Rabies
By Alexa Smith

Rabies Virus (Rabies); Etiological agent – Family – Rhabdoviridae. Genus- lyssavirus (1).

Transmission:
The virus can enter a host via a parenteral route. The saliva of the infected host will pass to the uninfected mammal after being bitten by the infected host. There are a few rare cases of mucosa transmission, if the saliva of the infected host comes in direct contact with the mucosa membranes such as the eyes, mouth, or nose. In extremely rare (laboratory) cases, the virus can be inhaled as an aerosol. (4)

Reservoirs:
Common reservoirs include foxes, skunks, coyotes, raccoons, and bats (5). The most frequently reported domestic reservoirs are dogs, cats, and livestock. (3) Rabies is a zoonose, meaning that it is a disease that is transmitted to humans via domestic or wild animal reservoirs (1)

General Characteristics
Rhabdoviruses are bullet shaped, single stranded RNA. There are 10nm glycoprotein spikes on the envelope surrounding the helical coils of RNA. The virus is a negative strand RNA virus, meaning it must carry RNA polymerase to transcribe a positive strand RNA (1). The virus encodes 5 viral proteins; N, P, M, G, and L proteins. The capsid is composed of N, L and P protein. These allow the virus to transcribe and replicate in the cytoplasm. The M protein is located in between the capsid and the envelope and contributes to the bullet shaped morphology of the virus. Glycoprotein spikes on the envelope allow the virus to bind to cell receptors (6).

Identification
The direct immunofluorescence test detects the presence of rabies antigens in skin and fresh tissues (brain). This is the most sensitive test that is performed on the infected animal post mortem (1). Unfortunately, in the early stages of disease in humans, direct immunofluorescence tests may return a false negative (2). Detection of the virus replication can also be used to confirm the rabies virus. Neuroblastoma cell cultures or mice can be inoculated to allow the virus to replicate quickly, then the cells undergo a direct immunofluorescence test to confirm the presence of rabies virus. The use of the polymerase chain reaction can be utilized to develop a fragment of the genome. Electrophoresis is then used to confirm the gene of interest. Serological test are the least effective way to diagnose rabies. Although, Fluorescent antibody neutralization test and rapid fluorescent focus inhibition tests can be used
to determine the titer of the antibodies (7). The positive diagnosis for rabies cannot be performed in one test and requires the use of multiple tests to confirm a positive result (7). Histopathology is an older detection method used before current methods were developed. This includes the presence of mononuclear infiltration, perivascular cuffing, lymphocytic foci, and negri bodies. This test is not effective or reliable. Electron microscopy and staining can be used to identify the structure of the rhabdoviruses. (1)

**Signs and Symptoms**

The early signs of rabies resemble the flu, with fever and weakness (1). Tingling and pain at the wound site are common. The incubation period varies more than any other acute infection, it may last from 5 days to up to 2 years after exposure, but normally about 30-90 days after exposure (2). The prodromal period usually lasts 2-10 days, this is where the first clinical signs and symptoms appear. This includes nonspecific symptoms, respiratory symptoms (sore throat and cough), gastrointestinal symptoms (vomiting, abdominal pain, nausea) or central nervous system symptoms (vertigo, irritability, nervousness and anxiety) (8). Some rare cases report agitation, photophobia, nightmares and depression (2). In the period of illness, the virus takes one of two forms. It becomes either furious or dumb. Symptoms of furious rabies form include irritability, hyperactivity and hydrophobia. Dumb form of rabies includes paralysis starting at the site of the bite. Eventually, coma and death occurs (10). There is no cure for the clinical disease of rabies. Nearly all cases of rabies disease, after clinical signs appear during the period of illness, are fatal. (9)

**Historical Information**

Rabies has been recognized since 300BC as noted in a paper written by Aristotle (11). Almost all cases of rabies were fatal until Louis Pasteur invented the vaccine in 1855. Pasteur also recognized from the characteristics of the disease that the etiological agent was a virus. This was confirmed in 1936, when the virus was first grown in a lab (12).

**Virulence Factors**

The virus encodes 5 viral proteins; N, P, M, G, and L proteins. The capsid is composed of N, L and P protein. These allow the virus to transcribe and replicate in the cytoplasm. The M protein is located in between the capsid and the envelope and contributes to the bullet shaped morphology of the virus. Glycoprotein spikes on the envelope allow the virus to bind to cell receptors (6).

**Control, Treatment, Prevention**

Vaccinating susceptible species will dramatically reduce the number of outbreaks of rabies. This can be done with the trap-vaccinate-release method (2). There is also an oral rabies vaccine which uses bait to attract a target species. The target eats the bait with the encapsulated, attenuated rabies virus vaccine inside. This is useful for larger scale vaccinations and is more effective at vaccinating large groups of target animals (5). In humans, a pre-exposure
vaccination is available for those who are at high risk, such as veterinarians. The next best method for preventing rabies in humans is avoidance of exposure to the disease. If a person is exposed to the virus, a post-exposure prophylaxis must be initiated as quickly as possible (2). This begins with the administration of human rabies immune globulin (HRIG). This provides antibodies to stimulate an immune response in the victim (15). Next, a schedule of four, 1 mL doses of either human diploid cell culture rabies vaccine (HDCV) or purified chick embryo cell culture rabies vaccine (PCECV), is given. The first dose is injected as soon as possible after infection. The following doses are given 3, 7, and 14 days after the start of treatment (14).

World-wide education and awareness of rabies virus is an excellent prevention method. In 2006, the global Alliance for Rabies Control created World Rabies Day. This helps educate those in countries with high prevalence and low awareness about the signs and facts of the disease. (16) A new vaccine is being developed and tested by researchers at the University of Georgia. This vaccine was created by adding a protein from the rabies virus to the parainfluenza virus 5 (PIV5). The PIV5 is harmless to humans and allows the rabies virus to be recognized by the immune system and create antibodies. In laboratory trials, 50% of mice exhibiting the clinical signs of the disease survived. If this vaccine can be adapted for humans, it will be the first effective vaccine at treating advanced rabies infection (22).

Local Cases

In 2011, Texas had the highest number of incidence cases in animals with 1,018 positive cases. These were heavily related to intense drought. Williamson and Travis county had the highest number of positive cases in Texas in 2011 (see figure below) (18). Most of these cases are skunks. Fortunately, these numbers have decreased significantly. In 2015, there were only 74 confirmed cases (19). The last human death from rabies in Texas was in 2013, a 34 year old man travelling from Guatemala was bitten by a dog in Guatemala and died in Texas from the disease (17). A 17 year old female was bitten by a bat in Texas in 2009 and she made a full recovery. In the United States of America, only 1 to 3 human cases are reported annually and only 34 cases have been diagnosed since 2003. (17)

Most Rabid Counties in Texas.

Confirmed cases in each county. 2011

1. Williamson County – 135
2. Travis County – 59
3. Burnet County – 57
4. Hays County – 29
5. Llano County – 26
5. Erath County – 26
7. Denton County – 25
8. Harris County – 24
9. Bastrop County – 23
10. Fort Bend County – 20
Global Cases

~59,000 deaths a year occur from rabies worldwide. Asia and Africa where healthcare availability and education of the disease are scarce, report 95% of all rabies related deaths (20). 3% of all rabies cases in Africa, where the incidence is extremely high, end in death. 1.5% of rabid bites in India result in death (see figure below) (21).

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<tr>
<th>INDIA,</th>
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<td>DEATHS:</td>
<td>19,290</td>
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Works Cited


