing and promptly handling exposures to a rabid animal.

Keywords: Rabies, Prophylaxis, Lyssavirus, Encephalitis, Zoonosis, Canines

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#### **CHAPTER 1 – INTRODUCTION**

"Rabies, one of the world's deadliest diseases, impacts 5 billion people, causing tens of thousands of deaths every year" (Global Alliance for Rabies Control, 2013). Rabies is a global threat and can be found on every continent, excluding Antarctica (World Health Organization, 2014). Although rabies serves as a prominent global public health threat, rabies is a preventable disease in humans by means of proper vaccination and education.

#### **History of Rabies:**

Rabies, a viral disease of mammals, is one of the oldest infectious diseases known to man and can be traced back more than 4000 years (Rupprecht, 2011). In looking through historical records, the first documentation of rabies occurred in the city of Eshnunna in 2300 BC where it was written, 'If a dog is mad and the authorities have brought the fact to the knowledge of its owner; if he does not keep it in, and it bites a man and causes his death, then the owner shall pay two thirds of a mine of silver' (Baer, 2007, pg. 1). One of the first documentations of a canine rabies case comes from a Greek philosopher named Democritus in 500 BC in which descriptions of a case of canine rabies was recorded in his papers, ("A short history of rabies," 2013). The disease of rabies is also written in early poems and books; In 800 – 700 BC Homer writes about the disease in a poem titled *The Iliad* ("A short history of rabies," 2013) and in 400 BC Aristotle depicts the disease in a book titled the Natural History of Animals (Hernandez, 2009). At the time of 400 BC, Greeks identified two gods for the prevention and cure of rabies. The god to prevent the disease was known as Arisaeus and the god said to cure rabies was known as Artemis ("A short history of rabies," 2013). The word "rabies" stems from the Latin word rabere which is defined as rave or rage. It is believed that the word *rabere* is rooted in the Sanskrit word rabhas which is defined as doing violence ("A short history of rabies," 2013). By 001 – 100 AD, rabies spread across the Roman Empire and in 1271, the first large rabies outbreak is recorded, 30 people die from rabies in Germany due to an invasion of rabid wolves ("A short history of rabies," 2013). In the 1400s, rabies spread across Spain, and in the 1700s, rabies made its way through Europe. In 1703, the first case of rabies was noted in the Americas by a priest in Mexico, and in 1953, the first case of bat rabies was recorded in the United States by the Centers for Disease Control and Prevention ("A short history of rabies," 2013).

As long as rabies has been known to man, myths about the cause, transmission and 'cures' for the disease have played an instrumental role in society and have impacted the health of animals and man. Some myths throughout history include the belief that witches cause rabies by spells and evil spirits, ambient temperatures cause rabies, or that a worm located in the base of the tongue of a canine caused rabies. It was believed that if this worm was cut and removed from the tongue, then the canine would be cured of the disease. Cauterization of wounds was also believed to cure the disease as, was having individuals physically suck the wound to remove the poisons. The same aforementioned worm was also believed to have magical powers to prevent rabies when injected. Other preventions for rabies included individuals eating cocks brains and consuming salted flesh from a rabid dog. Consuming maggots from a rabid dog were also believed to be a remedy (Baer, 2007). Furthermore, history reflects the belief of placing animal hair over the wound, would cure the disease as would having the child that was bitten by a rabid animal eat the raw heart or liver of the animal that bit them (Baer, 2007). Herbal remedies thought to cure rabies throughout history included utilizing the Angelica archangelica plant in a powered form as an external plaster. Ballota nigra plant leaves were beaten with salt and then applied to the wound. The *Pelteriga canina* plant was utilized whole with black pepper and then placed in milk, after which four doses were given to the individual or animal. The Julgans regia plant leaves would be placed in wine along with onions, honey and salt to use internally for the 'treatment' of rabies (Baer, 2007). To prevent coming in contact with a rabid animal, individuals were known to carry weasel tails as well as place the heart or tongue of a rabid dog in one's shoe (Baer, 2007). Prayer and divine intervention was another method utilized to prevent and 'cure' rabies throughout history. An example of this stems from the early centuries when Christians would travel to visit a well-known bishop by the name of St. Hubert in Europe. St. Hubert became known as the patron against rabies when it was believed that he 'cured' an individual with the disease by stating the words 'May the Lord Jesus heal you' as the individual believed to have rabies approached him (Baer, 2007). History reflects that this individual then walked away cured of the disease. This act resulted in visitations to St. Hubert from individuals around the world who believed they had the disease seeking out a cure. Individuals who owned canines suspected of having the disease from various parts of the world also visited St. Hubert to cure their canines of the 'madness'. St. Hubert utilized a metal rod in the form of a nail, known as St. Hubert's Key (Figure 1.1), to cauterize the wounds of animals

and humans that were bitten (St. Hubert Club, 2014). The idea of heating of the nail would allow for the disease to be killed once the nail was placed into the wound (they glyptodont, 2014). The role of St. Hubert led to revolt and the speaking out against superstitions in religion ("A short history of rabies," 2013). Myths about rabies continue to play an instrumental role in societies around the world. Religious and cultural beliefs are highly influential in rabies prevention and 'treatment'. Ironically, it is also currently believed that rabies is a rare disease which is not widespread around the world, whilst some share the belief that "nothing can be done to make an impact toward rabies elimination" (Rupprecht, 2011).

Although individuals were significantly influenced by the aforementioned myths for rabies cures and preventions, not all individuals were convinced of such beliefs. "Even in the 1st century, the optimism about curing rabies was not shared by Scribonius Largus, who affirms that a rabid patient is never cured..." (Baer, 2007, pg. 2). Whilst the source of rabies was questioned throughout history, it wasn't until the 1<sup>st</sup> century AD that the transmission of the disease from wild animals was recognized. In the New World, the first description of rabies transmission from a wild animal to man was documented in the early 16<sup>th</sup> century as a gentleman was dying from bites that were received from vampire bats. From the 1<sup>st</sup> century AD comes the 'first recorded attempt at defining the cause of rabies and prescribing treatments, as it was written in the words of a poem titled 'On Hunting' by author Grattius Faliscus (Baer, 2007). And in 1804 an individual named Zinke first demonstrated that rabies was transmitted through saliva. Zinke placed the saliva of a rabid dog onto an incision of another dog. The second dog began to fall ill on the seventh day, and by the tenth day obvious symptoms of the disease were present. This demonstration resulted in many articles being written about the pathogenesis (development of the disease) and 'treatment' of rabies throughout the 19<sup>th</sup> century. In 1879 Galitier proved that the disease could affect rabbits through an injection or by a bite of a rabid animal. Galitier's experiments and studies were followed by French chemist and microbiologist Louise Pasteur (Figure 1.2) who discovered that rabies is produced in the brain and spinal cord. Pasteur also discovered that if rabies was injected directly into the brain, then paralysis and death were inevitably the result. Pasteur's work proved that the brain is the fundamental organ in the pathogenesis of the disease. Pasteur then proceeded to develop the first vaccine against rabies. "The initial vaccination consisted of a series of inoculations prepared from dried spinal cord tissues from rabbits that had died from rabies, the 13<sup>th</sup> dose consisting of the most virulent

preparation" (Hooper, Roy, Barkhouse, Li, Kean, 2011, pg. 60). Pasteur's vaccine was then successfully utilized on fifty canines. In 1885 Pasteur took a step forward and utilized his vaccine on a young boy the day after the boy had been repeatedly bitten by a rabid canine. After several injections of the vaccine developed by Pasteur, the boy survived.

In 1921, thirty-five years following the work of Louise Pasteur, the first national program for canine vaccinations occurred in Japan. These efforts set a model for other countries to follow suit. The result of such endeavors lead to the World Health Organization (WHO) to set global recommendations that all canines should be vaccinated annually or every three years as approved by current vaccine labels. The WHO is an organization that "is the directing and coordinating authority for health within the United Nations system. It is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries and monitoring and assessing health trends" (WHO, 2014). The WHO continues to play a leading global role in the efforts towards rabies education and elimination on a global scale to this day.



Figure 1.1: Photograph of St. Hubert's Key, utilized to cauterize wounds to 'cure' rabies (The Glyptodont, 2014).



Figure 1.2: Photograph of Dr. Louis Pasteur, French Chemist whom developed the first rabies vaccine (Bio.True Story, 2014).

#### **Rabies Virus Introduction and Pathogenesis**

As a result of scientific advancements through time it is known that rabies is not the result of witches spells, ambient air or worms of the canine tongue as previously discussed. Rabies is an acute virus that affects the central nervous system and is almost unvaryingly fatal. Rabies is a zoonotic disease that can be transmitted from animals to humans and is primarily spread through the bite of an infected mammal through saliva. Other routes of transmission include aerosol transmission, mucosal contact (i.e., mouth, nose, eyes) licking of broken skin, transplantations of organs and corneas, and penetration of the skin from a scratch where bleeding occurs. It is important to note that non-bite transmissions rarely cause rabies in humans (Rupprecht, 1996) and that human to human transmission, aside from transplantations, has never been documented (International Travel and Health, 2014). In the United States, 5 human rabies cases out of 154 were a result of non-bite incidences from 1950 through 1980 (Rupprecht, 1996). Two cases resulted from laboratory-acquired infections and two cases were cave explorers, all of which were undoubtedly exposed to high concentrations of rabies virus (Rupprecht, 1996). The fifth human rabies case resulted from a transplant of a cornea which was received from a patient that was dying from an unsuspecting case of rabies encephalitis (Rupprecht, 1996).

The rabies virus is highly neurotropic (affects or attacks the nervous system). Once the virus enters an individual, it may replicate within the tissue (at or near the entry site) and remain sequestered (segregated or secluded) during incubation. The virus will then enter the peripheral nerves and travel to the central nervous system where it will continue to replicate, then travel out to the organs, including the salivary glands. The salivary glands are the primary exit portal in which the virus is excreted and passed on to other hosts. In humans, five general clinical stages for rabies are recognized: incubation, prodromal stage, acute neurologic phase, coma and death or very rarely, recovery (Rupprecht, 2011). In humans, the incubation period can be anywhere from ten days to ten years whilst the average incubation is three to six weeks (Rupprecht, 2014). The prodromal stage consists of nonspecific signs, such as headache, fever, nausea, sore throat, anxiety, increased sensitivity to noise and light, hallucinations, fear of air (aerophobia), fear of water (hydrophobia), etc. Additional abnormal signs can also occur during the prodromal stage, such as increased libido, nightmares, depression, insomnia, etc. The acute neurologic phase is where signs of dysfunction within the central nervous system become apparent. During the onset

of the acute neurologic phase, encephalitis (inflammation of the brain) occurs in which the central nervous system becomes dominated by the virus. At this time, the disease is then classified into one of two forms: hyperactivity, known as furious rabies, or paralysis known as paralytic rabies (also known as dumb rabies). "At the end of the acute neurologic phase, periods of rapid, irregular breathing may begin; paralysis and coma soon follow. Respiratory arrest may occur thereafter, unless the patient is receiving ventilator assistance, which may prolong survival for days, weeks, or longer, with death due to other complications" (Rupprecht, 1996). Whilst ventilation assistance can prolong the clinical signs of rabies, it will rarely affect the outcome of the disease itself. Once the onset of symptoms occurs, rabies is nearly one hundred percent fatal. "Rabies has one of the highest case-fatality ratios of any infectious disease" (MMWR, 2011).

The rabies virus is best described as an enveloped, rod or bullet shape (bacilliform) (Figure 1.3) in its appearance (morphology). One end of the virus particle (also known as virion) appears flat (planar) while the other end of the virion has a rounded appearance (hemispherical).

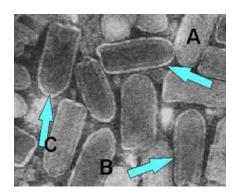


Figure 1.3: Photograph of the rabies virus. Negatively stained rabies (Rhabdovirus) as seen through an electron microscope. Notice the bullet shape of the virus (A). See the "bee hive" like striations of the RNP (B). Notice the glycoprotein spikes in the outer member bilayer (C) (Centers for Disease Control and Prevention, 2014)

The origin of the virus is that of the Mononegavirales order (WHO, 2012). The Mononegavirales order contains numerous viruses, all of which cause harmful diseases in humans. Viruses in the Mononegavirales order are single-stranded, nonsegmented, negative-stranded ribonucleic acid (RNA) genomes (CDC, 2013). Within the Mononegavirales order, the bullet-shaped viruses are classified in the Rhabdovirdae family which consists of 12 genus species (WHO, 2012). Rabies is part of the Lyssavirus genus (WHO, 2012). To better understand how these names were identified, the Greek words rhabdos means 'rod' and lyssa means 'rage' (Wunner, 2007). The rabies virion is approximately 180 nanometers (nm) long and 75 nm wide (CDC, 2013). Rabies is an RNA virus, as previously mentioned, in which the virus particle (virion) encodes five different proteins. These proteins are nucleoprotein (N),

phosphoprotein (P), matrix protein (M), glycoprotein (G) and polymerase (L) (CDC, 2013). The basic structure of the rabies virus is depicted in Figure 1.4 while Figure 1.5 depicts the relative size and order of the proteins.

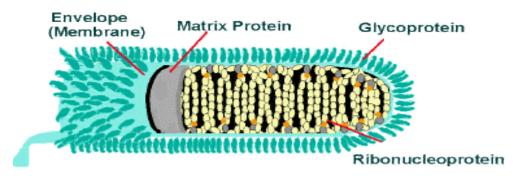


Figure 1.4: Rabies virus (virion) is rod or bullet-shape with spike-like glycoprotein covering the surface. The ribonucleoprotein is composed of RNA encased in nucleoprotein (Centers for Disease Control and Prevention, 2014)

#### Rabies Genome



Figure 1.5: The rabies virus encodes five proteins; (N) nucleoprotein, (P) phosphoprotein, (M) matrix protein, (G) glycoprotein and (L) polymerase. The order and the size of the proteins is imperative as this makes up the virus (Centers for Disease Control and Prevention, 2014).

It is important to note that the location of these five proteins and the RNA determine the structure of the rabies virus. While this paper will not go into detail in describing the replication and strategies of the rabies virus, it is important to understand the virus and how it affects individuals and continues to survive and infect new individuals.

All rhabdoviruses, including the rabies virus, include two major structural components. These two components are a helical ribonucleoprotein core (RNP) and a surrounding envelope. The L and the P protein are associated with the RNP as they aid in the replication process. The G protein which is spiked, as depicted in Figure 1.4, is located on the surface of the virion as it is used to physically attach to the host cell membranes (Rupprecht, 1996). The M protein is associated with the RNP and the envelope which plays a key role in virion assembly and egress

(Okumura, Harty, 2011). The M protein is also known to play an important role in giving the virion its bullet-shaped appearance (Wunner 2007). Without going into great detail, the N protein encapsidates (encloses) the genomic and antigenomic RNA. The genomic includes an individual's full DNA sequences (Web definitions, 2014).

The life cycle of a rabies infection begins by the attachment of the virion to the surface of the cell membranes in which penetration of the virion is initiated. It is important to note that most often the virion attaches to a receptor molecule that will permit the virion to enter the susceptible cell membranes (Wunner, 2007). The life cycle of the rabies infection can be divided into three phases. The first phase, as discussed, includes the attachment of the virion to susceptible cell membranes by which the virion then enters the host cell. This phase initiates the infection process. This phase of the life cycle is considered to be the most difficult phase (Wunner, 2007). The second phase of the life cycle includes replication of the virion in the host cell. The third phase consists of final replication of new virions which are then released (budding) from the cell to attach to new host cells, starting the life cycle process over again. The life cycle process is seen in Figure 1.6.

"Rabies is a fatal disease. Clinical management of rabies patients should include adequate sedation and care in an appropriate medical facility with suitable emotional and physical support" (WHO, 2012). If intensive care is not provided, death normally occurs within two weeks of the onset of clinical signs, although typically, death results in seven to ten days after the first clinical sign (WHO, 2012). It is important to note that there currently is no cure for rabies after the onset of clinical symptoms. An experimental approach, known as the Milwaukee protocol, has been utilized around the world on approximately 40 patients. This protocol involves inducing the patient into a coma state and administering antiviral drug treatment. Out of the 40 patients around the world, there are 4 reported survivors (Centers for Disease Control and Prevention, 2013). "Despite these observations, rabies must still be considered 100% fatal for practical purposes, and preventive measures remain the only way to guarantee survival after a bite by a rabid animal" (Centers for Disease Control and Prevention, 2013, pg. 1).

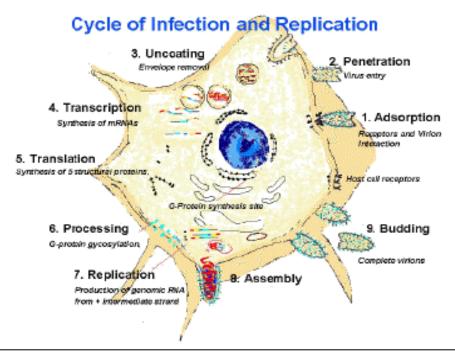


Figure 1.6: Steps of the life cycle of the rabies virus/virion for infection and replication in a susceptible host cell (Centers for Disease Control and Prevention, 2014).

#### **Rabies Diagnosis**

As aforementioned, rabies is part of the Rhabdoviridae family and is caused by a Lyssavirus which is an acute progressive encephalitic disease that can affect all mammals. It has also been discussed that "rabies has one of the highest case-fatality ratios of any infectious disease" (Compendium of Animal Rabies Prevention and Control, 2011). Rabies is a difficult disease to diagnose as it mimics the signs of other diseases and is often misdiagnosed in the early stages when clinical signs first appear (World Organization for Animal Health, 2009). Although a variety of testing methods exist, it is important to note that a negative test does not rule out a rabies infection.

In animals (all mammals excluding humans) rabies can be diagnosed, however, the animal must first be euthanized (put to death) as tissues from the brain must be collected and tested. Two tissues from the brain are required for testing and in order to successfully rule out a rabies diagnosis, the cerebellum and the brain stem must be test negative. Brain tissue is required as the rabies virus resides in the nervous tissue and not blood as other viruses (Centers for Disease Control and Prevention, 2014). The testing method utilized is the Direct Fluorescent

Antibody test known as the DFA test. Whilst other testing methods exist, the DFA test is the gold standard for rabies diagnosis and must be performed according to standard protocol (Compendium of Animal Rabies Prevention and Control, 2011). The DFA test utilizes antibodies that attach to the rabies virus (antigen) in the brain samples if the animal is positive for rabies. When the animal is positive for rabies the samples will show a green-apple fluorescent color when viewed under a fluorescent microscope (Figure 1.7), this green-apple fluorescent will not be viewed for a negative sample (Figure 1.8). Whilst the DFA test and other methodologies are beneficial in diagnosing rabies, it has been proven through public health surveillance and pathogenic studies that euthanizing an animal is not always necessary. For animals that have a low probability of being rabid after biting an individual, the animal may be quarantined for 10 days to rule out rabies. If the animal survives on and after the 10<sup>th</sup> day, than the rabies virus was not present in the saliva at the time of the bite. This quarantine is effective as the salivary gland is an exit route and the animal will not survive the virus longer than 10 days once the virus is shedding in the saliva (Compendium of Animal Rabies Prevention and Control, 2011).

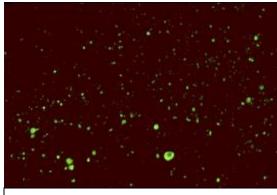


Figure 1.7: DFA test viewed through a fluorescent microscope that is positive for rabies, (Centers for Disease Control and Prevention, 2014).



Figure 1.8: DFA test viewed through a fluorescent microscope that is negative for rabies, (Centers for Disease Control and Prevention, 2014).

For humans, a test does not exist for diagnosing rabies infection prior to the onset of clinical disease, and unless the rabies-specific signs of hydrophobia or aerophobia are present, the clinical diagnosis may be difficult (World Health Organization, 2013). Once clinical symptoms are present, several tests are available as no single test is sufficient in diagnosing human rabies ante-mortem (before death). Ante-mortem diagnosis includes detecting the antigen or nucleic acids of the rabies virus or by virus isolation. Samples utilized to detect rabies from

humans include saliva, corneal impressions, eye wash fluid, central spinal fluid (CSF), tears, and skin biopsies (nuchal). The nuchal biopsies are taken from the nape of the neck as the rabies virus is found in cutaneous nerves, which are located at the base of the hair follicle (World Organization for Animal Health, 2009). Serum may also be tested to look for antibody production against the rabies virus. Antibody production is also tested for when testing the CSF. It is important to note that antibody production in the CSF can result from individuals that have previously been vaccinated against rabies. It is also noteworthy that antibody response from a true rabies infection occurs in the late stages of the illness and the individual may die prior to this occurrence, resulting in a negative CSF test for circulating antibodies at the time of death. These samples may also be utilized for post-mortem (after death) diagnosis in humans along with samples of the brain from the infected individual. As a result, "postmortem diagnosis is usually by immunofluorescence to detect viral antigens in the brain" (WHO, 2013, pg. 3).

#### Rabies Vaccine, Prophylaxis and Immunoglobulin

Several scientific and technological advancements have progressed since following the days of Louis Pasteur when the first rabies vaccine was developed in the 1880s. Injectable animal rabies vaccine is currently approved for dogs, cats, ferrets, horses, sheep and cows. The vaccines provide a variation of duration of immunity from 1 to 4 years (Compendium of Animal Rabies Prevention and Control, 2011). In reference to domesticated animals, local governments are tasked with ensuring that effective vaccine programs are maintained. Animal vaccines may be administered intramuscularly (in the muscle) or subcutaneous (under the skin).

Controlling rabies in wildlife is extremely difficult (Compendium of Animal Rabies Prevention and Control, 2011); however, the vaccination of free ranging wildlife or selected wildlife populations can be beneficial. The oral rabies vaccine (ORV) was developed and designed to vaccinate certain wildlife species in the form of a sachet (Figure 1.9). The sachets are approximately the size of a matchbox and along with the vaccine the sachet can include fishmeal to attract certain animal species (Figure 1.10). The sachets are distributed in the animal's environment by air and ground personnel. Once the animal finds and bites into the sachet the animal then swallows the vaccine and is then vaccinated for rabies. ORVs have been utilized in Europe since 1980, Canada since 1985 and the United States since 1990 (United States Department of Agriculture, 2012).

ORVs have been successfully utilized to vaccinate raccoons, foxes, and coyotes in the United States. The attempt to successfully vaccinate skunks with ORVs in the United States was attempted in the state of Texas during the routine ORV baiting in February 2014 (Forsyth, 2014).



Figure 1.9: Photograph of coated sachet baits containing rabies vaccine only utilized for ORVs, (United States Department of Agriculture, 2012).



Figure 1.10: Photograph of ORV baits containing fishmeal and rabies vaccine, (United States Department of Agriculture, 2012).

It is important to note that translocation of wildlife has made a significant impact in the spread of rabies. As a result, the translocation of known rabies carrier species should be prohibited (Compendium of Animal Rabies Prevention and Control, 2011).

In respect to human rabies vaccines (prophylaxis), two areas of emphasis exists 1) pre-exposure prophylaxis and 2) post-exposure prophylaxis. Pre-exposure prophylaxis is aimed at vaccinating individuals that have a risk of being exposed to the rabies virus. Pre-exposure prophylaxis is used as a preventive measure. Individuals in this category include veterinarians, individuals traveling to an area with increased risks to rabies (endemic), animal control officers, wildlife officers or laboratory personnel working with the rabies virus (WHO, 2014).

Individuals in this group are considered high risk or continuous. Pre-exposure prophylaxis should be considered for all individuals that consistently have the potential to be exposed to the rabies virus or have frequent potential contact with animals that can carry the rabies virus. These individuals are considered moderate and low risk or frequent and infrequent (Table 1.1). Pre-exposure prophylaxis consist of three doses of vaccine administered intramuscularly on day 0 (day of first vaccine), 7 and 21 or 28 (Centers for Disease Control and Prevention, 2014).

Table 1.1: Rabies Pre-exposure Prophylaxis Guide, (Centers for Disease Control and Prevention, 2014).

| Rabies Pre-exposure Prophylaxis Guide |   |   |  |  |
|---------------------------------------|---|---|--|--|
| Risk<br>Category                      | Nature of Risk  | Typical Population  | Pre-exposure<br>Recommendations  |  |
| Continuous                            | Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, nonbite, or aerosol exposure. | Rabies research laboratory workers; rabies biologics production workers.  | Primary course. Serologic testing every 6 months; booster vaccination if antibody titer is below acceptable level. |  |
| Frequent                              | Exposure usually episodic, with source recognized, but exposure also might be unrecognized. Bite, nonbite, or aerosol exposure.             | Rabies diagnostic lab workers,<br>spelunkers, veterinarians and staff, and<br>animal-control and wildlife workers in<br>rabies-enzootic areas. All persons who<br>frequently handle bats. | Primary course. Serologic testing every 2 years; booster vaccination if antibody titer is below acceptable level.  |  |
| Infrequent                            | Exposure nearly always  | Veterinarians and terrestrial animal-   | Primary course. No serologic   |  |

control workers in areas where rabies is

uncommon to rare. Veterinary students.

Travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care including

U.S. population at large, including

persons in rabies-epizootic areas.

Table 1.2: Rabies Post-exposure Prophylaxis Guide, (Kentucky Public Health Practice Reference Section, 2010).

biologics is limited.

| Rabies Post-exposure Prophylaxis Guide |               |   |  |  |
|--|---------------|---|--|--|
| Type of vaccination                    | Route         | Regimen   |  |  |
| Primary                                | Intramuscular | Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV); 1.0 mL (deltoid area), one each on days 0,* 3, 7, and 14 |  |  |
| Booster†                               | Intramuscular | HDCV or PCECV; 1.0 mL (deltoid area), day 0 and 3   |  |  |

<sup>\*</sup>Day 0 is the day the first dose of vaccine is administered.

Rare

(population

at large)

episodic with source

exposure.

recognized. Bite or nonbite

Exposure always episodic

or nonbite exposure.

with source recognized. Bite

testing or booster vaccination.

No vaccination necessary.

<sup>†</sup>Persons in the continuous-risk category should have a serum sample tested for rabies virus neutralizing antibody every 6 months, and persons in the frequent-risk category should be tested every 2 years. An intramuscular booster dose of vaccine should be administered if the serum titer falls to maintain a value of at least complete neutralization at a 1:5 serum dilution by Rapid Fluorescent Focus Inhibition Test.

Post-exposure prophylaxis is aimed at vaccinating individuals that have possibly been exposed to the rabies virus. 'Have possibly' been exposed is stated as individuals may not be aware they have been exposed or bitten. An example is when a bat is found in the same area such as; a bedroom or tent, of an infant, adult or child (includes intoxicated or mentally disabled individuals). Bats have small sharp teeth and often times the bite is unnoticed. Bite marks from a bat can go unnoticed and often disappear in a short time frame. Post-exposure prophylaxis for individuals that have not been previously immunized for rabies include four intramuscular doses on days 0 (day of first vaccine), 3, 7 and 14 (Centers for Disease Control and Prevention, 2011). Individuals that have previously been immunized and have documentation of virus neutralizing antibody production in response to the initial rabies immunizations will receive two booster doses at days 0 (day of first vaccine) and 3 (Table 1.2). Rabies immune globulin (RIG) is also administered with post-exposure prophylaxis for individuals that have never previously received rabies prophylaxis. Two types of RIG exist that are administered around the world, human rabies immune globulin (HRIG) and equine rabies immune globulin (ERIG). RIG is an injection that is administered around the wound as RIG should be infiltrated where the teeth and saliva penetrated into the skin (Centers for Disease Control and Prevention, 2014). "Rabies immune globulin is a sterile solution of antibodies that provides individuals with immediate short-term protection against rabies" (Government of Saskatchewan, 2014, pg. 1). RIG is administered on day 0, the same day the first dose of post-exposure prophylaxis is administered. RIG is administered as the antibodies provide short passive immunity to protect against the rabies virus while the individual's body is in process of producing antibodies from the prophylaxis (Mayo Clinic, 2014). RIG is administered according to body weight, 20 IU/kg (Centers for Disease Control and Prevention, 2013). Table 1.3 outlines the three categories that exist to determine if an individual is to receive RIG along with the 4 dose post-exposure prophylaxis.

Immunocompromised individuals receive a 5 dose regimen for post-exposure prophylaxis, administered on days O (day of first vaccine), 3, 7, 14 and 28 (Centers for Disease Control and Prevention, 2011). Immunocompromised individuals also receive one dose of RIG on day 0. For infants and children post-exposure prophylaxis and RIG is the same regimen as adults (Centers for Disease Control and Prevention, 2013). Pregnant women, unless immunocompromised, are directed to follow the 4 dose post-exposure and RIG regimen (Center for Disease Control and Prevention, 2010).

| Category of Exposure | Type of exposure to a domestic or wild <sup>1</sup>  | Recommended Post-exposure Prophylax                    |
|----------------------|--|--|
| Category of Exposure | animal suspected or confirmed to be                  | Recommended Post-exposure Propriylax                   |
|                      | ·  |  |
|                      | rabid, or animal unavailable for testing             |  |
| I                    | Touching or feeding animals                          | None, if reliable case history is available            |
|                      | Licks on intact skin                                 |  |
|                      | Contact of intact skin with secretions or            |  |
|                      | excretions of a rabid animal or human case           |  |
| II                   | Nibbling of uncovered skin                           | Administer vaccine immediately <sup>2</sup> . Stop     |
|                      | Minor scratches or abrasions without                 | treatment if animal remains healthy                    |
|                      | bleeding   | throughout an observation period of 10                 |
|                      |  | days <sup>3</sup> or is proven to be negative for rabi |
|                      |  | by a reliable laboratory using appropriat              |
|                      |  | diagnostic techniques.                                 |
| III                  | Single or multiple transdermal bites <sup>4</sup> or | Administer rabies vaccine immediately a                |
|                      | scratches, licks on broken skin                      | rabies immunoglobulin, preferable as so                |
|                      | Contamination of mucous membrane with                | as possible after initiation of post-                  |
|                      | saliva (i.e. licks)                                  | exposure prophylaxis. Rabies                           |
|                      | Exposure to bats⁵                                    | immunoglobulin can be injected up to 7                 |
|                      |  | days after first vaccine dose                          |
|                      |  | administration. Stop treatment if anima                |
|                      |  | remains healthy throughout an                          |
|                      |  | observation period of 10 days or is prove              |
|                      |  | to be negative for rabies by a reliable                |
|                      |  |  |
|                      |  | laboratory using appropriate diagnostic                |

<sup>1</sup> Exposure to rodents, rabbits or hares does not routinely require rabies post-exposure prophylaxis.

<sup>2</sup> If an n apparently healthy dog or cat in or from a low-risk area is placed under observation, treatment may be delayed.

<sup>3</sup> This observation period applies only to dogs and cats. Except for threatened or endangered species, other domestic and wild animals suspected of being rabid should be euthanized and their tissues examined for the presence of rabies antigen by appropriate laboratory techniques.

<sup>4</sup> Bites especially on the head, neck, face, hands and genitals are category III exposures because of the rich innervation of these areas.

<sup>5</sup> Post-exposure prophylaxis should be considered when contact between a human and a bat.

The first step of defense when bitten or scratched by any animal is proper wound care and management. At the time of the bite or scratch immediately wash the wound aggressively for several minutes with an abundant amount of soap and water. This action can significantly decrease the risk for rabies as it physically decreases the amount of saliva and rabies virus from the wound (WHO, 2013). Medical consultation immediately follows this crucial first-aid step of washing of the wound for determining the appropriate action. "It is important to remember that rabies is a medical urgency but not an emergency. Decisions should not be delayed" (Centers for Disease Control and Prevention, 2011, pg. 1).

#### **Human Rabies Case**

When discussing the rabies virus, pathogenesis, diagnosis and prophylaxis; it is often hard to put it into perspective the events that take place and how an individual is affected from the rabies virus and why rabies is such an important public health concern. To better understand, a human case from 2011 will illustrate the timeline from exposure to death disclosing the physical characteristics and final impact of the disease for one individual.

In January 2011 Private First Class (Pfc.) Kevin Shumaker (Figure 1.11), 24 years old, received a bite to his right hand from a feral dog while deployed in Afghanistan. As Pfc. Shumaker was preparing for a new military assignment, on August 14<sup>th</sup>, 2011 he experienced shoulder pain and paresthesia (unexplained burning, tingling or pricking on the skin) during his travel to Fort Drum, New York from Grafenwöhr Germany (Morbidity and Mortality Weekly Report, 2012). Prior to August 14<sup>th</sup>, 2011 Pfc. Shumaker was medically listed as a healthy individual. Pfc. Shumaker began to have symptoms of nausea, vomiting and fever. August 15<sup>th</sup>, 2011 Pfc. Shumaker visited an emergency room where he was released (Morbidity and Mortality Weekly Report, 2012). August 15<sup>th</sup> and 16<sup>th</sup>, 2011 Pfc. Shumaker visited a chiropractor for the reasons of pain and then August 17<sup>th</sup>, 2011 Pfc. Shumaker made a second emergency room visit and again was released (Morbidity and Mortality Weekly Report, 2012). The diagnosis for both emergency room visits were listed as gastritis and neck tendonitis. August 18<sup>th</sup>, 2011 Pfc. Shumaker was having difficulties swallowing and on August 19<sup>th</sup>, 2011 he was evaluated by the medical team at Fort Drum (Morbidity and Mortality Weekly Report, 2012). At this time Pfc. Shumaker's symptoms were ataxia (lack of muscle control) and syncope (partial or complete loss of consciousness) in which the medical team at Fort Drum sent him to the same emergency room that he previously visited on two occasions the few days prior (Morbidity and Mortality Weekly Report, 2012). At the time of his arrival Pfc. Shumaker was dehydrated, lucid (easily understood) and hydrophobic and showing signs of aerophobia (Morbidity and Mortality Weekly Report, 2012). Pfc. Shumaker advised he received a bite from a dog while in Afghanistan. As a result of this knowledge and the aforementioned recent medical history, rabies was suspected. The New York State Department of Health (NYSDOH) and the Centers for Disease Control and Prevention (CDC) were then immediately notified. On that same day, August 19th, 2011, Pfc. Shumaker was transported to a second hospital (Morbidity and Mortality Weekly Report, 2012). At the time he arrived he was becoming agitated and combative.



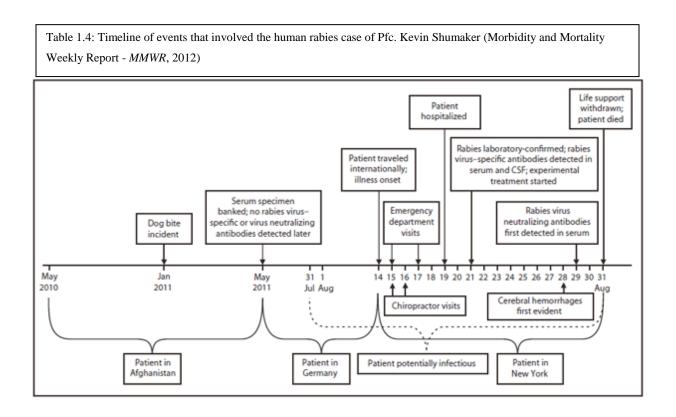
Figure 1.11: Private First Class Kevin Shumaker. Photo taken October 28, 2010 (Mail Online, 2012).

Upon his arrival, serum, saliva, CSF and a nuchal biopsy samples were taken and submitted for rabies analysis. On August 20<sup>th</sup> and 21<sup>st</sup>, 2011 the test results revealed rabies virus antigen in the hair follicles from the nuchal biopsy and viral RNA was revealed in the saliva and CSF (Morbidity and Mortality Weekly Report, 2012). The CDC confirmed that rabies virus antibodies were detected in the serum and CSF. On August 19<sup>th</sup>, 2011 the Milwaukee Protocol was implemented as a life saving measure for Pfc. Shumaker (Morbidity and Mortality Weekly Report, 2012). Pfc. Shumaker was intubated, his pupils were dilated and his nervous system was not functioning properly. Although no brain abnormalities were present a pacemaker was

inserted due to complete heart blockage. On August 20<sup>th</sup>, 2011 intracranial pressure was monitored by the placement of and external ventricular drain (Morbidity and Mortality Weekly Report, 2012). August 21<sup>st</sup>, 2011 he suffered from a severe form of diabetes and on August 22<sup>nd</sup> there was severe brain swelling and acute respiratory distress (Morbidity and Mortality Weekly Report, 2012). Small brain hemorrhaging began on August 28<sup>th</sup> and on August 30<sup>th</sup> severe brain hemorrhaging was documented (Morbidity and Mortality Weekly Report, 2012). Family was advised that Pfc. Shumaker would unlikely recover and life support was ceased on August 31<sup>st</sup>, 2011 (Morbidity and Mortality Weekly Report, 2012).

It is noteworthy to mention that a serum sample of Pfc. Shumaker from May 2011 was tested at the CDC in August 2011 and no specific rabies antibodies were found in this sample (Morbidity and Mortality Weekly Report, 2012). This indicates that Pfc. Shumaker did not receive post-exposure prophylaxis or RIG following the dog bite to the right hand.

Table 1.4 represents the timeline of the incidents that occurred from the time Pfc. Shumaker was in Afghanistan to the time of his unfortunate death from the rabies virus.

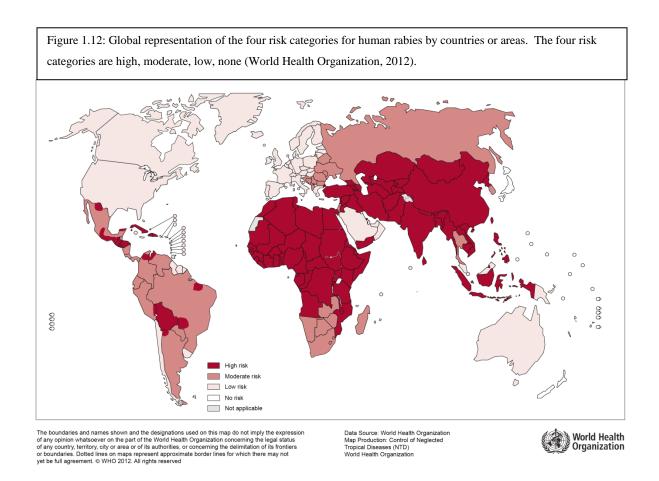


#### **Global Burden of Rabies**

As stated by the World Organization for Animal Health (OIE), rabies is found on 6 of the 7 world continents, Antarctica is the exception (OIE, 2014). Globally, dogs are the main source of rabies as over 95% of human deaths result from infected dogs (Briggs, 2013). According to current statistics provided by the Partners for Rabies Prevention an average of 61,000 human deaths occur annually from rabies (WHO, 2012). Of those deaths, up to 60% are children under the age of 15 years old (Global Alliance for Rabies Control, 2013). It is known that 84% of the 61,000 human deaths occur in rural areas (WHO, 2012). These rural areas are in "poor, remote regions where healthcare provision is minimal, and reporting even more so, plus awareness among the general population almost non-existent" (Briggs, 2013). "And because most cases tend to be isolated, the statisticians tend to miss the big picture worldwide, which is that one person dies very eight minutes" (Briggs, 2013). Underreporting, misdiagnosis, poor surveillance and the lack of infrastructure result in an underestimation of knowing the true burden of the disease on a global scale (WHO, 2012). Over 95% of the human deaths from rabies occur in Asia and Africa (Global Alliance for Rabies Control, 2013) with India reporting the highest incidence globally (WHO, 2012). Figure 1.12 depicts the global distribution of risk for human rabies (WHO, 2012). It is estimated that 3.3 million people live with the risk of rabies every day (Global Alliance for Rabies Control, 2014).

Whilst it is known that rabies impacts life on a physical, social and psychological level, rabies also impacts the world on an economic level. In 2013 it was assessed that canine rabies results in \$124 billion USD annually for global economic output (Global Alliance for Rabies Control 2013). While loss of human life is the most devastating impact of rabies, loss of human life also results in the highest financial cost (Global Alliance for Rabies Control, 2013). The financial cost takes into account the deaths and the future lost earnings of the individuals that have died, which is known to directly impact the communities (Global Alliance for Rabies Control, 2013). The next highest financial cost of rabies is the cost of rabies prophylaxis (Global Alliance for Rabies Control, 2013). In reviewing specific costs around the world, we find that in the United States the CDC estimates that \$300 million are spent on rabies prevention annually (WHO, 2012). Although fox rabies has been eliminated from Western Europe, \$6.5 billion USD is spent annually on post-

exposure prophylaxis (WHO, 2012). In taking a direct look at post-exposure prophylaxis, in Asia and individual pays 3.87% of their gross national income for a full series of post-exposure prophylaxis while an individual in Africa will pay 5.80% (WHO, 2012). To put this into perspective, this constitutes the pay of working 51 days for the individual from Africa and 31 days for the average individual in Asia (WHO, 2012).



In looking back to the year 1985, it is documented that Latin America and the Caribbean had an annual cost of \$30 million USD from loss of livestock directly resulting from vampire bat rabies.

The economic cost of rabies is substantial. "Rabies is the deadliest disease on earth with a 99.9% fatality rate" (Global Alliance for Rabies Control, 2014), and due to the result of growing populations of humans and canines around the world the economic cost of rabies along with the burden of human deaths will also continue to grow (WHO, 2012).

#### **CHAPTER 2 – FIELD EXPERIENCE**

#### **Global Alliance for Rabies Control:**

In 2006/2007 the Alliance for Rabies Control (ARC), a Non-government Organization, (UK charity number SC037112) was established by a group of rabies experts and scientific stakeholders with the mission of one day eliminating human deaths from rabies and to relieve the burden of rabies in animals, especially dogs (Stukey, 2102). Months following in 2007, the Global Alliance for Rabies Control (GARC), a Non-government Organization, was established in the Unites States as a 501c3 class non-profit organization (Stukey, 2012). From these two non-government branches, the World Rabies Day campaign was developed and the first annual global World Rabies Day occurred in September 2007. The mission of the World Rabies Day campaign "is to raise awareness about the impact of human and animal rabies, how easy it is to prevent it and how to eliminate the main global sources" (WorldRabiesDay.org, 2001, pg. 1). World Rabies Day persists today with global events taking place year round to continue this mission. The Partners for Rabies Prevention (PRP), as aforementioned, was an initiative of GARC developed in 2007. The PRP is a working group of global experts from the WHO, OIE, GARC, the Food and Agricultural Organization of the United Nations, research scientists, representatives from industry, UBS Optimus Foundation and representatives from the Bill and Melinda Gates Foundation (GARC, 2014). As we are aware that rabies is 100% preventable in humans, GARCs vision is "a world free of human rabies" (GARC, 2014, Pg. 1). For my field experience, I had the honor of teaming up with GARC to implement programs and secure resources for educational campaigns and distribution of resources on a global scale. The tasks that I performed with GARC are as follows in the paragraphs below.

#### **Zach Jones Memorial Fund**

One of my unique opportunities was to work with the Zach Jones Memorial Fund (ZJMF), a 501c3 non-profit organization that was established in 2006, by Mr. and Mrs. Larry Jones in honor of their son Zachary "Zach" Ross Jones. At the age of 16, Zach awoke to a bat in his room after napping, and without hesitation the bat was released to the outdoors. Weeks

following this incident, May 2006, Zach became ill and was diagnosed with rabies. On May 12, 2006 Zach died of rabies (Zach Jones Memorial Fund, 2013). Larry and Connie Jones, of Humble Texas USA, established the fund to honor Zach's life and to promote rabies education, in hopes of preventing another family from facing the same tragic loss. The mission of ZJMF "strives to raise funds in order to assist with educational awareness, early detection, and ultimately the cure for rabies. ZJMF also grants scholarships to graduating seniors from the Atascocita High School" (JZMF, 2014, Pg. 1).

It was with great honor that I had the opportunity to write a grant and submit a proposal to ZJMF. The intent was to secure funds and prepare a project that would share Zach's story and educate adolescents on rabies awareness and control across the USA. I completed and submitted a proposal that was reviewed and accepted by GARC to present to ZJMF. The proposal was to educate 1 million adolescents about bats and their role in transmitting rabies. The backbone of this project was to educate adolescence on what rabies is, how to prevent it and what to do in the event of an exposure, or possible exposure. The project design included the development of a poster for display and an educational video in English and Spanish. An electronic survey was also anticipated so that data could be collected on the existing needs of rabies educations for this target audience. The dissemination of the products (video, poster and link for electronic survey) would happen through existing partners of GARC that currently have programs established with adolescents. In order to reach 1 million adolescent children, the products need to be received by approximately 30,000 classrooms. Projected costs listed in the proposal were listed at \$46,445 USD (Table 2.1). The proposal requested that 50% of the listed amount come from ZJMF, which would total a donation of \$23,222.50 USD to GARC. The remaining \$23,222.50 USD was be support from existing funds already secured by GARC for educational initiatives. ZJMF immediately accepted the proposal and submitted a donation check of \$18,000 USD for these initiatives to GARC. The title of the proposal was 'Zach "Z" Jones US Rabies Education Proposal'. News of the ZJMF donation and acceptance of the proposal was received and the project targeting adolescents for bat and rabies education began immediately. A small working group, in which I held a leading position, was immediately formed and included members of GARC and the CDC. The working group consisted of rabies experts, scientists, a translator and a graphic designer. The goals and agenda of the poster were presented to the working group, that the focus was bats and rabies targeting adolescents. As photos and write-ups were instantly

physically displayed on the poster had to be age appropriate to be the most effective. The poster was not to allow for interpretations and questioning as the topic was critical. The poster had to be direct and factual while physical space to accomplish this was limited. Individuals in this working group were physically spread out across the USA. As a result, in order to communicate effectively and efficiently conference calls were held weekly and the email system was utilized heavily for ongoing conversations and sharing of graphics.

| Table 2.1: Projected cost of 'Zach "Z" Jones US Rabies Education Proposal (Stukey, 2014) |                          |
|--|--------------------------|
|  | 3,711.04                 |
| 19"X25" Panel Size Poster/4 Color Process Inks/80# Gloss Coated Text Paper               |                          |
| Envelopes for shipping   | 2,237.44                 |
| Non-profit Postage   | 743.31                   |
| Including DVD /Computer Compatible Video in Packet for Mailing                           | 4,600                    |
| Copying of DVD/Computer Compatible Video (Includes protective jacket)                    | 20,700                   |
| Electronic Survey (GARC will handle logistics & statistics)                              | 400                      |
| Poster Design (Handled by GARC & Independent Graphic Design Artist)                      | 700                      |
| Cost per packet that is mailed out comes to  | 1.06                     |
| Program design, coordination and implementation  | 12,000                   |
| Administration 3%  Total   | 1,353<br><b>\$46,445</b> |

After much deliberation and reflection, the working group unanimously agreed on a final poster design and the poster was published in English (Figure 2.1) and Spanish (Figure 2.2). The poster is titled "Bats Can Have Rabies". Upon completion, the poster was presented on GARCs webpages for immediate downloading and usage in both English and Spanish for educational use around the world. The posters were available for download and printing in a variety of sizes to best meet a variety of needs. At this time I also comprised and outreach campaign to the State Public Health Veterinarian's (SPHVs) across the USA, as they are often involved in public health education in the school systems. The outreach was at no cost to the SPHVs as printing and shipping costs of the posters were covered through this grant. Attention of this outreach was noticed among nurses and health departments which allowed for further outreach on educating

communities on the importance of bats and rabies. These efforts resulted in 1000+ 11"x17" and 18"x24" posters being printed in English and Spanish and distributed to Maine, Florida, North Carolina, Kentucky, Minnesota and Arizona.

Figure 2.1: Educational poster designed to educate adolescents across the USA on behalf of the Zach Jones Memorial Fund – English version. (Stukey, 2014) VE RABIES NEVER TOUCH A BAT Did you know... · Rabies is a deadly disease transmitted through the saliva of an infected animal Not all bats have rabies but most human cases of rabies in the US are caused by bats • Bat bites often leave small minor wounds but still require prompt medical attention Rabies is a preventable disease · Bat-proof homes and buildings by eliminating open areas where bats may enter . If you find a bat in your home call the health department so it may be tested for rabies · If bitten, wash the wound with soap and water and seek medical care immediately For more information, visit: www.cdc.gov/rabies/bats orldRabiesDay.Org

Figure 2.2: Educational poster designed to educate adolescents across the USA on behalf of the Zach Jones Memorial Fund – Spanish version. (Stukey, 2014)

# LOS MURCIÉLAGOS PUEDEN PROPAGAR LA RABIA NO TOQUE NUNCA A UN MURCIÉLAGO

#### Sabía usted que.....

- La rabia es una enfermedad mortal transmitida por la saliva de un animal infectado.
- No todos los murciélagos propagan la rabia. Sin embargo, los murciélagos ocasionan la mayoría de los casos de rabia en humanos en los Estados Unidos.
- Aunque la herida producida por una mordedura de murciélago sea pequeña, debe tratarse lo antes posible.

#### La rabia es una enfermedad prevenible

- Es posible evitar que los murciélagos entren en su casa o en cualquier otro edificio, sellando las aberturas por las que puedan acceder.
- Si un murciélago entra en su casa, llame al Departamento de Salud Pública, para que haga pruebas de laboratorio al animal.
- Si sufre una mordedura, lave bien la herida con agua y jabón, y vea a un médico lo antes posible



Directly following the completion of the "Bats Can Have Rabies" poster, I began to work on the video segment of the grant. The video was to mirror the same goals as the poster as well as educate adolescents on the importance of bats in our ecosystem. The first step in this process was to consult with a production team and outline the project goals and retain a quote to provide to team members of GARC for approval. This was successfully accomplished and Knowlera Media, LLC was secured as the production company. It came to my attention that Knowlera and GARC previously had a successful working relationship on previous endeavors. I believe this worked in our favor on planning the timeline of events. Once a payment of 50% of the quote was submitted, Knowlera contract requirement, I began to work directly with a team from Knowlera in great detail. I advised that the video was targeted to be approximately 12 minutes in length. Knowlera advised that I submit an outline of the topics to be included in the video along with a brief paragraph on each topic. This task was completed and Knowlera advised on a format for script writing. Knowlera suggested that I have an introduction and break out the topics into segments. It was also identified that I needed to outline the expert(s) and narrator(s) for this video. After brief discussions with GARC, I identified that I would narrate as a world renowned individual should be the expert. After much deliberation, I contacted colleague Dr. Charles Rupprecht (global rabies expert) for consultation and without hesitation he agreed to be the video expert. As I was outlining my talking points prior to my call with Dr. Rupprecht I learned that he just signed a contract with GARC as Director of Research.

Moving forward I consulted with members from GARC and the CDC on the variety of rabies topics that could be discussed and ranked their importance. I then stepped back and thought at great length, what would Zach's family hope to accomplish in this educational video? I outlined items and topics, that if known at the time of Zach's exposure, Zach's situation could have had a different outcome. As a result of this reflection, the following segments with a brief description were outlined and submitted to the production team:

- Segment 1: Introduction to rabies
- Segment 2: About Rabies (general scientific information)
- Segment 3: Rabies and bats
- Segment 4: Preventing exposures
- Segment 5: Exposures

- Segment 6: How bats benefit the ecosystem
- Segment 7: Closing

Knowlera advised to begin writing the script with the recommendations that each segment be no longer than 300 words or 2.5 - 3 minutes in length to hold the attention of this target audience. A sample script was sent to my attention so that I could better understand the format style Knowlera was looking for and what they were accustomed to working with. After reviewing this format in great detail, I began to write the first draft of the script. Upon completion of the draft I submitted it to Dr. Rupprecht for review and advisement. The initial drafted script that I sent to Dr. Rupprecht was 1,169 words which equals to 12.10 minutes of video. During this time of writing I was also thinking of a location in which to film the video. I envisioned a variety of locations to utilize for filming to best capture the attention of our audience. As thoughts of a location ensued Dr. Rupprecht and I finalized a draft we were both in agreement with. I presented this draft to the production team for review and consultation. The production team then combed through the script and we began consulting on photos and film footage (known as B-Roll footage) that would be ideal for use, as giving the audience visuals is a powerful learning tool. Whilst Knowlera and I were focusing on photos and B-Roll footage, Dr. Rupprecht presented the drafted script (as it was a continuous work in progress) to colleague's at Bat Conservation International (BCI), headquartered in Austin Texas. BCI is an organization that began in 1982 and is the world leader in bat conservation. BCI has accomplished many successful endeavors in scientific research and on the ground bat conservation. BCI aids in establishing self-sustaining conservation efforts around the world and works with universities, scientists, conservationists and wildlife professionals (BCI, 2013). BCI quickly examined the draft and submitted their input for consideration. BCI is accustomed to working with adolescents and the public on bat behavior and conservation in which their feedback was most beneficial.

I was introduced to the BCI team and we continued to work together on script edits. As our work together continued and I learned more about BCI I knew I wanted to film this video in Texas with their involvement. I approached this idea to Dr. Rupprecht and he was in agreement. Involving BCI in the filming process would also aid in building relations between GARC and BCI for future collaborations. I proposed the idea to BCI and it was unanimously agreed upon,

we were filming in Texas. As edits continued on the script and researching for film footage continued, BCI and I began to identify areas of interest for filming of the video. Areas of interest included; Bracken Cave, home of the world's largest bat colony, located on the suburban area of San Antonio (BCI, 2013); BCIs headquarters in Austin or at private bat rehabilitation facilities. I consulted with Knowlera and was advised that outdoor filming was not ideal as all the elements could not be controlled, such as; lighting and shadowing. It was agreed that the filming would take place at BCIs headquarters in Austin. On the day of filming, team members from BCI, Dr. Rupprecht and I met for final edits on the scripts. The script was segregated into segments for the narrator and the expert, me and Dr. Rupprecht. It was important to have BCI involved as much as possible therefore Dr. Rupprecht and I approached two team members with BCI about narrating the script segments on bat behavior and bats in the ecosystem and they accepted. Filming lasted a full day and at the end of the day a member from BCI, the production team and I visited a private bat facility to film bats demonstrating their natural behavior. Following the filming process it was time to put all the pieces of the video together. During this process Dr. Rupprecht and I discussed having a teenager give a brief introduction on the importance of bats and rabies and how this video could indeed save their life. The thought process was that we would be more apt to capture the attention of our adolescent audience by having one of their peers speak directly to them. During the process of writing up another 3-5 sentences and identifying a teenager, Dr. Rupprecht presented the idea of having Ms. Jeanna Giese give this opening introduction. Ms. Giese is the first documented human rabies survival case without receiving rabies prophylaxis (Lite, 2008). As Ms. Giese is a colleague, I contacted her with the idea and she accepted with enthusiasm. During this phase of the project, the video we had to date was projected out to a focus group that included adolescents the same age as our target audience. The focus group submitted feedback in which Dr. Rupprecht and I reviewed and incorporated into the editing process. Ms. Giese's introduction was filmed in her home and the production team was able to edit it into the video. The final edit was to include a photo of Zach as the video first starts with a dedication to him. The video was successfully completed and all goals were accomplished. The video length is a total of 7 minutes and 22 seconds in length and has been released to GARC for private and public distribution. Knowlera also completed a 2 minute edited version of the video for immediate internet distribution and has been made available at monkeysee.com or via link https://www.youtube.com/watch?v=Zjg\_FHqlFnU.

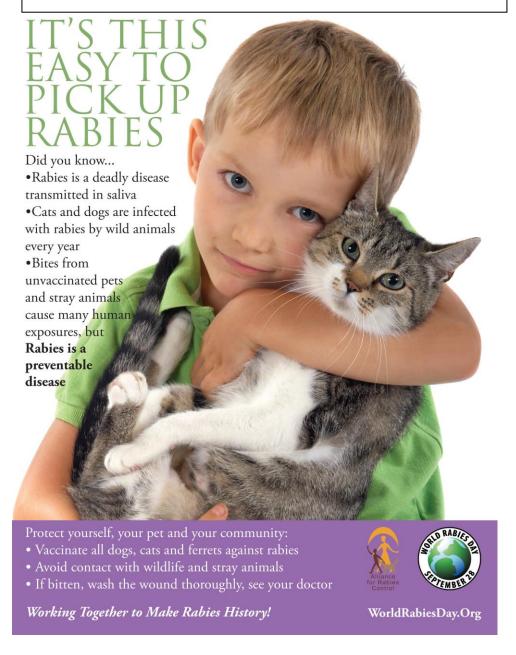
#### **Shelter Program Development & Vaccine Distribution Program**

In teaming up with GARC, I was also fortunate to develop a shelter program for the World Rabies Day campaign. The goal of the shelter program was to develop and share educational materials and network with animal shelter organizations and facilities on a global scale. Goals of the educational components were to focus on rabies, animals and rabies, responsible pet ownership, animal behavior and pet populations. A secondary goal was to build a rapport with humane educators to further extend this education into communities and villages to youth of all ages. My initial approach was to identify key existing materials that could be used to educate in a variety of ways for adults and youth. Once I identified a handful of key materials I worked with GARCs graphic designer to design a webpage specifically for the shelter program. This webpage was to be located within the World Rabies Day website. Key educational material that I utilized included brochures, posters, videos, public service announcements (Figure 2.3), animal quarantine recommendations, human rabies prophylaxis guidelines and lesson plans for teachers and humane educators to utilize. I also designed a power point and drafted a rabies fact sheet for posting onto the webpage. The concept was to provide these key documents with ease to areas of the world that had internet and printing capabilities. This would allow individuals to simply access the items to utilize right off an internet receptive device (computer, phones, etc.) for their specific teaching needs or print of the materials in a variety of available sizes to distribute throughout classrooms, communities, or whatever the appropriate setting might be. The webpage was also a resource for individuals to simply utilize to answer specific questions about animals, rabies and vaccines. Making the website user friendly allowed for individuals of all ages to access the information with ease.

A shelter program listserv was also developed and managed as part of the shelter program to keep current communications with animal shelters, humane organizations, students, government officials, military personnel, and youth all over the world. Updated materials, articles, newsletters, and World Rabies Day events were distributed throughout this listserv to keep all parties well-informed of the latest topics and events. Within its first few months of development the listserv included over 250 contacts.

An additional component that was developed as part of the shelter program with success was an animal vaccine program for World Rabies Day events held across the USA.

Figure 2.3: A public service announcement (PSA) made available to the public.



I proposed to GARC the idea of partnering up with a global animal rabies vaccine producer for a mass donation of animal rabies vaccines to distribute as a donation to animal welfare organizations. The initiative was to reach out to animal welfare organizations across the USA to promote animal rabies vaccinations and to increase involvement in the World Rabies Day campaign. A set number of vaccines would be distributed to organizations that submitted an application in which I would develop and manage. GARC had an interest to see how this would develop and permitted me to move forward. Prior to approaching a vaccine producer I identified

target groups that I felt were in most need that should benefit from these vaccines through the humane organizations. The target groups I identified were companion pets up for adoption, feral felines and low income households. I also instilled a rule that each organization would receive a limited amount of 250 animal rabies vaccines. The reason for this is that from experience I knew the humane organizations that were in most need of such a donation consisted of the smaller organizations. Lack of funding prevents a large number of the small humane organizations from vaccinating their adoptive animals with rabies. The geographical areas where these small organizations are located also tend to lack community regulations on rabies vaccine requirements and public health education and the importance of vaccination. This vaccine incentive would allow for community education and vaccinating animals in the most needed areas across the United States. I drafted a formal letter and first contacted Pfizer Animal Health on this initiative. Following a few conference calls outlining the logistics that were envisioned and answering pending questions, they accepted. Pfizer agreed to donate the animal rabies vaccines as well as ship the vaccines directly to the organizations veterinarian and cover all shipping costs. I developed a two page application that was to be completed by an executive board member or the organization's veterinarian and submitted to my attention for review and acceptance. The application was uploaded to the shelter program webpage along with the eligibility requirements. A brief write up on the vaccine initiative was sent out through the listsery that was developed and through GARCs social media outlets. I partnered with The Humane Society of the United States Feral Cat Program to be certain we reached out to feral cat organizations across the US as they were an important target group. Thousands of applications were received and reviewed for acceptance. I developed an excel database in which the following information was submitted directly to Pfizer for vaccine distribution:

- Name of Organization
- Legal Name of Organizations Veterinarian and License Number
- Veterinarian's Legal Mailing Address (Excluding PO Boxes)
- Pfizer Account Number (New or Existing)
- Animal Welfare Organization's EIN Number
- Animal Welfare Organization's Contact Information

As a result of this endeavor over 250,000 animals were vaccinated for rabies and over 1000 communities received public health education on rabies and the importance of vaccinations and responsible pet ownership. Majority of these communities hosted a free or low-cost rabies vaccination clinics and animal adoption days (Figure 2.4) whilst dispersing rabies information and consultation. A total of thirty two states within the United States received the donated animal rabies vaccine and hosted community events.

Figure 2.4: A young female interacts with a canine at a low-cost animal rabies vaccination clinic and adoption day event in Las Cruces New Mexico (Stukey, 2014)

#### Involvement in 'Day-to-day' Operations on a Global Level

Being involved in daily operations allowed me to gain insight and to appreciate how rabies affects the daily lives of animals and man and the importance of the eradication of this disease on a global level. It has also allowed me to see how 'on the ground projects' are, and can, make an impact. My involvement in daily operations consisted of multiple activities. These activities included ongoing consultations with humane organizations, partners, veterinarians, military personnel, youth organizations, nurses, government officials, and police and animal

controls officers around the world. Consultations comprised of a variety of events, stemming from proper administration of prophylaxis, project initiatives, securing resources, compendium guidelines, and rabies education in general. I was actively involved in GARCs infrastructure as I was included in conference calls for ongoing projects and internal resource development. My input was solicited for the review and writing of articles in newspapers, newsletter, brochures, webpages, posters and magazines. I assisted with drafting a 'media talking points' document that was released to veterinarians across the United States as well as take a leading role in 'lesson plans' development to be distributed for global use targeting youth ages 6 -14. Correspondingly, I developed a two page checklist for individuals and organizations looking into hosting or physically hosting a community animal rabies vaccine clinic. This was immediately uploaded and distributed on GARCs webpages, social media and list-servs. This document served two purposes, 1) allow individuals and organization to simply check off the outlined items in need as they physically prepared for their clinic, to ascertain nothing was missed and 2) allow interested individuals and organizations whom had never undertaken an animal rabies vaccine clinic to review and determine what resources ideally should be secured and the design of running the clinic.

I was fortunate to have several opportunities that allowed for me to work within all realms for GARC. I worked with a dynamic group of people from around the world which enhanced my education and understanding of rabies as a whole. I have gained trusted colleagues that I will forever be entwined in both my professional and personal life. This was such a valuable experience that in some ways just cannot be defined. The only shortcoming, it came to an end. If I had to pick one overall lesson from my entire experience, I would have to quote Dr. Briggs when she stated in a conversation that I was having with her once, "that one person can indeed make a difference" (Briggs, 2013).

#### CHAPTER 3 – CONCLUSIONS & RECOMMENDATIONS

#### **Conclusion**

Rabies is a neurological disease that has affected the lives of animals and man for centuries. Rabies is known as the deadliest disease to man with a 99.9% fatality rate (GARC, 2014) and is found on every continent excluding Antarctica (WHO, 2014). This disease cost lives and impacts culture, religion and economics devastating communities globally. Annually, rabies claims the lives of 61,000 (WHO, 2012) humans, which is grossly under reported as 84% (WHO, 2012) of the deaths occur in rural areas in the poorest countries. Majority of these human deaths, up to 60%, are children ages 15 and younger (GARC, 2013). Asia and Africa result in majority of the human annual deaths, 95% (WHO, 2012) with India having the highest fatality rate (GARC, 2013). Human and animal prophylaxis, in conjunction with proper wound management, have proven to prevent and control the virus, however, limiting factors prevent successful distribution and administration. These factors include lack of government infrastructure, culture and religious beliefs, lack of funding for the vaccines, location of vaccine administration and more. Whilst rabies can occur in all mammals, 95% of human deaths result from infected canines (Briggs, 2013). Rabies is 100% preventable in humans and can be eradicated in canines through successful vaccination programs. Individuals and organization around the world, such as the Global Alliance for Rabies Control, spend tireless efforts on building and establishing educational rabies programs and vaccine incentives. Although there has been great success in these efforts, it is still not enough as people continue to die from rabies. Rabies cost the world an astonishing \$124 billion USD annually (GARC, 2013) and as long as populations continue to grow for humans and canines, the cost and economic burden will also continue to grow.

#### **Recommendations**

As human and canine populations continue to grow, the cost and economic burden will also continue to grow (WHO, 2012). In order to reduce the burden of rabies there is a need for further solid foundation for prevention and control. Canine rabies can be eradicated with proper

animal vaccination distribution and administration in conjunction with an ORV program. As obstacles exist for free roaming canines, additional efforts with ORV must be implemented. ORV would provide crucial benefits for saving lives and decreasing the economic burden in the poorest areas. Contraception initiatives with vaccine programs and ORV also promise to enhance the control of rabies globally (Rupprecht, 2011). Minimizing human exposures to infected animals is also essential. Ensuring prompt wound management and proper administration of prophylaxis (and RIG) for exposed individuals is critical. Further use of effective blueprints and international advocacy for prevention and control is needed on a global scale. In reference to research, additional studies are necessary for development of recommendations that are science based. Well-designed studies are needed for additional data in the following areas; potential shedding of virus in milk, PEP protocols for domestic animals, earliest age at which rabies vaccine is most effective, viral shedding periods for domestic livestock and lagomorphs and the ecology of rabies in wildlife species (Compendium of Animal Rabies Prevention and Control, 2011). Rabies is 100% preventable in humans and the eradication of canine rabies is obtainable through vaccine and contraceptive campaigns. Implementing national programs with effective surveillance and control efforts are imperative as is obtaining political commitments globally.

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