Literature review examining the biological, epidemiological, and pathogenic properties of a neglected tropical disease: Rabies

by

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Abstract

Neglected tropical diseases (NTD) such as rabies represent a balance between properly investing in public health infrastructure, health education, and clinical research. Known problems of rabies include the high case fatality rate, endemic spread, and vaccination/treatment cost. Current research on these topics is often fragmented between journals and divided between endemic vs. non-endemic countries. Creating a centralized review of the most up to date literature is critical for enhancing public health professionals'/clinicians' intellectual arsenal against this disease. Acquisition of the appropriate literature was accomplished by carefully screening through research articles. One of the common themes throughout all articles analyzed is the debate on whether to invest more in rabies deterrence. This review aims to showcase the need for scientific community to take rabies more seriously, as it is one of the few infectious diseases today that continues to evade eradication methods in conjunction with an extraordinary death rate.

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1.0 Introduction

This essay is a literature review detailing the current knowledge in rabies pathogenesis, virology, and epidemiology in countries where cases remain consistently at or above endemic levels. Data sources were compiled using PubMed and the World Health Organization's expert consultant rabies manual. Endemic countries represent the biggest concern of ultimately controlling this virus and its contained spread. Investigations into the historical rates of rabies acquired infections in India as well as Africa and Eastern Europe pose more questions than answers. India itself continues to account for 35% of all rabies infections globally. (1) It's interesting to note that the disease itself has been practically eliminated from other countries including most of Western Europe and the United States, minus a few sporadic cases yearly. There must be some underlying cause, whether it be poor public health infrastructure or community cultural practices that account for the repeated transmission of the virus. (1)

Pathogenesis & Virulence characteristics will also be examined in detail with specific highlights including viral replication methods, steps in the pathogenic process, and the molecules involved in immunological processes. Rabies differs from other viruses in that it targets the central nervous system by methods of immune evasion/apoptosis of infected neurons. In addition to documenting the microbiology of the virus, this essay discussion will also discuss key epidemiological findings of the virus and control methods that can hamper its spread throughout the countries listed. Finally, relevant literature will be examined on vaccine/treatment methods for rabies as well as a deep dive into the future recommendations for public health, including implications for global health.

1.1 Methods

Data sources were compiled for this review using PubMed and the World Health Organization's expert consultant rabies manual. PubMed showcases a wide variety of rabies literature so careful attention was placed upon the countries listed. Sources were analyzed and synthesized to provide an adequate synopsis of current rabies research and methodological developments. Thirty-five initial articles were found, and these were filtered through certain criteria. Selection criteria for studies included in this review focused on relevant findings on viral replication, general epidemiology, pathogenesis, outbreak prone counties, demographical factors, and government response. This whittled the final reference total to twenty-five sources. Search strategies focused on studies primarily in the English language, as there were many in other languages.

1.2 Rabies, a Viral Encephalitis

Rabies is a negative-stranded RNA virus that belongs to the rhabdovirus family, genus *Lyssavirus.* It is mainly spread through the bite, scratch, or lick of an infected mammalian host. Symptoms of rabies are divided into three specific stages: prodromal, furious, and paralytic. In the prodromal stage common symptoms include fever, itching, and pain at the wound site. Furious stage rabies includes the textbook hydrophobia (fear of water), hallucinations, muscle spasms, and coma. Paralytic stage symptoms showcase increasing paralysis and a worsening fever, in addition

to sensory dysfunction. Any warm-blooded animal can become infected including dogs, bats, skunks, or even humans. Human to human transmission is rare with most cases being from animals. Saliva from an infected host can transmit the virus if it encounters the nose, eyes, or mouth of a victim. It's worth noting that the virus is nearly always fatal once symptoms begin to show but there is a vaccine that is highly effective.

After a typical human infection by bite, there is a delay in viral movement that can last for weeks to months. Viral binding is initiated by linkage to the nicotinic acetylcholine receptors at the neuromuscular junction. Once binding has been successful, rabies virus is internalized via receptor mediated endocytosis which triggers the fusional of the viral membrane into the endosomal membrane. (2) These actions further release virus into the cytoplasm. The virus then travels toward the spinal cord with the axons of the peripheral nerves. Dissemination then follows within axons in the central nervous system alongside neuroanatomical pathways. In terms of cellular replication, rabies proliferates in the neurons which causes neuronal dysfunction. (2) Research is on-going, but hypotheses are placed on this being the reason for poor clinical outcomes of infection. During this time, the virus cannot be easily detected within the host, and vaccination may still confer cell-mediated immunity to prevent symptomatic rabies (2). Once the virus reaches the brain it will cause encephalitis which is the beginning of the symptomatic phase. At this point the virus is nearly always fatal in over 99% of worldwide cases. (2)

Rabies diagnosis methods include fluorescent antibodies, which is a test backed by the World Health Organization (W.H.O) These antibodies can bind to specific rabies induced antigens which then allow pathologists to visualize the virus under electron microscope. An important note, rabies diagnosis is almost always confirmed with a brain sample collected after autopsy. The diagnosis can also be made from saliva and urine samples, but they might not as reliable as the

brain ones. Given this information, it's critical that mass vaccination programs be implemented in historically poorer countries like India.

It's also important to note that up until the 1950s, the rabies virus was considered unique. This uniqueness was quickly disrupted when virus samples from shrews/bats serologically tested from Nigeria & Lagos, presented new viral data to scientists studying them. The genomic structure of the virus group has shown how complex they are, and their potential for virulence factors. Typical virus structure includes a modular genome organization that encodes five structural proteins. (2) These proteins include an RNA polymerase (L), nucleoprotein (N), phosphorylated protein (P), matrix protein (M), and an external surface glycoprotein (G) The combination of these three virus discoveries lead to the term of rabies serotype being introduced (2). Another incident involved a case in South Africa, which ultimately lead to the discovery of a 4^{th} virus leading to what we have today (2).

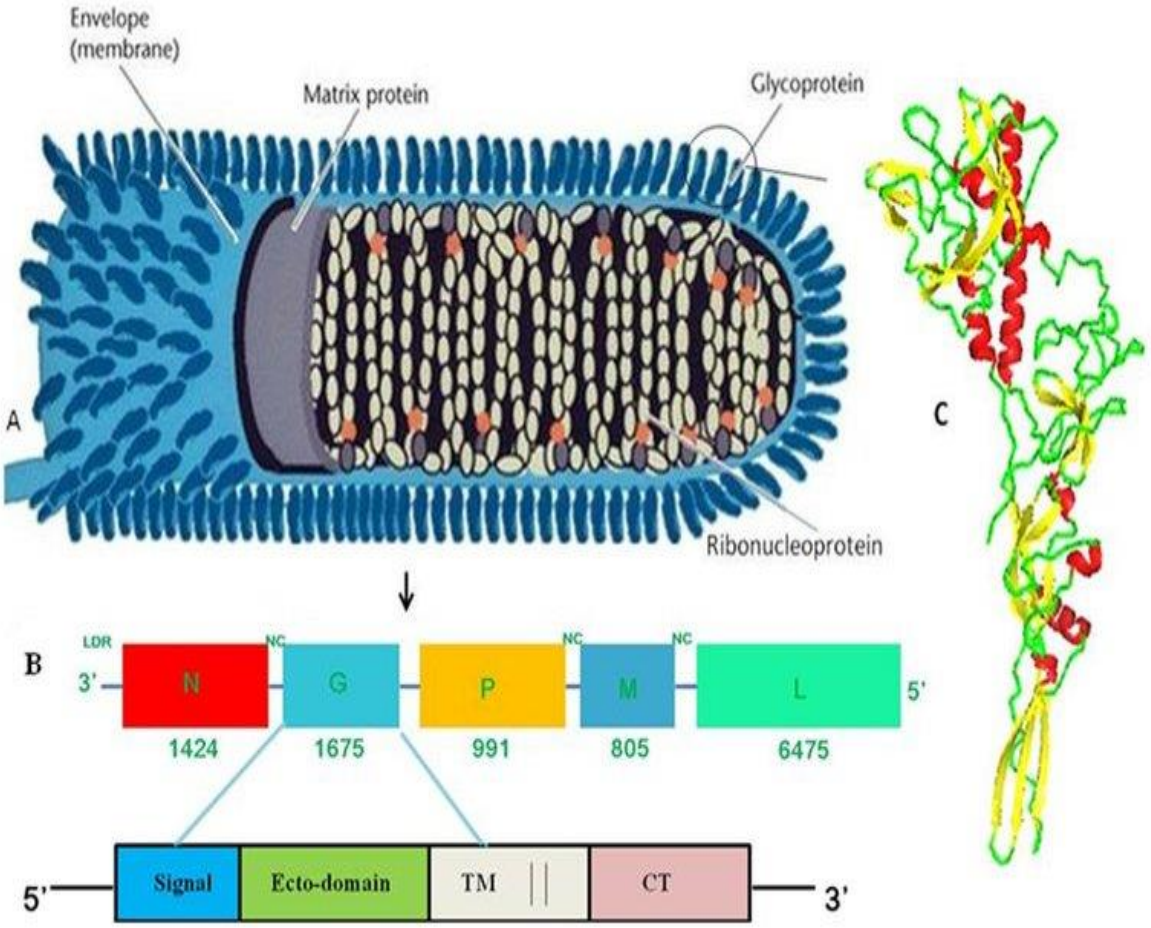

Figure 1

(A. Diagram showcasing the cell structure of a rabies virion. B.) protein structures encoding different genome of rabies virus comparing lengths. *Notice glycoprotein G is shown with signal, ectodomain, and transmembrane. C.) Three-dimensional structure of Rabies virus glycoprotein.) (source: Int.J.Curr.Microbiol.App.Sci (2017) 6(12): 2064-2085)

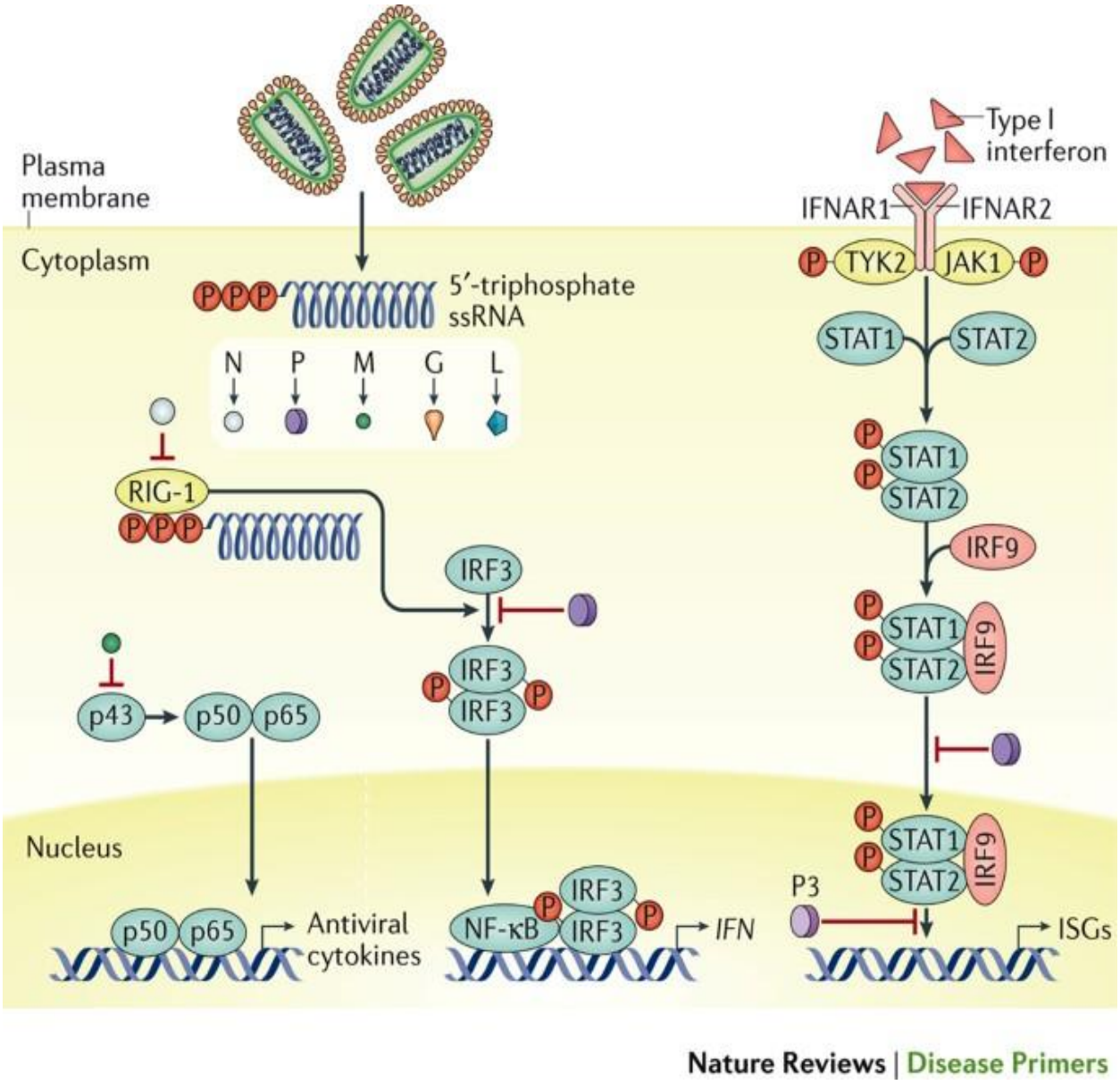

Figure 2

(Viral infection triggers numerous signaling cascades, including the induction of the genes encoding type I interferons and chemoattractive and inflammatory responses, resulting in an antiviral environment and efficient innate immune responses.) (Source: nature.com/Rabies infection characteristics)

2.0 Pathogenesis Characteristics

Pathogenesis starts once the virus has infiltrated the port of entry, which normally occurs through wound surfaces sustained during bites or through the mucosa. Intact skin provides protection from viral entry and proliferation, which makes a thorough skin self-examination paramount if individuals are going to be handling rabid animals. If the virus is successfully able to cross into the body, however, it uses transportation systems along the central nervous system. Transportation properties of rabies virus come from the G protein that plays a unique role in cell-cell spread and viral transport. (3, 4) Studies conducted in rats and rhesus monkeys show that rabies migrates exclusively in the retrograde direction.

Multitudes of proteins may be involved by current research places the blame on the G protein. This G protein is thought to play a dominant role in trans neuronal spread of the viral infection. (4) Before it can reach the CNS, virions are carried by specific vesicles that allow them to adequately travel along the sensory motor axons. (3, 4, 5) The incubation period varies widely with some cases ranging from 5 days to several years, with the usual onset being between 2-3 months post infection. (3, 4, 5) The rate in which viral replication reaches its critical threshold depends mainly on the amount of virus transmitted during bites and proximal location of the bite. Bites occurring near the lower extremities will take longer to manifest symptomatically than say a bite on the neck.

Going in further detail involves looking at the site of the initial bite. Once bitten by an infected host, neuropathic pain emerges roughly at the site and radiates throughout the dorsal root ganglia. (7) Innate immunity responses then contribute to the increased inflammatory state as

macrophages and other cells rush to the site of injury. While this discussion raises questions on the immunology of the disease, it's important to note that there is no definite approach to whether an individual infected with rabies will develop fast onset symptoms, or slower more progressive ones. The consensus among experts is that host immune factors play a role in susceptibility to the virus. In that regard, two main clinical subversions of human rabies can develop after infection: Furious & Paralytic.

The two main modes of viral migration and spread are: centripetal retrograde transport (CRT) or centrifugal spread (CS), both of which have widely different microbiological arenas that can affect speed. In CRT, the virus moves quickly since neuronal populations are infected simultaneously (3, 5). Speeds in CS are often slower, which can be attributed to diffusion rather than possibly active transport methods. (3, 4, 5) Centrifugal spread also occurs along nerves to multiple organs. (4) During one of the predominant phases, widespread neuronal transfer occurs within the CNS and infection of the root ganglia happens with central connections. (3-4, 5) The peripheral axons of the root ganglia lead to infection of a wide variety of muscles/surfaces including: skin, hair follicles, salivary glands, heart muscles, and lungs. (3-4, 5) There are many others, but by the time of the first clinical symptoms, the virus has already replicated widely enough throughout the CNS. (6).

Pathogenicity elements mainly correlate with the rate of viral RNA synthesis and slated production of infection particles. (6) Research has shown that viral mRNA and genomic RNA produced by chimeric viruses mainly suggests that transcription and regulation are controlled by the M protein, which can be considered a transacting factor. (6) Regulation of viral replication is considered one of the most important factors in viral pathogenesis, with specific focus on preserving the neuronal network in which rabies uses.

2.1 Apoptosis

According to the current literature, the correlation between apoptosis and rabies virus infection continues to grow. (6) Apoptosis is critical in the removal of rabies infected cells through programmed cellular death. This differs from other viruses that have exploited highly regulated apoptotic cascades by blocking it within cells. Studies analyzed have made it apparent that RNA viruses can multiply rapidly, producing an overwhelming number of virions before hosts can initiate an adequate immune response. (7) While making the connection between the two biological events is important, understanding how this relates to virulence is critical for developing treatment strategies for the future.

Two pathways have been identified that have an important role in apoptosis events during rabies infection. The first is an extrinsic pathway that has been found to be initiated by cell surface receptors. These receptors are activated through the enzyme caspase-8. (7) The second pathway is an intrinsic pathway that forms in the mitochondria and is activated through caspase-9. One final pathway, which forms from a flavoprotein caspase is released from the mitochondria beings the final independent pathway. (7) These three pathways are all affected by the apoptosis-inducing factor when it enters the cytoplasm. Research has also shed light on two of the proteins responsible for apoptosis, M and G. The M protein targets mitochondria and induces mitochondria apoptosis by means of caspase-dependent/independent pathways. (7) The P protein has been shown to mediate functional disturbances in the mitochondria which leads to apoptosis. Both events occur later during the late stages of infection. Apoptosis is one of many immune responses to viral infection that the body has. While this defensive tactic has many benefits in combatting infection,

this process also contributes to the spread of the virus. More scientific research is needed to determine the role of apoptotic cellular processes in the context of rabies infection. (7)

2.2 Pathogenesis/Virulence Main Points

Virulence factors of rabies virus are determined by the rate of viral uptake, cell to cell spread, viral replication and G protein expression. (6) Kinetics of viral uptake are interrelated with the rate of virus expression. Pathogenicity factors are mainly determined by encoded proteins, including the G protein which is considered high divergent. The G protein can be responsible for fast viral entry and regulation between expression and replication. Rabies virus triggers cellular apoptosis in inflammatory cells. This can interfere with the release of cytotoxic cytokines and possibly prevent cellular lysis.

Further points discovered through the literature detail how neuroinvasiveness and neurovirulence both play a role in determining the lethality of rabies. (6) Rabies has effectively developed strategies that allow it to bypass the blood brain barrier and reside in the brain. Determining which site in the brain the virus infects is conducted by innervation through motor neurons. Once in the brain, the virus can then be intermittently excreted in the saliva and be ready to transfer to a new host. These factors are all mediated through its movement along a host's central nervous system. Structural integrity of a hosts CNS is important during rabies infection due to viral adhesion methods of travel. Pathogenic rabies infection has developed immunological evasion abilities that allow it to keep the expression of RNA, antigens, and proteins low. (6)

The literature reveals the most effective ways of studying apoptosis in rabies pathology, mainly through the use of animal models, such as mice. (7) Mice models provide a glimpse into the pathogenic properties of rabies induced infection through studies conducted in labs. Expression of dormant genes is decreased in the rabies infected neurons, which may result in a repression of protein synthesis. (7) Mice that were infected in the lab with rabies also show impairment of serotonin, a neurotransmitter involved in many critical functions. The discovery of nonexistent immunological responses in humans 7-10 post clinical symptoms also provides clues into the pathogenesis of rabies. (7) Theories on this suggest that the rabies G protein provides immunological suppression to the CNS through a complex strategy developed through mutation.

3.0 Furious (Encephalitic) Rabies

Of the two well-known forms, encephalitic rabies presents the clinical symptoms most people recognize to be consistent with disease presentation. The hallmarks of furious rabies include fever, general malaise, and a strong presentation of an excitement state. Neurological symptoms follow soon after which can include hydrophobia (fear of water), agitation, and hyper salivation. After this, a common theme of seizures, coma, and respiratory failure occur in nearly all cases. (8) Episodes of rapid rabies may result from stimuli which may involve patients' sense of touch, hearing, or what they see. (8) It's important to note also that furious rabies accounts for nearly all human cases reaching upwards of 80% of cases. (8)

Scientific debate surrounding the most prominent form, furious rabies, presents a unique challenge that warrants further discussion. Observations include analyzing the animal vector where the bite came from, wound size and location, and the incubation period. Prior history of rabies vaccination must also be documented. In encephalitic rabies, the anterior horn of the spinal cord in mammalian victims appears to be perturbed. Denervation begins at the site and may progress or remain clinically normal throughout the course of infection. Functional muscle weakness near the proximal site remains nonexistent in the beginning, while the motor neurons also function adequately.

4.0 Paralytic (Dumb) Rabies

The second form of rabies, albeit lesser known, is paralytic rabies which accounts for 20% of cases on average. (8) The early clinical manifestations of PR, which include headaches, fever, and wound site paralysis may present challenges to clinicians since this form is nearly indistinguishable from another disorder, Guillain-Barre syndrome (GBS). Clinicians should pay special attention to the signs of paralytic rabies, which includes urinary problems, something GBS suffering patient's lack. (9) Dumb rabies is nearly confined to a single animal vector, rabid vampire bats, and many individuals who have received post exposure therapies. (10) Possible pathological causes of paralysis in dumb rabies require further inquiries but newer signs point to anterior horn cells. Scientific consensus points to demyelination factors that may be the sole contribute source of weakness seen in this form.

5.0 Rabies Epidemiology

5.1 Rabies in India

Over three-quarters of cases in India occur in rural communities with poor access to diagnostic facilities and post-exposure prophylaxis, which are key to preventing development of disease. (1) Besides the poor infrastructure, there is a consensus among infectious disease experts at local/regional health clinics that many residents of India lack the proper education on how to identify rabies & what to do if exposed.

The government of India has handled the disease in such a unique way as well as other notable NTDs. Surveillance systems were developed, tested, and deployed throughout hard hit areas to assist local health leaders in keeping track of the rabid dog population. This effort to combat rabies and other infectious diseases was instrumental in the establishment of a wide network of research institutes in India. (1) The knowledge of that should present the idea that rabies is taken seriously among Indian government leadership circles. This is not the case, however, given the fact that the government itself labels rabies a disease of the poor and of no concern to affluent Indians.

Most rabies infected individual cases in India have been identified as rural, male Indians. (1) Many of these cases occur where most of the male population are unvaccinated and adopt stray dogs as “pets” for companionship or for food later. Epidemiological surveys conducted presented a case load of 2 cases per 100,000 residents and identified dogs as the main culprit representing 95% of cases. (1) Finally, the incubation period timeframe varied widely from as small as two

weeks to as large as six months with a mean time of three months. Variance in the incubation period occurs due to difference in amount of the virus introduced to the wound, severity, and distance of the wound to the CNS. (1)

From the early 1990s to the early 2000s India has reported 30,000 human rabies deaths. These case numbers are important because at the time India accounted for 60% of the global mortality for the disease. Concerning the 30,000 human rabies deaths, the majority of those were children under the age of 15. (11) This shows that children are an extremely vulnerable group in that country when it comes to contracting infectious diseases such as rabies. Detailed observations of those 30,000 deaths revealed the main clinical features were lower extremity bites, followed by upper extremity bites, and then head/face.

The rural community is at particular risk when it comes to rabies infections. These communities are often resource limited and forced to improvise medicines to help those that are sick. Barriers to adequate care are abundant with some residents instead seeking out traditional medicine. (26) Reasons for this include distance to the nearest health clinic, high cost of the rabies vaccine, lack of vaccine availability, and lack of transportation. (26) Research has shown that some of these individuals prefer traditional healers over modern health due to general distrust in outsiders, and that combatting this distrust is complicated and will take time. (26)

The main methods used were community surveys that allowed researchers to collect important epidemiological data of the rabies problem. A survey population of 10 million was considered, based on the earlier reported incidence of 30 000 deaths annually. This population was whittled down through a careful selection of desirable parameters such as age, socioeconomic status, and overall health at the time. To establish the severity of rabies endemicity, researchers

collected infectious disease records from over 20 medical schools spread out across the country. (11)

After obtaining this data, researchers fanned out across different districts plagued by rabies cases and went to homes of rabies patients. Death information was collected by interviewing a surviving family member over the age of 18. These individuals were screened for reliability and to prevent false data from being entered into the community survey pool. Once enough data was collected the samples were analyzed using a simple software program such as SPSS. (11)

5.2 Rabies in Africa

European colonization is believed to have spread canine rabies across the continent during that conquest period. Today, canine rabies cases account for nearly all reported cases in Africa. (14) Given this, there are detailed reports of sporadic cases occurring from time to time but those have only been documented in Southern African countries. Here, canids such as jackals and foxes are the primary host for rabies. (15) In terms of countries most affected, Nigerian cases remain at the highest since vaccination campaigns started against the disease in Africa. Thousands of people are estimated to die in Nigeria each year from an otherwise preventable disease. (16)

One of the main things Nigeria lacks is a national rabies control program. They represent a nation that still grapples with an endemic zoonosis with high disease levels of burden and constant, repeated outbreaks. (17-18) Diving deep into this topic uncovered a primary reason for the outbreak issues that Nigeria continues to face: dog markets. The dog meat market provides small business owners with essential forms of income to survive in an otherwise limited economy.

While owners provide valuable commodities to their local village residents in terms of food, they face significant risk in going into this market chain. By going out into the field and collecting dogs, many of which are rabid, they are constantly exposed and risk infection.

Studies have also shown that dog butchers often fail to be vaccinated or use PPE when handling the dogs. (19) Findings like these represent a paramount public health concern that needs to be addressed through health education/promotion targeting dog butchers. Another note is how these dogs are getting transported throughout the country. Unchecked dog transportation represents a significant public health concern for rabies control methods. Quiet dog movements across state borders represent obstacles to effective campaigns.

Studies conducted in Nigeria showcase the quality of health education between urban and rural centers when it comes to rabies knowledge. (20) Assumptions can be made if the urban community lacks basic knowledge when it comes to rabies, the rate in rural communities must be even higher. Conducting studies in rural areas presents logistical challenges to researchers who often face long drives into unknown territory, wildlife concerns, and hostile parties. In terms of creating awareness, conventional methods such as providing health education to rural villages, leaving pamphlets, and focusing on responsible dog ownership seem to be the way to go. Good dog ownership can be stressed through a mass campaign that involves the use of television for urban areas, to village announcements for rural ones. (21)

5.3 Rabies in Europe

Rabies in Europe provides a unique look into how supposedly higher income countries have successfully eliminated disease cases. When it comes to animal reservoirs, the most important one today is the red fox (*Vulpes vulpes*). (22) Dog rabies, a reservoir prevalent in so many poorer countries, has practically been eliminated in Europe. As the European population expanded there was an epidemic in red foxes from a spillover event that occurred during the 1940s. (23) Campaigns were launched to decrease the red fox population through the means of trapping, but those failed, and the virus was allowed to persist. (24)

After failing to repeatedly reach the required threshold, development turned to an oral vaccine. In the 1980s, a mass vaccination campaign was implemented across the EU after small trials were deemed effective. These campaigns have shown remarkable success in controlling infection throughout the red fox populations in the EU. Showcasing that point, in 2019 only a small number of animals were documented and the elimination of rabies in mammals has been achieved by 2020. (25) Table 1 list the number of cases per animal reservoir over the course of almost 10 years.

European rabies cases have been relatively stable over the course of past few decades, but caution should still be addressed. Reported data suggest there are two main groups of individuals that are increased risk for contracting rabies in this part of the world. People who handle puppies of unknown vaccination status, and do not consider it a risk of exposure, and people who are scratched by an animal who do not seek medical attention. (25) Both causes can be lessened by increasing rabies public health messaging campaigns across Europe. Through the swift action of the European government and its partnerships across the globe, dog rabies campaigns can quickly

be implemented in todays technologically connected world. Gone are the days of tossing fliers out of airplanes or using privatized health segments in newspaper.

Table 1: Number of animal rabies cases reported from EU/EEA countries in foxes, raccoon dogs, farmed animals, dogs and cats, 2010-2019 (n= 3,323)

Animals	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**Total**
Foxes (*Vulpes vulpes and Vulpes lagopus*[a])	643	331	503	544	319	99	14	2	6	3	2,464
Raccoon dogs (*Nyctereutes procyonoides*)	15	11	4	0	1	3	1	0	0	0	35
Farmed mammals[b]	75	51	70	85	56	11	10	3	1	1	363
Dogs (*Canis lupus familiaris*)	41	47	65	74	27	14	3	1	1	0	273
Cats (*Felis catus*)	42	29	45	39	18	12	2	1	0	0	188
Total	816	469	687	742	421	139	30	7	8	4	3,323

Source: Data for 2010 to 2018 were reported to the European Food Safety Authority using the Data Collection Framework; data for 2019 were reported via the Animal Disease Notification System of the European Commission. Data downloaded on 17 December 2019.

5.3.1 Table Discussion

There is a gradual decline in cases with a small spike in between 2012-2013, and a sharp drop off in 2014-2015. This drop off can be attributed to the rapid deployment of the oral vaccine to red fox populations. Chart details also include other rabies infected mammalian species dominant in the EU. Since Europe represents a large portion of the world's tourist economy, travelers to countries need to heed the warnings about engaging local wildlife. Pre-exposure vaccination should be followed if a travel thinks they may be exposed to a possibly rabid animal. If exposed, seek immediately medical attention at the local clinic or hospital for post exposure prophylaxis. While the overall risk remains relatively low across countries in Europe, there remains a small chance of exposure regardless of where individuals go.

6.0 Vaccination & Prevention Strategies

6.1 Dog Bite Prevention/Vaccination as a Critical Challenge

One of the biggest challenges to the rabies epidemic in these countries is how healthcare professionals and government officials implement a preventative strategy for dog bites. As discussed above, dog bites account for most rabies infections in the countries listed. Dogs, especially males, can be territorial and dangerous if provoked into an attack. Caution should be taken when encountering new stray dogs or keeping ones in the household as a pet. It's critical to treat all unknown dogs as possible rabies carriers unless their vaccination status is known. Once healthcare teams are ready to be deployed, they face another challenge: Catching stray dogs is not easy. These are hardy, streetwise animals, not lumbering, overweight Labradors. The dogs see the dog catchers coming a mile off, setting off a chase which may or may not result in a dog being caught, immobilized, and given a shot. (13) Most local city authorities, already dealing with other important issues like pollution, tend to treat dog vaccination as a low priority.

Another major issue India and Africa are facing is the challenge of mass vaccination campaigns across the country in rabies endemic areas. Healthcare professionals need to overcome the logistic challenge of tracking down stray dogs (who could potentially number in the tens of millions) and giving them the vaccine. (13) This is not to mention the nightmare of stockpiling enough rabies vaccine with which to begin the campaigns. India's government has listed rabies as "low concern" meaning governmental funding to prophylaxis treatments has been reduced to negligible amounts. Healthcare lobbying for increased rabies vaccines needs to be made a priority

if change is to occur. One strategy that has shown promise in India is the "OneHealth (OHA) approach". This partnership involves using collaborative, multisectoral, and trans directional methods between local, regional, and global partners to help fight help issues. (13) Scientists working for the OHA realize that people's health is closely related to the health of animals that they share the environment with. Studies analyzed in the literature paint the OHA as a cost-effective means of adequately implementing a program that can turn the tide in the rabies fight. OHA methods are centered on three main pillars: Rabies surveillance, health education, and dog vaccination. While many of these concepts have been addressed above, this approach can be modeled and applied to other countries that have continued cases.

6.2 Changing Rabies into a "Notifiable Disease"

Local governments need to declare rabies a "notifiable" disease like polio or tuberculosis, and they need to place more emphasis on the deaths it causes. Essentially, it means the government would pay proper attention to it, measuring the incidence rate, monitoring progress, and allocating resources and funds. (13) With its status beginning updated, rabies would now be placed under the umbrella of infectious disease surveillance and be taken seriously instead of an issue left to dog owners/sellers.

Below the governmental level, rural communities around the country need to make sure they are taking an active approach in spaying/neutering stray dogs. There is only so much leadership can accomplish without the active participation of the people. Local community leaders must disseminate education pamphlets on what symptoms to look out for on a potentially rabid

dog/how to report that using the surveillance system. These pamphlets can be requested from regional health departments or even federal ones if there is funding. In terms of trusting the guidance in these pamphlets, that ties back into the other point in reaching out and building trust with these communities. If there is some form of trust, they would be more likely to listen to the information.

6.3 Challenges in Rabies Eradication

One of the biggest challenges in making adequate rabies progress is defining the burden of disease in endemic countries. Experts from agencies like the CDC in North America and W.H.O. in Switzerland have fanned out across rural communities to help identify the true burden countries are facing. Besides defining the burden of disease, training the healthcare workforce in India, Africa, and Europe requires more funding/time than is currently being done. Certain rural communities are resource poor and there are not enough well-trained epidemiologists, laboratory workers with expertise in rabies diagnostic testing, and medical and veterinary care providers with knowledge about proper rabies exposure evaluation methods in addition to giving post exposure therapy.

6.4 Vaccination

Current knowledge on rabies treatment consists of administering a live-attenuated virus-based vaccine prophylactically. Due to the high mortality rate of rabies infection, only inactivated vaccines are approved for human use. The rabies vaccine triggers both CD4+ T cell responses as well as CD8+, both of which play a pivotal role in the cellular immune response. (28) Studies on future vaccines against rabies have begun with manipulating the rabies virus genome that have led to some startling results. Findings have shown that the virulent wild-type rabies virus can be attenuated through passages in cultured cells. In addition, further studies have shown the molecular basis for phenotypes. (29) Going even further, it may be indicative that it might be possibly to develop revolutionary therapeutics that have increased immunogenicity. (30) These tools would hopefully incorporate strategies such as targeting viral genes, insertion of proinflammatory cytokines, and using genetic tools to engineer the rabies virus genome. Since the development of the rabies vaccine by Louis Pasteur, the treatment tool has only become more refined and effective. Cell-culture vaccines today are highly effective and efficacious, while being also safe, and easily accessible if funding is there. Besides the vaccines themselves, research discussions have centered on the idea of administering them before exposure occurs in high-risk groups such as the young and old. This public health strategy would effectively reduce the incidence of rabies cases in endemic prone areas.

7.0 Recommendations for Public Health

Researchers need to focus more on cultural practices, logistical hurdles, and communication methods if they want to make a dent in number of rabies cases per low-income burden countries. Public health education is at the core of everything healthcare professionals/public health workers need to do to make a difference in the communities they treat. Every effort should be made to connect with rural communities to better understand their way of life dealing with stray dogs and how they feel about the virus. By getting to know them, researchers can tailor their message scientifically to make it easier to understand.

Logistics concerns can be solved by mass coordination between public health facilities and hospitals across the country. I briefly discussed above that turning rabies into a "notifiable" disease is the first course of action needed to trigger cooperation. If this doesn't work, bring in outside agencies from across the global in addition to stronger efforts by the CDC/WHO. Finally, the last thing that needs to be mentioned is communication. Many residents of are poor and illiterate making communication methods hard to accomplish. There needs to be a strong push in getting rural community members educated so they can understand basic public health and in the case of rabies, what to do if they get bitten.

7.1 Discussion/Conclusion

Concluding thoughts on this topic have showcased how governments treat infectious diseases in their borders. Most of the time this is through neglectful inaction, and only moving the bare minimum in helping residents that live within their borders. Relevant information on rabies was located across the spectrum and paints a grim, but hopeful, outlook on combatting this terrible virus. If governments want to move forward towards total eradication by a certain date, this requires the mass coordination of multiple stakeholders across the globe. Federal action such as mass shipping vaccines, training doctors/public health staff, and building up infrastructure needs to be implemented if there is to be any movement toward eradication. Problems such as lack of funding, education, and technical systems can be addressed if the commitment is there. Interpreting this information presented requires a multitude of responses in the realms of scientific, governmental, and humanitarian areas.

Rabies is a terrifying disease that has disproportionately affected vulnerable populations across the globe. After conducting this review, the need for first-class treatment methods has become apparent. While a single treatment method exists, this must be expanded into a rapid deployment of multiple treatments so one day, clinical rabies will no longer be a death sentence for so many. Improving healthcare will be able to save these individuals so they can go back to their families.

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