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Review Article

Recent advances in vaccines and therapeutics for Nipah virus

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ABSTRACT

The Nipah virus (NiV) is a newly discovered zoonotic paramyxovirus that affects people and causes serious, frequently fatal respiratory and neurological conditions. Following an encephalitis outbreak among pig farmers in Malaysia and Singapore, the virus was initially identified, and subsequent outbreaks in Bangladesh or India took place virtually annually. Due to NiV's high pathogenicity, the pandemic potential spread, and lack of licensed vaccines or therapeutics, research and development is needed to create highly sensitive and precise diagnostic tools, antivirals, and vaccines that will aid in preventing and controlling outbreak situations in the future.

Keywords: Nipah, Paramyxovirus, Vaccination

INTRODUCTION

The first cases started at the end of September 1998 in villages near the town of Ipoh in the state of Perak, Western Malaysia, where pig farming was an important sector.[1] Cases continued in this area until the beginning of February 1999. The second cluster occurred in December 1998 and January 1999 near Sikamat, a small city in a different state, Negeri Sembilan. The third and largest cluster began in December 1998 near the town of Bukit Pelandok, but the situation remained constant.[1] Because 4 serum samples from 28 patients in this epidemic area tested positive for Japanese B encephalitis (JE), which had previously caused porcine-associated outbreaks in Malaysia, at first the cases were attributed to immunoglobulin (Ig)M that is specific to the JE as well as JE nucleic acids were found in some of the patients' samples.[2] The majority of the patients in this outbreak were adult males as opposed to children, which is unusual for JE.[3] In contrast to a disease spread by mosquitoes, a large percentage of victims had direct physical contact with pigs. As many as 33% of symptomatic cases among family members in the same home were clustered (1), suggesting a higher attack rate than the JE virus, which only causes symptoms in one out of every 300 infected people.[4] Anti-JE measures failed to halt the rise in new cases, and many patients had already received JE vaccinations.

In addition, there were reports of sick animals, including sick pigs that developed a severe barking cough and died from the illness, which was also not a symptom of JE. The distribution of the affected villages was notable because, despite being close to Chinese farms that had cases of encephalitis, there were no instances recorded from the Malay villages. The majority-Muslim Malays make up Malaysia's largest ethnic group and are prohibited from coming into close contact with pigs or pig products.[5] Researchers at the University of Malaya discovered a virus

in early March 1999 that, based on its outward appearance, belonged to the Paramyxoviridae family, which does not include the JE virus. Additional testing revealed that the virus was interacting with antibodies to the Hendra virus (HeV), and subsequent viral genome sequencing at the Centers for Disease Control and Prevention revealed that the new virus differed from the HeV by around 20%.[6] All affected pig farms in the outbreak locations underwent pig culling procedures. More than 1 million pigs were slaughtered in phase I, which involved culling in regions where outbreak cases had materialized. Phase II involved surveillance at every pig farm in the nation. All pigs at the infected farms and at farms within a 500-meter radius were slaughtered. Farms were considered positive if three samples tested positive for the Nipah virus (NiV). This process took 3 months to complete.[7] On May 27, 1999, the final fatality involved a human being. By that point, Malaysia has had 265 instances of acute NiV encephalitis, resulting in 105 fatalities.

Meanwhile, by the end of February, the outbreak had reached Singapore, which had just begun importing live pigs from Malaysia. Abattoir workers were identified as the source of four instances of encephalitis that were admitted to three different hospitals within a few days of one another. It was announced to the Ministry of Health. On March 3, 1999, imports of pigs from farms in Negri Sembilan were halted. On March 19, 1999, all imports of pigs from Malaysia were blocked, and the two abattoirs in Singapore were shut down for an investigation and thorough cleaning. The case–control study revealed that substantially more case patients than control participants had contact with live pigs. All 11 case patients worked at one of Singapore's two abattoirs. Two to 3 weeks before the onset of the illness in patients, pigs from Malaysian regions impacted by Nipah were imported and slaughtered, which would be consistent with the paramyxovirus' anticipated incubation period. Additionally, the nucleotide sequences of the reverse transcription-PCR products obtained from the Singaporean cases were the same as NiV sequences from cases and pigs in Malaysia[8] discovered a link between pigs from Malaysia and human NiV infection in Singapore. The outbreak was put an end with a restriction on the importation of live pigs from Malaysia, and the ban is still in effect today for the importation of pork and goods containing pork from peninsular Malaysia. Since 2001, NiV outbreaks have continued to occur practically yearly in Bangladesh and India.[9]

The Philippines' National Epidemiology Center was informed in 2014 that there had been human fatalities in two villages on the island of Mindanao. Investigation into the outbreak led to the discovery of more human fatalities, nonfatal infections, concomitant neurologic illness, and multiple abrupt horse deaths. 17 people met the case definition in this instance (11 with encephalitis, 5 with influenza-like illness, and 1 with meningitis). The most recent event this year when Nipah-associated encephalitis in Kerala State, India, claimed the lives of 17 people.[10]

Except for henipaviruses, all agents tested negative for a variety of neurotropic infections. Additionally, IgM antibodies and neutralizing antibodies against NiV were found in 3 individuals. It was believed that the virus may be transmitted to people by close contact with infected horses, coming into contact with contaminated bodily fluids while sick horses were being killed, and/or eating undercooked meat from infected horses. Although the total death rate was 53%, individuals with acute encephalitis had a fatality rate of 82%.[11]

There were reports of person-to-person transmission in the Malaysian outbreak, particularly in the households of the affected index patients. There were no reports of any major illnesses, encephalitis, or hospital admissions among any of the 300 healthcare workers in the three hospitals that had cared for 80% of the patients with encephalitis in the study.[12] However, third serum samples from 3 nurses who had treated encephalitis patients associated with an epidemic contained NiV IgG antibodies that were positive. Despite the fact that they exhibited no signs of encephalitis and that blood tests revealed no IgM response and no anti-NiV neutralizing antibodies, the authors nevertheless came to the conclusion that these were false positives. One of them was a staff nurse who also experienced magnetic resonance imaging modifications resembling those observed in acute NiV. She had no prior contact with pigs, but she had cared for the sick patients, therefore it is likely that she had an asymptomatic or moderate NiV infection.

In Bangladesh and India, where multiple outbreaks were caused by person-to-person transmission, the situation was drastically different. Between 2001 and 2007, approximately half of the cases found in Bangladesh involved human-to-human transmission.[13] The Faridpur outbreak in 2004 provided the best example of person-to-person transmission, with the chain of transmission eventually affecting 34 people over 5 generations.[14] The morbidity and mortality of Nipah virus in different regions across the world are mentioned in Table 1.

CLINICAL EVALUATION OF PATIENTS

In humans, the incubation period lasted 4 days to 2 months, with more than 90% occurring in 2 weeks or fewer.[15] Patients initially displayed symptoms of fever, headache, lightheadedness, and vomiting, which progressed into a diagnosis of acute encephalitis. An aberrant doll's eye reflex, pupillary reflexes, vasomotor alterations, seizures, and myoclonic jerks were among the major symptoms of brainstem dysfunction that was seen in many

individuals.[15] Aseptic meningitis, widespread encephalitis, and focal brainstem involvement were just a few examples of the varied and multifocal neurological involvement. Cerebellar symptoms were very typical. Relapse and late-onset encephalitis, some of which occurred months or years after the acute sickness, were distinct and unique characteristics of NiV infection: In Tan's group of 160 cases, 12 (7.5%) of them experienced relapses after recovering from acute encephalitis, while 3 (3.4%) of them experienced late-onset encephalitis (where the initial infection did not result in neurological manifestation).[16] The longest late-onset encephalitis onset delay was 11 years.[17] In a different series, a sizable majority of the participants had personality changes and clinical symptoms like depression, while others struggled with concentration, language, and/or visual memory problems.[18] In addition, there were variations in neurological manifestations.

Segmental myoclonus was a prevalent feature in the Malaysian instances, although Bangladesh and India did not frequently experience it. Nearly one-third of 22 people, who recovered from NiV, according to a research, had ongoing neurologic and cognitive impairment. Over half of them experienced behavioral and neuropsychiatric alterations comparable to those in the Malaysian and Singaporean instances, and nearly all of them had debilitating chronic fatigue syndrome.[19]

INVOLVEMENT OF RESPIRATORY SYSTEM

Although the effects of NiV infection on the neurological system are well known, involvement of other organ systems was observed to varying degrees. Although it was not evident from the Malaysian series whether respiratory involvement was a result of aspiration or ventilator-associated pneumonia, it was recorded in 14–29% of patients. In Singapore, two of the 11 patients had encephalitis, whereas the other eight patients had merely respiratory symptoms. Respiratory involvement was more prevalent in patients in Bangladesh and India, accounting for 50–70% of cases, with some suffering acute respiratory distress syndrome.

INVENTION OF VIRUS

University of Malaya virologists discovered a virus in the cerebral fluid of a patient with encephalitis in the beginning of March 1999. Syncytia formed in vero cells that had been injected with cerebrospinal fluid samples from three fatal encephalitis cases.

Studies using electron microscopy on the virus revealed traits that are typical of viruses in the Paramyxoviridae family. The initial isolate was made from clinical material from a fatal human case from Kampung Sungai Nipah, a community in Negeri Sembilan, hence earning the moniker NiV.[6]

CLASSIFICATION OF VIRUS

NiV is the second Henipavirus belonging to the Paramyxoviridae family. The closely related HeV, which was found during an inquiry into the 1994 deadly illness outbreak in horses and humans in Australia, is the prototype virus of the genus. The equine morbillivirus was initially thought to be a potential new member of the Morbillivirus genus; however, a subsequent whole-genome investigation found numerous significant molecular markers of HeV that were not shared by any of the known Morbilliviruses. The idea that HeV and NiV are novel paramyxoviruses that do not fit into any of the current genera in the family and that a new genus must be created to accommodate them was confirmed by additional examination of the NiV genome sequence classification.[20] In 2002, the International Committee for Virus Taxonomy approved the establishment of the new genus Henipavirus.

EPIDEMIOLOGY IN ANIMALS

Host animals

Fruit bats, also called flying foxes, belong to the family Pteropodidae and are the primary reservoir hosts of both NiV and HeV.[21] Neither virus, whether it is acquired spontaneously or artificially, seems to induce clinical illness in bats experimentally.[22]

Host range

Tradition has it that interspecies transmission is uncommon and that the host range of paramyxoviruses is constrained.[23] NiV, in contrast, has a fairly wide species tropism. NiV naturally infects pigs, horses, dogs, cats, people, and several species of bats.[24,25] In addition, NiV has been demonstrated to infect guinea pigs, hamsters, ferrets, squirrel monkeys, and African green monkeys in experiments. EphrinB2/B3 molecules, which are substantially conserved in all mammals, are used by NiV as their entrance receptors, contributing to the vast variety of species tropism.[26,27]

As a result of these forest fruit bats migrating to planted orchards and pig farms, it has been hypothesized that the initial transmission of NiV from bats to pigs in Malaysia happened in late 1997 or early 1998 by contamination of pig swill by bat excretions. In Malaysia from Indonesia, where El Nino-related fires and drought struck from 1997 to 1998.[28] Malaysian flying foxes are very migratory, migrating hundreds of kilometers between roosting locations in a year, and they have home ranges that extend outside of Malaysia to encompass Indonesia and Thailand, according to

studies utilizing satellite tracking.[29] Furthermore, NiV was demonstrated to be contagious in populations of flying foxes in Indonesia Chong HT, *et al*. They also demonstrated that the virus was identical to strains found in Pteropus vampyrus in peninsular Malaysia.[30]

PREVENTION OF DISEASE

Since there are few treatment options, prevention should be the main focus of NiV care.

Interventions to stop farm animals from contracting NiV by consuming fruit tainted by bats are among the preventive techniques. Farms should not be located next to fruit trees that draw bats in order to prevent the quick transmission of disease among animals. Instead, they should be built to minimize overpopulation. However, because they go against social and cultural conventions, efforts to cut back on the intake of fresh sap in general would not be well received. Other, preferable strategies include putting up physical barriers to keep bats away from sap and keep them from contaminating it.[31]

TREATMENT AND OUTCOME

Anticonvulsants, the management of secondary infections, mechanical breathing, and rehabilitation made up the majority of the therapeutic options. Ribavirin was used as an empirical treatment for the outbreak in Malaysia because of its ability to pass the blood-brain barrier and broad-spectrum efficacy against DNA and RNA viruses. In an open-label trial of Ribavirin in 140 patients compared to 54 controls, Chong *et al*. showed a decrease in mortality (54% in the control arm against 32% treatment arm, $P = 0.011$).[32]

Between September 1998 and May 1999, Malaysia experienced 265 instances of Nipah encephalitis, with an estimated 105 deaths, for a mortality rate of close to 40%. From the start of symptoms to death, the sickness typically lasted 16 days. Positive viral culture from the CSF and significant brainstem involvement were linked to mortality.[33]

Mortality rates have been substantially higher, nearing 70%, in Bangladesh and India. This is likely due to the respiratory tract's increased involvement in the Bangladeshi-Indian outbreaks, the pathogenicity of the 2 virus strains differing, as well as less developed medical facilities, like critical care units.

ANTIVIRAL DRUGS

Ribavirin and chloroquine

Because of its broad-spectrum antiviral efficacy against both DNA and RNA viruses, ribavirin was the first medication utilized during the 1998 NiV outbreak. In this instance, it was claimed to have a mortality reduction of 36% in treated patients with no discernible side effects.[34] Chloroquine, an antimalarial medication, proved very effective *in vitro* when used either alone or in conjunction with ribavirin. However, *in vivo* NiV infection models including hamsters, ferrets, and AGMs have shown chloroquinavir to be ineffective.[35,36] Ribavirin was only able to postpone death in a hamster model of NiV, indicating that improved patient care and empirical treatment may have been more responsible for the decrease in mortality reported in humans during the 1998 outbreak.[35,36] Other antivirals As NiV antivirals, fusion inhibitors and nucleoside inhibitors have also been researched. A heptad-based peptide fusion inhibitor with a cholesterol tag, NiV-Fc2 could bind to effectively prevent infection and NiV membrane fusion *in vitro*. This also shown modest therapeutic success in combating NiV in the Model of a hamster.[37] In addition, the minor nucleoside inhibitor R1479 been successful *in vitro* against henipaviruses as well as other paramyxoviruses and could be developed into a. therapeutic spectrum, similar to ribavirin.[38]

Favipiravir (T-705)

A purine analogue antiviral drug called favipiravir (T-705) has been approved for treatment against new influenza strains in Japan, and it has through numerous phase 2 and 3 clinical trials. are still going on in Europe and the US. Favipiravir has shown effectiveness against a variety of members of the Paramyxoviridae, Filoviridae, and Arenaviridae families of RNA viruses, as well as other RNA viruses, the Bunyavirales order, etc. We have now established the efficacy of favipiravir as an antiviral agent against henipaviruses. Favipiravir prevented the replication and transcription of the NiV and HeVs *in vitro* during micromolar concentrations. In the Syrian hamster model, oral administration twice daily or 14 days of subcutaneous favipiravir treatment completely shielded animals exposed to a deadly NiV dosage. This is the first instance of an *in vivo* henipavirus infection treatment that has succeeded. Drug molecule implies that favipiravir should be further evaluated as an antiviral treatment option for henipavirus infections.[39]

As NiV antivirals, fusion inhibitors, and nucleoside inhibitors have also been investigated. NiV-Fc2, a heptad peptide-based cholesterol-tagged fusion inhibitor, inhibited NiV membrane fusion and infection *in vitro*. In the hamster model, this inhibitor also had some therapeutic efficacy against NiV. R1479, a small nucleoside inhibitor, has also been shown to be effective *in vitro* against henipaviruses and other paramyxoviruses, and has the potential to be modified as a broad spectrum therapeutic, similar to ribavirin. The Antiviral drugs used in the treatment of Nipah virus infection are mentioned in Table 2.

MONOCLONAL ANTIBODIES

m102.4

A phage-displayed antibody library was used to isolate a human monoclonal antibody (mAb) specific for the G glycoprotein of

Table 1: Morbidity and mortality of Nipah virus in different regions across the world.[15]

Month and year	Location/Country	Number of cases	Number of death	Mortality rate (%)
September 1998–April 1999	Perak, Selangor, Negeri Sebilan (Malaysia)	265	105	40
March 1999	Singapore	11	1	9
January–February 2001	Siliguri (India)	66	45	68
April–May 2001	Meherpur (Bangladesh)	13	9	69
January 2003	Naogaon (Bangladesh)	13	9	69
April 2004	Faridpur (Banglasdesh)	36	27	75
January 2004	Rajbari (Banglasdesh)	31	23	74
January–March 2005	Tangail (Bangladesh)	12	11	92
January–February 2007	Thakurgaon (Bangladesh)	7	3	43
March 2007	Kushtia, Pabna, Natore (Bangladesh)	8	5	63
April 2007	Naogaon (Bangladesh)	3	1	33
April 2007	Nadia (India)	5	5	100
February 2008	Manikgonj (Bangladesh)	4	4	100
April 2008	Rajbari and Faridpur (Bangladesh)	7	5	74
January 2009	Gaibandha, Rangpur and Nilphamari (Bangladesh)	3	0	0
January 2009	Rajbari (Banglasdesh)	1	1	100
February–March 2010	Faridpur, Rajbari, Gopalganj, Madaripur (Bangladesh)	16	14	87.5
January–February 2011	Lalmohirhat, Dinajpur, Comilla, Nilphamari and Rangpur (Bangladesh)	44	40	91
February 2012	Joypurhat, Rajshahi, Natore, Rajbari and Gopalganj (Bangladesh)	12	10	83
January–February 2013	Gaibandha, Natore, Rajshahi, Naogaon, Rajbari, Pabna, Jhenaidah, Mymensingh (Bangladesh)	12	10	83
February 2014	Manikganj, Magura, Faridpur, Rangpur, Shaariatpur, Kushtia, Rajshahi, Natore, Dinajpur, Chapai Nawabganj, Naogaon	18	9	50
March–May 2014	Tinalon and Midtungok (Philippines)	17	9	53
February 2015	Nilphamari, Ponchoghor, Faridpur, Magura, Naugaon, Rajbari (Bangladesh)	9	6	67
May 2018	Kozhikode, Malappuram (India)	19	17	89
June 2019	Kochi, Kerala	1	0	0

henipaviruses. This mAb, m102.4, has demonstrated strong cross-reactive neutralizing efficacy against both HeV and NiV and is specific for an epitope in the Ephrin-B2 and Ephrin-B3 receptor binding regions of G.[40] At various periods after exposure, m102.4 can stop illness in ferrets and non-human primates that have received an evenly fatal dose of both NiV-M and NiV-B.[41-43] Although there may be a feasible therapeutic window of usage, this sort of passive immunization would be best suited as a post-exposure treatment in future outbreak situations.[43] On compassionate grounds, m102.4 has been given to 11 people who are at high risk of being exposed to HeV since 2010. No negative side effects have been reported to date, and a phase 1 clinical safety investigation in people is now being conducted to further examine this antibody.

VACCINATION IN ANIMALS

Animals are entirely protected from high dose NiV challenge by a subunit vaccination based on a recombinant soluble and oligomeric version of HeV G (sG), with no clinical symptoms or indicators of virus multiplication or pathology. High quantities of cross-reactive NiV-specific IgG and nAbs are produced in vaccinated cats, ferrets, and AGMs.[44-46] Later, this subunit vaccine was created and given Australian approval to be used as the Equivac® horse vaccination.[47] A cell-mediated immune response is also necessary to give protection, according to results of another investigation that revealed pigs immunized with HeV sG did not generate high cross-reactive nAb responses to NiV post challenge.[48] An orthologous recombinant NiV sG-based vaccine candidate that provides full protection against NiV challenge in cats has been developed.[44]

VECTORED VACCINES

The hamster model used in one of the first NiV vaccination and challenge studies documented involved weakened vaccine viruses that produce recombinant NiV F and/or G.

Whether the glycoproteins were expressed separately or in concert, Recombinant vaccinia vaccines were able to offer protection against after a NiV challenge, total protection. Also accurate was this after passive transfer of the hamsters' vaccine-induced antibodies high nAb titers to uninitiated hamsters.[49] A canary pox vaccination moreover, a vector (ALVAC) has been created that expresses NiV F, G, or Pigs have been immunized using both glycoproteins and a procedure called without histopathology or viral shedding, an experimental model observable in animals who had received vaccinations.[50] Therapeutics and pre-clinical vaccines against NiV are enumerated in Table 3.

VESICULAR STOMATITIS VIRUS (VSV) VECTORS

Candidate vaccines have been developed using a variety of VSV vector platforms. This involves using live attenuated recombinant VSV (rVSV) expressing NiV F, G, or N[51-53] or pseudo typing replication-defective VSV lacking its envelope G protein (VSVDG) with NiV F or G. Single-dose injection

Table 2: Antiviral drugs used in the treatment of Nipah virus infection.

Antiviral drug	Class	Year	Mode of action
Ribavirin	Nucleoside analogues	1998	Mainly act by the inhibition of viral polymerase enzyme
Favipiravir.[39]	Purine anlogues	2018	This molecule acts as a substrate for the RNA-dependent RNA-polymerase enzyme, which misidentifies it as a purine nucleotide, inhibiting its activity and causing viral protein synthesis to stop

Table 3: Therapeutics and pre-clinical vaccines and against NiV.

Channel	Targeted antigen	Schedule of vaccination	Dose	Animal models
m102.4 Human monoclonal antibody.[40]	HeV G/NiV	IV 15 mg/kg, 1, 3 or 5 days post challenge, then again after 2 days	IT 5×10^5 PFU NiV-M	Ferret
		IV 50 mg (24 h before) Pre challenge dose (10 h after) post challenge dose	ON 5×10^3 TCID50 NiV-M	African Green Monkey
Polyclonal serum.[41]	NiV F and/or G	IV 0.2 mL of antiserum	IP 1×10^3 PFU NiV-M	Hamster
Recombinant vaccinia virus.[42]	NiV F and/or G	SC 10^7 NiV F	IP 1×10^3 PFU NiV-M	Hamster
Recombinant canarypox virus.[43]	NiV F and/or G	IM 10^8 PFU NiV F	ON 2.5×10^5 PFU NiVM	Pig
Recombinant VSV.[54]	NiV F and/or G, or N	IM 1×10^7 PFU NiV-B F, G or F and G	ON 5×10^3 PFU NiV-M	Ferret
		IM 1×10^6 infectious particles NiV-M F	IP 10^5 TCID-50 NiV-M	Hamster
Recombinant adeno associated virus.[55]	NiV G	IM (2.1010 infectious particles) D (1.1010) for mice; IM (6.1011) for hamster	IP-10^4 PFU NiV-M	BALB/c mice Hamster
Recombinant measles virus.[55]	NiV G	IP 2×10^4 TCID50 NiV G for hamster. Boost after 21 days	IP-10^3 TCID50 NiV-M	Hamster
		SC 1×10^5 TCID50 for NiV G for AGM. Boost after 28 days	IP-10^5 TCID50 NiV-M	African Green Monkey
Recombinant subunit.[54]	NiV/HeVsG	SC 4, 20 or 100 g HeVsG. Boost after 20 days	ON 5×10^3 TCID50 NIVB	Ferret
		SC 100 g NiVsG or HeVsG. Boost after 2 and 4 weeks	SC $5\times10^2/5\times10^3$ TCID50 NiV-M	
Venezuelan equine encephalitis virus replicon particles.[56]	NiV F or G	Footpad inoculation 3.1×10^5 infectious units. Boost after 5 and 18 weeks		Mice
VLPs.[57]	NiV F, G and M	IM 30 g VLP. Boost after 21 and 42 days	IP 1.6×10^4 PFU NiV-M	Hamster
		OR IM 30 g VLP	OR IP 3.3×10^4 NiV-M	

VSV: Vesicular stomatitis virus, VLPs: Virus-like particles, NiV: Nipah virus , HeV: Hendra virus, sG: Soluble G, EID50: 50% Embryo infectious dose. IV: Intravenous, ON: Oronasal, IT: Intratracheal, IP: Intraperitoneal, IM: Intramuscular, ID: Intradermal, SC: Subcutaneous, PFU: Plaque forming units, TCID50: 50% tissue culture infectious dose. m102.4 is currently in phase 1 trials in humans. HeVsG licenced for use in horses

of these vaccines, which were created utilizing both NiV-M and NiV-B strains, was able to completely protect Syrian hamsters, ferrets, and AGMs exposed to lethal levels of NiV.

Animals immunized with NiV F or Gene expressing vectors showed high nAb titers, low viral RNA/antigen levels, and no signs of disease.[51,52,54] Interestingly, only partial protection was given in hamsters vaccinated with rVSV expressing NiV-N, suggesting a potential role for both the cellular and non-neutralizing antibody responses in protection from disease.[53]

PARAMYXOVIRUS VECTORS

It has been demonstrated that a recombinant measles virus vaccination expressing the NiV glycoproteins totally shields hamsters from NiV challenge. AGMs that received two doses of the same vaccination, however, were only partially protected and showed symptoms of neurological illness.[55] It has also been described to use a recombinant Newcastle disease virus strain that expresses the NiV G or F envelope proteins as a paramyxovirus vectored platform. In these experiments, CD8 T cell responses and nAb responses were produced when administered singly or in combination, and immunogenicity was assessed in both mice and pigs.[56]

OTHER VIRUS VECTORS

It has been demonstrated that giving mice three doses of Venezuelan equine encephalitis virus replicon particles carrying NiV F or G induces highly powerful nAb responses.[57] The NiV G protein-expressing adeno-associated viral vector has also been described and put to the test in a hamster model. Hamsters were protected against a deadly NiV challenge with just one dose of this vaccine, which also produced strong nAb reactions.

VIRUS-LIKE PARTICLES (VLP)

The NiV F, G, and M proteins were successfully expressed in mammalian cells to create VLP These have been tested in a BALB/c mouse model and have been shown to induce a nAb response as well as protect vaccinated hamsters against NiV challenge after a three-dose regimen as well as a "single-shot" regimen.

The success of the mAb m102.4, which has now advanced to phase 1 clinical trials in humans, is encouraging even if the development of antivirals and immune modulators is still in a very early stage. However, unlike m102.4, no vaccine candidates have yet reached the stage of human clinical trials. This is in part because to the extremely challenging aspect of conducting Phase 3 effectiveness studies on relatively uncommon diseases like Nipah. The ideal candidate would be cost-effective and useful in an outbreak emergency since it would offer high levels of protection after a single dose of immunization. The "One Health" strategy to immunization is beneficial for preventing and controlling the NiV disease in cattle and limiting its spread to people.

CONCLUSION

NiV was an entire different virus when it first appeared exactly 20 years ago. NiV outbreaks have been reported in several countries over the last two decades, including Malaysia, Singapore, and Bangladesh, with the most recent reports coming from Kerala, India. Because of the high mortality and mobility rate of NiV infection, such outbreaks have posed a significant threat to the economies and community health of affected countries. Furthermore, expert scientists have speculated that NiV could be the next pandemic agent to emerge after COVID-19. As a result, it is critical that public preparedness and awareness, particularly in affected areas, be implemented in order to control and effectively contain NiV outbreaks. Furthermore, prohibiting pig transportation in affected areas and improving hygiene practices at pig operation centers are strongly advised. Furthermore, cooperative efforts should be made. In the recent research with the Syrian hamster model, favipiravir administered twice daily or once daily subcutaneously for 14 days completely protected animals challenged with a lethal dose of NiV. This first successful *in vivo* treatment of henipavirus infection with a small molecule drug suggests that favipiravir should be investigated further as an antiviral treatment option for henipavirus infections. Furthermore, collaborative efforts should be made to accelerate the development of specific treatment regimens to prevent the spread of NiV.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflict of interest.

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