Nipah: The history, and future, of one of the world's most lethal viruses

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B.S., Biology and Community Health

Tufts University, 2022

Submitted to the Program in Comparative Media Studies / Writing in partial fulfillment of the requirements for the degree of

Master of Science in Science Writing

at the

Massachusetts Institute of Technology

September 2024

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ABSTRACT

The Nipah virus kills around three quarters of people who contract it, making it one of the most lethal viruses known to infect humans. The virus first emerged in 1998, when hundreds of pig farmers in Malaysia fell ill with fevers and encephalitis, or brain inflammation. Nipah has caused smaller outbreaks in nearby Bangladesh nearly every year since then.

The Malaysian farmers appeared to have been infected directly from their pigs, rather than from each other. For a time, there was no clear evidence that Nipah could spread from humans to other humans. That changed in April of 2004, when investigators responding to a Nipah outbreak in a remote district in Bangladesh discovered that the virus was spreading person to person.

Pteropus fruit bats, which are native to South Asia, were identified as the natural reservoirs of the Nipah virus. Researchers have spent the last two decades studying the virus' transmission in bats and how the virus spills over into humans. Institutions across the world have even recently started developing Nipah vaccines.

Scientists believe the Nipah strains that currently circulate in humans are likely not transmissible enough to ignite a pandemic in people. That could change. Whether the virus one day evolves to spread better within humans, or hits a particularly susceptible place and thrives, officials worry about what could happen if Nipah ever affects larger populations. The Nipah virus is just one of many zoonotic pathogens that scientists are studying to understand how humanity can prepare for future deadly pathogens.

Emily Gurley, an American epidemiologist, was working in an old cholera ward on April 7, 2004, when she made a chilling discovery. At the time, Gurley was an employee for the International Center for Diorrheal Disease in Bangladesh, also known as ICDDR,B. The ward was near a remote village in Faridpur, a district in Bangladesh, where she and two of her colleagues had arrived the day before to investigate an outbreak of a mysterious illness.

The cement ward housed over a dozen sick villagers who had recently developed fevers. Many now had splitting headaches and unrelenting coughs. The sickest patients had suffered through an altered mental state and were now unconscious, including an older woman.

A concrete partition divided the ward, which was a short walk from a main hospital building and had originally been built to isolate cholera patients, into two small chambers. The rooms were crowded. Gurley's team had arranged for the sick villagers to come to the hospital earlier that day, and now most patients had a family member caring for them at their bedside. The investigators had brought enough protective masks, gloves, and gowns for themselves, but not enough for everyone in the ward.

"We were completely unprepared for what we found," Gurley told me.

Gurley's job was to collect information and try to identify the outbreak's cause. She circled through the ward and interviewed patients or their caregivers. She asked when they got sick, what symptoms they had, whether anyone else in their household was ill. It soon became clear that many of the patients were relatives, several of whom lived near each other.

Meanwhile, a thunderstorm raged outside and the hospital's power went out. Windows with wooden shutters were closed to protect patients from the rain.

It was dark by the time Gurley left the ward to get some rest. When she returned the next morning, she learned that two of the patients had died overnight. One was the older woman, who had arrived at the hospital unconscious. The other was a coughing man she had interviewed at length the night before. She was shocked. The man had been very sick but didn't seem mere hours from death. What could have killed him so quickly?

The Faridpur district's civil surgeon suspected the villagers had been infected with the Nipah virus, a deadly pathogen that destroys the lungs and brain of its victims. Nipah had been discovered five years earlier when over two hundred farmers in Malaysia each got infected from an infected pig. Nearly half of the farmers died. No treatments were available to reduce symptoms and there was no cure.

To try to understand the path of the Faridpur outbreak, Gurley started charting how many patients fell sick each day. Called an epidemic curve, this can help researchers visualize whether an outbreak is ongoing and, when combined with patient histories, can give clues as to how an outbreak started.

The computer Gurley had brought to the ward was dead, and she had no way to charge it, since

the electricity was scarce. She drew the curve by hand, listing each patient's name next to the day they had developed symptoms. What she found concerned her.

Several patients were members of a local Islamic sect whose leader had recently died of the same illness. Many were his family members. The villagers appeared to have been infected by him. But was that even possible?

"At the time, there were no reports of Nipah being spread person to person," Gurley said.

Yet it was the best explanation for the epidemic curve she had drawn.

Gurley showed one of her colleagues, a clinical epidemiologist named Jahangir Hossain, her paper. Perhaps the pathogen wasn't Nipah, the pair reasoned — perhaps it was some other deadly infection. A year earlier, a never-before-seen virus called severe acute respiratory syndrome, or SARS, had infected 8,000 people across 29 countries and killed nearly 800. One of the patients that died before Gurley arrived had received an X-ray, and clinicians thought his lungs looked as though he had tuberculosis.

The team had been face to face with several patients for hours. Maybe the unknown pathogen was Nipah, maybe it was something else. No matter what the virus was, Gurley started to wonder — had she been exposed?

The Nipah virus is now recognized as one of the most lethal pathogens in the world. There is still no cure. The most common strain kills about three quarters of the people it infects. Its severity is often compared to the likes of Ebola, an African virus that in 2014 caused one of the scariest outbreaks in recent memory. There are only a handful of viruses that kill people as efficiently.

Nipah causes fever and encephalitis, which is the medical term describing the inflammation of brain tissue. The headache is caused by the infection's swelling of the brain. Many of Nipah's victims eventually develop seizures, go into a state of delirium, fall unconscious, and die.

Patients in Bangladesh and India also develop respiratory symptoms. Their last waking moments are often spent in an altered mental state as they battle a relentless cough. It is a horrific way to die.

The virus moves remarkably fast. Most patients die within six days, and the ones that survive don't always make a full recovery. About a third of survivors have long-term neurological damage.

There is one saving grace. Nipah does not spread very efficiently between people. Only one out of every ten Nipah patients, for example, will infect another person. Experts believe that the

Nipah virus strains that have infected humans so far are unlikely to trigger a pandemic.

That could change. We live in an increasingly connected world. The COVID-19 crisis demonstrated how rapidly a new virus could emerge and cause a global emergency. Epidemiologists worry that if Nipah evolves to spread more easily, or hits the wrong place at the wrong time, it could cause a disaster.

For the most part, we cannot predict when or how a new virus will emerge. That doesn't mean we can't prepare. The last few decades have introduced tools to study viral genetics and their most mysterious properties. Nipah is just one of many deadly viruses that are forcing scientists to grapple with the question — how can we prepare for future deadly pathogens?

Earth is a world of viruses. There are more than 380 trillion individual viruses in the human body at any given moment — about 10 viruses for every human cell. They are tiny. The smallest Nipah virus particles compared to the diameter of a human red blood cell are the same size as a man compared to the Statue of Liberty.

Most viruses are benign to us. Viruses are essentially just genetic material encased in a shell. They cannot replicate on their own, and instead must hack the replication material of other cells to reproduce. It's often in a virus's best interests to keep its host alive for as long as possible, since viruses who do not eradicate their hosts may have a better chance at reproducing and spreading their genetic material.

Many of the most successful viruses spread efficiently and kill sporadically. The ability to spread, called a virus' transmissibility, is why SARS-CoV-2 was so good at traveling across the globe. It is highly contagious, and in the grand scheme of things, does not kill most of the people it infects. Hosts that live longer are then able to infect more and more people.

Nipah is, on the other hand, highly lethal but not very transmissible. There is a widespread thought that viruses with such high mortality rates are unlikely to cause larger epidemics, since they often kill their hosts very quickly.

But whether they slowly evolve to spread better, or they infect somewhere particularly susceptible and thrive, highly fatal pathogens may be able to spread efficiently under the right circumstances. If Nipah were to one day become transmissible enough to ignite a pandemic, experts want to be ready.

"A lot of people who are not directly involved with Nipah will not know that this is a pandemic potential pathogen," Mahmudur Rahman, an epidemiologist who served as the Director of the Institute of Epidemiology, Disease Control and Research in Bangladesh for 12 years, told me. "That understanding is lacking."

Most of the world's viruses remain unidentified. It is often only when they cause a crisis, killing

large numbers of people, that scientists start paying attention.

The first recorded Nipah outbreak started as a pig epidemic. In 1970, a large pig farm opened in Northern Malaysia. The farm grew rapidly, and by 1980, it housed over 30,000 pigs and was a one stop shop for raising them. Piglets were born, weaned, and fattened up for market all in one place.

By the end of the twentieth century, the Malaysian pig industry blossomed into a billion-dollar business. In the midst of the success, farmers at the large farm in Northern Malaysia planted mango trees on land next to the pig farms in 1983 in hopes of selling the fruit.

This was their crucial mistake. Flying foxes, huge furry fruit bats from the genus *Pteropus* with a wingspan up to the size of a human adult, are native to South Asia. They are considered a nuisance by locals, who actively shoot at the animals to prevent them from stealing fruit. The bats, desperate for places to feed, found refuge in the large farm's mango trees.

At some point, Nipah-infected bats spread the virus to the pigs, possibly by urinating or dropping contaminated fruit into the pig pen. The pigs then got infected, many of whom developed respiratory and neurologic symptoms. But most of the pigs recovered. Even though pigs are quite physiologically similar to humans, less than five percent of them die from Nipah.

The pig population may have been expected to develop herd immunity to the virus, causing the epidemic to eventually fade. But because the industrial pig farm was constantly breeding new piglets to fatten and eventually sell, the virus had regular batches of fresh hosts to infect. Nipah thus incubated there, slowly spreading within its porcine hosts.

The first farmers developed encephalitis in 1998. Malaysian scientists initially believed the infection was an outbreak of Japanese Encephalitis, a virus spread by mosquitoes and native to Southeast Asia. But Japanese Encephalitis is mostly found in children, and it rarely kills. Adult farmers were dying too often for such a diagnosis to make sense.

A Malaysian virologist named Paul Chua identified the Nipah virus in 1999. He personally escorted infected patient samples, carefully packaged in his carry-on, to a lab in Colorado run by the U.S. Centers for Disease Control and Prevention. There, he saw Nipah under a microscope for the first time.

The Malaysian government took swift and draconian measures to stop the outbreak. They sent in the army to kill nearly a million pigs in farms throughout the country. Soldiers pushed screaming pigs into pits and shot them.

The culling economically decimated the country's pig farming industry. But it worked. Nipah has not been detected in Malaysia since 1999.

In the end, the Nipah outbreak in Malaysia infected over 250 people, 105 of whom died. It remains the largest Nipah outbreak ever recorded. Still, investigators saw one hope: the virus only appeared to spread directly from pigs to farmers.

“One of the dogmatic things people would talk about in the Malaysia outbreak was ‘well, at least it didn’t spread between people,’” Jon Epstein, a veterinarian and disease ecologist who helped study the first Nipah outbreaks on Malaysian pig farms, told me in an interview.

It didn’t take long for scientists to realize that Nipah was not restricted to Malaysia. Smaller outbreaks popped up in Bangladesh from 2001 to 2003. The Nipah strain that circulates in Bangladesh is more lethal than the Malaysian one, killing closer to three quarters of patients. Patients with the Bangladeshi strain suffer from encephalitis but also have respiratory symptoms, including severe coughing fits.

Respiratory symptoms are alarming because they can make viruses more transmissible. Nipah spreads through bodily fluids, and it can latch onto saliva droplets ejected when a sick person sneezes or coughs. Patients with the Bangladeshi Nipah strain often cough a lot, meaning they may discharge infected respiratory droplets into the air.

There were no labs in Bangladesh that could confirm Nipah cases in 2004. Soon after Emily Gurley learned Nipah could be spreading between people in the Faridpur district, her team traveled back to their headquarters in Dhaka, the capital of Bangladesh, and shipped blood samples from the sick patients to a CDC lab in the United States.

Confirming a Nipah outbreak took a few weeks. In the meantime, Gurley and Hossain checked in with each other after their potential exposure in the ward: are you feeling okay? You don’t have a fever today, do you? As Gurley monitored herself in Dhaka, her mind turned to the villagers in Faridpur. She was anxious to return and find out more about the unknown illness.

“Outbreak investigations in general, and this one in particular, are very high stress, rather emotional situations,” Gurley told me. “That stress comes from witnessing something really horrible that’s happening to people and being tasked with telling that story, but also solving the mystery.”

The team didn’t know if the outbreak was ongoing. Gurley and her colleagues soon returned to Faridpur, where they spent months investigating the outbreak to determine how it started. In May, a team of anthropologists — experts trained to gather information from remote communities very different from their own — arrived and interviewed the victims’s families, neighbors, and healthcare professionals. Their stories, which the anthropologists later published, revealed a detailed picture of the outbreak.

Most of the sick villagers had been in contact with the religious leader, a man whom the

anthropologists referred to under the pseudonym Afsar Monir. The sect Monir led identified under Islam, Bangladesh's state religion. The sect's followers were criticized by other Muslims. They did not pray five times a day, and they did not fast during Ramadan. They sang and smoked copious amounts of tobacco and ganja. Monir's teachings earned him love from his followers, but his teachings also disgruntled other villagers, who claimed his practices went against Islamic rule.

Monir directly infected 22 people, meaning he was the mysterious disease's superspreader. He was not the first case. In March, a few weeks before Gurley arrived, Monir visited his son's mother-in-law, who was dying herself of the unknown illness in a nearby village. He comforted the woman and repeated lines from the Quran as he held her hands. Monir then returned to his village, where he soon got sick.

Monir's family members and followers rushed to care for him as he had cared for the dying woman. They stayed with him the night before he died, feeding him, massaging him, blessing him. They held his head in their laps, even as Monir coughed incessantly, sending respiratory droplets into the air.

In the weeks following his death, Monir's loved ones died one by one. Twelve of his family members got sick, four of whom survived. Caretakers tried to reduce fevers with home remedies, like dousing their loved one's heads with water, to no avail.

The virus killed shockingly quickly. Villagers had their own explanation for why people were dying. They blamed *asmani bala*: a curse imposed by Allah, placed upon Monir's followers for their unconventional practices.

"Allah was angry and wanted to punish people by killing them," one villager said, according to the report by the anthropologists.

There was little anyone could do to help the sick villagers. Some family members withdrew patients from the hospital ward so they could die surrounded by loved ones, and because it was easier to move a person while they were still alive.

Distrust brewed between villagers and the outbreak's responders. A rumor emerged that health care providers were purposefully killing patients in the hospital to stop the outbreak. One mother described how her son and step son were admitted in good spirits, having walked to the hospital while singing. When their condition deteriorated, the mother discharged them. The boys later died.

"If they had not been taken to the hospital they would have lived," the woman told the anthropologists. "They killed my son in the hospital. They pushed an injection and my son died."

The CDC confirmed the villagers had Nipah around three weeks after the team sent the blood samples. Gurley had escaped the virus' incubation period, which is the period before symptoms

develop in which the virus grows inside of a person. None of her colleagues fell ill, either, and neither did any of the hospital's caregivers.

“I think we were very lucky,” Hossain told me. The thought that he might have been infected and might die had crossed his mind. Still, Hossain said he worried not for himself, but for the sick villagers.

Seven more people got sick while the team waited for test results. In the end, Nipah had infected 36 people in Faridpur, 27 of whom died.

The news that Nipah could spread person to person alarmed scientists around the world. Outbreak responders for a massive Indian viral outbreak in 2001 — which infected 66 people, killing 45, and was originally suspected to be measles — reviewed their data and later announced that Nipah may have been spreading among people there as well, including several healthcare workers. Responders poured into Bangladesh in the spring of 2004.

Joel Montgomery was a young epidemiologist for the CDC sent to investigate how Nipah was spreading. Bangladesh is one of the most densely populated countries in the world, with nearly 140 million people living in the country in 2004. If transmission between people occurred there, in a country roughly the size of the state of Georgia, Montgomery worried the deadly pathogen could spread across the world.

“That was pretty alarming and scary, and still is,” Montgomery, now the Chief of the CDC’s Viral Special Pathogens Branch, told me in an interview.

Montgomery and Gurley had become good friends during an earlier Nipah outbreak in January. Now, they wondered whether the January outbreak might hold the key towards determining where the virus had come from in Faridpur.

The January outbreak hit a pair of villages in a nearby township called Goalanda. At the time, the virus did not appear to spread between people. Ten out of 12 villagers died, most of whom were little boys. Gurley, Montgomery and Hossain wondered whether the virus was secretly brewing in an intermediate animal host, similar to what had happened on Malaysian pig farms. But pork is rarely eaten in Bangladesh, and no pigs were being raised in the Goalanda villages, meaning they were not likely to blame this time.

“Bangladesh is predominantly Muslim, so there’s not a lot of pigs,” Montgomery said. “We were all scratching our heads about how this outbreak started.”

The team examined whether the boys had gotten sick from close contact with cows, sheep, goats, and even dogs and cats. No luck. They started looking elsewhere.

“We just walked through the village and said ‘what are all the ways that someone could come into contact with a bat here?’” Gurley recalled.

Gurley stopped to take a picture of a lone date palm tree, which leaned sideways and had a clay pot tied around one of its branches.

“We were like, ‘that’d be a pretty good way,’” Gurley said. “Add it to the questionnaire.”

Sure enough, the investigators learned that nearly all the sick boys often climbed trees. When the Faridpur outbreak broke out later that Spring, they once again asked whether victims had interacted with trees.

The team discovered that the dying woman who Afsar Monir visited in March had contracted the virus from her adult nephew. The nephew had gotten sick shortly before his aunt, and also died. He was the first case, and Gurley traveled to his village to investigate.

“He lived in a village that was just lined by date palm trees,” Gurley said.

Climbing trees alone couldn’t explain why the villagers got Nipah. Somewhere up the trunks, they had to have unknowingly been exposed to bats.

Gurley and Montgomery learned during their outbreak investigations that in the winter, Bangladeshi villagers tapped trees with a spout to harvest a sweet, cloudy liquid called date palm sap. The villagers would often boil the sap to create molasses, but if the sap was fresh enough, they would drink it raw.

Raw date palm sap is considered a delicacy in Bangladesh. The young epidemiologists suspected it could also be secretly contaminated with Nipah. Still, they didn’t have enough evidence yet to prove it.

In 2005, two men took charge of outbreak response teams in Bangladesh. Stephen Luby, an American epidemiologist who was affiliated with CDC, took over at ICDDR,B. His counterpart for the Bangladeshi government’s Institute of Epidemiology Disease Control and Research was an epidemiologist named Mahmudur Rahman. The men were quick friends.

Over the next several years, Luby, Rahman, and Gurley found time and time again that drinking raw date palm sap was consistently associated with contracting Nipah. At one point, a veterinarian at ICDDR,B installed night vision cameras on the date palm trees. The footage revealed that at night, fruit bats nibbled on sap flowing from the tree and urinated into collection pots.

Just like in Malaysia, the bats were looking for food in the trees. Epidemiologists advised villagers to be careful collecting date palm sap. Luby’s team suggested putting bamboo cages around their trees to keep out any bats. Rahman’s institute told the public to not drink date palm

sap at all. Some villagers were skeptical of the advice, but others believed the government and took matters into their own hands.

“The Bangladeshi population is quite resilient,” Rahman told me. He said in one outbreak, “people actually put cow dung on the shaved part of the trees so that they could not collect any more sap.”

Twenty years have passed since Gurley first discovered Nipah could spread among people. Outbreaks have continued nearly every year. She continued studying Nipah in the years immediately following Afsar Monir’s death, leaving Bangladesh in 2009 to earn her Ph.D. at Johns Hopkins. Once done, she flew back to Dhaka to lead ICDDR,B’s Program for Emerging Infections. She settled at Johns Hopkins as a professor in 2017 following a terrorist attack in Bangladesh’s capital.

I visited Gurley in East Baltimore in January 2024. Her office is on the sixth floor of the School of Public Health. A window overlooks industrial buildings and the Patapsco River in the distance. It’s a long way from Bangladesh, but a small version of the country’s flag still hangs on her office wall.

Gurley has shoulder-length silver curly hair and speaks with a smile, a testament to the kindness her collaborators mentioned when they described their experiences working with her. During the two hours I spent with her, she recounted detailed stories of past Nipah outbreaks and walked me through her concerns of humanity’s viral threats, occasionally turning to her computer monitor to show me data or photographs of her in the field two decades ago. At one point, she played with the corner of a hardcover Infectious Disease Epidemiology textbook on her desk — for which she is the latest version’s editor — and told me her story.

She was raised in a rural town in Northern Georgia, in the foothills of the Appalachian mountains. Her father was a firefighter and diver who started the first underwater rescue unit in Atlanta. For the first decade of her life, she only left the state twice. Then, when Gurley was 10 years old, her father died in the line of duty. A year later, her mother remarried a physician who had just taken a job in Bangladesh with the United States Foreign Service. The family packed their bags and moved across the world.

The outbreaks in 2004 were two of the first infectious diseases she ever responded to, having started at ICDDR,B the previous fall. Gurley is now one of the world’s foremost Nipah experts, going back to the time she discovered the virus could spread between people. She has seen firsthand how tragic Nipah outbreaks can be, and worries about what could happen if Nipah ever caught on in a larger human population.

Larger Nipah outbreaks in Bangladesh and India would be horrific. Under the right circumstances, the virus may one day be able to travel further. The worst case scenario would be for Nipah to become capable of fueling large epidemics with efficient spread between people

across the world — in other words, a pandemic.

The Nipah strains that have infected humans so far are likely not transmissible enough to trigger such a monumental crisis. In order to thrive in humans, a new strain that's better at spreading between people would likely need to emerge.

"I think Nipah is important because of what it could become," Gurley said. "The likelihood of that happening is something we don't know, and frankly, aren't smart enough to judge. So it seems prudent to keep an eye on it."

To understand how such a Nipah strain could one day emerge, scientists have spent decades learning more about where the virus comes from. Jon Epstein, a veterinarian and disease ecologist, traveled to Malaysia in 2003 to study the relationship between *Pteropus* fruit bats and Nipah. Epstein had recently graduated from veterinary school, and he wanted to know how common the virus was in bats. He figured the best way to do this was by catching bats by hand.

For the next five years, Epstein and his colleagues surveyed Malaysia in search of the flying mammals. They found bat colonies sleeping high up in the trees in remote mangrove forests and on mountain tops, far away from humans who shot at them in villages. The team would wake the bats up, carefully catch them in nets for testing, and then release them back into the wild.

"Everywhere we looked, bats seemed to have antibodies against Nipah virus," Epstein told me. "That was the real signal to us that this was a virus that was circulating widely in bats around Malaysia."

There was one thing that puzzled Epstein. Lots of bats had antibodies to the virus, meaning they had gotten Nipah before. But it was really hard to find animals actively shedding the virus. Epstein and his colleagues reasoned that bats must not get infected for very long, and must not get very sick. Under those circumstances, the virus might be expected to eventually die out. Why, then, was Nipah so common?

Epstein began attaching satellite collars to captured bats to track their movement. What he found intrigued him. The bats' geographic range was much larger than had ever been recorded. Some of them flew for hundreds of miles, crossing country borders from Indonesia to Thailand. Along the way, they would interact with other bat communities, linking fruit bats across South Asia.

"Different bat colonies are connected to each other because they migrate," Epstein said. "It's effectively one big population where the virus can circulate wherever there are susceptible bats available."

Nipah does not affect bats the same way it affects other mammals, like humans or pigs. This may be due to a bat's unique immune system. Bats use up a lot of energy when they fly, which

causes inflammation. Some ecologists believe the mammals evolved an ability to suppress this inflammation, which would otherwise take a toll on their bodies. This feature, on top of allowing bats to tolerate the stress of flight, may also make them more resilient to viral infections.

“I’ve caught bats that are infected and look perfectly healthy,” Epstein said. “They don’t even break a sweat.”

When scientists looked into bat organs, they began finding trace amounts of Nipah. The virus appeared latent; too low to show up on Epstein’s tests, but potentially able to reinfect bats later on. Nipah has possibly been circulating this way in bat populations for thousands of years, mutating countless times to create the strains that exist today.

According to some of the scientists I spoke to, there are a few scenarios under which a more transmissible Nipah strain — one perhaps capable of causing larger epidemics or even a pandemic — could emerge and make its way into humans.

One scenario is that a more transmissible Nipah strain may already be circulating in bats but has not yet made its way to a human host. The geographic range of *Pteropus* fruit bats extends from Australia all the way to Madagascar. Those bats could carry millions of copies of Nipah and similar viruses, many of which are slightly different from each other. In theory, one of these mutated Nipah strains could be the one that spreads more easily between humans. Were that to be true, it could only be a matter of time before the wrong bat pees into a date palm sap collection pot.

A second scenario would be for Nipah to make it into an intermediate host, like a pig, similar to what happened in Malaysia. It might then be able to incubate in mammal populations to evolve versions of the virus that are more selective towards spreading in animals similar to us. If Nipah were to infect more humans, it might be able to similarly adapt.

“The nightmare scenario is that you get a variant that is efficiently transmitted on a respiratory tract and retains its 75% case fatality rate,” Luby, now a professor at the Stanford School of Medicine, said. “That would be worse than any other historical pandemic.”

Luby believes the likelihood that such a devastating Nipah strain emerges is low. But because the scenario is so deadly, he says it makes sense to invest in preventing it.

Even if Nipah itself never becomes better at spreading between people, there is the worry that one of its undisclosed cousins might. Nipah belongs to a family of viruses called the paramyxoviruses. Measles, one of the most transmissible viruses in human history, is the family’s most infamous member.

Nipah and its closest relative, Hendra — a deadly bat-borne virus that has killed over 100 horses and four humans in Australia since 1994 — belong to a genus within the paramyxovirus family called the henipaviruses. Four other henipavirus species have been discovered since then.

Only one of them, Langya virus, discovered in 2018, is known to cause human disease.

“We’ve seen some henipaviruses that don’t cause disease. And then of course, we have Nipah virus, which causes severe disease in Bangladesh, India, Malaysia,” Epstein, who is now the Vice President for Science and Outreach at the nonprofit EcoHealth Alliance, said. “What we don’t know is what lies in between. It’s possible that some of those viruses are more easily transmitted among people.”

One of the reasons SARS-CoV-2 was so devastating when it appeared in late 2019 was because it had never been seen before. Yet because scientists had spent decades studying its cousin, SARS, a vaccine was ready in record time. Should a more transmissible, as-of-yet unknown henipavirus ever come to the fold, scientists may hope to similarly turn to Nipah research.

“The more we learn about Nipah virus, the better off we are for some of these henipaviruses that are newly discovered or are yet to be discovered,” Montgomery told me.

The scale of a virus with a 75% kill rate causing sustained large outbreaks is hard to imagine. One of the closest frames of reference would be to refer to the history of Ebola, which kills around 50% of its victims, on average.

Ebola was first discovered in 1976 on the banks of the Ebola river in Zaire (in the modern day Democratic Republic of the Congo). The virus wiped out villages in neighboring countries for the next several decades, infecting anywhere from just a couple of people to over 300. The outbreaks were tragic, mainly impacting villagers in rural areas. Still, the number of positive cases recorded before 2013 paled in comparison for what was to come.

In 2014, the virus spread into Guinea, Liberia, and Sierra Leone. The three West African countries had never experienced Ebola outbreaks before. They were not prepared. Healthcare systems in densely populated cities crumbled as over 28,000 people fell ill. By the time the epidemic faded two years later, over 11 thousand West Africans were dead.

Ebola’s ascendancy in West Africa was a wake-up call on how pathogens with high case fatality rates could, in certain situations, cause large epidemics. Nipah has never come close to causing a similar crisis, which could be attributed to factors that make Ebola’s transmissibility higher between people.

“The transmission of Nipah virus between people is not as efficient as Ebola, and so I think that the chance is much smaller that such a big outbreak would happen” Emmie De Wit, a virologist at the National Institute of Health's Rocky Mountain Labs in Hamilton, Montana, said. “Could that change? Certainly.”

Ebola cases started waning by 2016, and towards the end of the epidemic, healthcare experts began giving people an experimental vaccine. The vaccine had been in development for

decades, but at the outbreak's start, it had been tested only in animals. Scientists at Merck, the pharmaceutical company behind the treatment, ramped up production at the start of the 2014 epidemic. The company got permission to start clinical trials and run emergency vaccination campaigns after many people had already died. By 2016, they knew the vaccine was over 95% effective.

Thousands of lives have likely been saved by the Ebola vaccine, which has been used in the last five years to fight back outbreaks in the Democratic Republic of the Congo. Still, people lamented how more people in West Africa could have been saved had a vaccine been ready from the start.

A group called the Coalition for Epidemic Preparedness Innovations (CEPI) launched in 2017 with the goal of funding vaccines that could stop future epidemics. The coalition's founding members and financial supporters include the countries of India, Norway, and the Bill and Melinda Gates Foundation. CEPI's initial deadly virus shortlist highlighted Ebola, Middle Eastern Respiratory Syndrome, Marburg, and Nipah.

Institutions across the world have worked to develop Nipah vaccines for the last seven years. Although none of the vaccines have been formally approved so far, researchers may be getting close. Two CEPI-funded vaccine candidates — one developed at Oxford and another at the NIH — started testing their vaccines for safety in humans in the last two and a half years. Other entities, including Moderna and the CDC, are also developing shots.

Traditional human clinical trials involve giving people a vaccine, sending them into their daily lives, and seeing if they are more or less likely to contract a virus than their unvaccinated peers. The approach works well for common viruses like the flu. But because Nipah is so rare, it may be impossible to tell how effective the vaccines are without a large epidemic occurring.

CEPI's goal is to get Nipah vaccines as ready as possible. The organization is hoping to get the treatments through Phase I and II clinical trials, which is where researchers figure out whether the shots are safe, what dose to give, and whether they produce an immune response in people. Successful Phase I and II trials can take around three years. In the case of an emergency — the virus one day mutates to be more spreadable, infects a city that doesn't know how to control it, or a combination of both — researchers may then be able to more quickly deploy the new vaccine.

The Nipah virus has possibly been circulating in bats for thousands of years. Villagers in remote Bangladesh have been collecting date palm sap for centuries, meaning Nipah may have eradicated several small villages in the last millennium. But the virus probably stopped there. Ancient villagers who didn't get sick likely fled outbreaks. With no more bodies to infect, and nowhere else to go, Nipah would die out before ever reaching the outside world.

Such an impromptu quarantine may be less feasible in today's world. Even in the last 20 years,

the pathway from rural Bangladesh to Dhaka has drastically shortened. Gurley's trip from ICDDR,B headquarters to Faridpur took at least five hours in 2004. Today, a bridge connects two sides of the Padma river, meaning travelers between the two regions no longer need to hitch a ride on a slow-moving ferry. The journey takes just under two hours today.

Such infrastructure improvements have benefitted the lives of people living in rural Bangladesh. They also mean a sick Nipah patient could more easily make it into a hospital in Dhaka, one of the most densely populated cities in the world.

For Gurley, the 2014 Ebola epidemic showed how a shift in the circumstances a deadly virus emerges in could precede the spread of larger outbreaks. One possibility, she and De Wit believe, is that Nipah could take advantage of transmission within healthcare facilities in Bangladesh's capital. During the COVID-19 pandemic, hospitals around the country expanded their supply of ICUs with ventilator support. Intubation is an invasive procedure, and Gurley worries that clinicians could introduce infected respiratory droplets into the air while intubating a Nipah patient.

"Those kinds of invasive techniques, I fear, could lead to super spreading events if the infection control environment isn't as good as it needs to be," Gurley said. "The shifting context can create opportunities for spread and changes of transmission, even, that we may not have fully considered."

The government of Bangladesh has invested in rigorous Nipah surveillance systems. But in a different country, where perhaps the virus isn't as heavily monitored, a more infectious strain might be able to spread between people for longer before it was noticed.

"Asian mega cities are connected to dozens and dozens of countries by direct flights," Gurley said. "Depending on how infectious it was, how difficult it was to identify, it could get pretty far before it was recognized."

Even with Bangladesh's robust surveillance, there's a chance disease hunters are missing Nipah cases. Most people who develop encephalitis in South Asian countries never receive a formal diagnosis. Gurley is certain some of them have Nipah.

"We spend a lot of time every year raising money just to get the funds to do the careful surveillance and testing needed to identify Nipah patients," Gurley said. "But it's not something that's commonly happening in routine health care systems."

Most Nipah cases are isolated events. A single person gets infected from a bat, falls ill, and either recovers or dies before infecting anybody else. Occasionally, people get the virus from infected batches, or each other, at the same time. But no outbreak has come close to causing a sustained epidemic. So far.

Nipah outbreaks are tragic for the victims and families involved. A vaccine could one day be used to protect those who come into contact with infected people during outbreaks, including

healthcare workers and loved ones. But in the absence of a more transmissible strain emerging, or the virus hitting the wrong place at the wrong time, the vaccine may never have to be used to prevent a global catastrophe.

Then again, Nipah continues to surprise us. In 2018, the virus killed 21 people in Kerala, a state in southern India over a thousand miles away from Bangladesh. The state had never reported Nipah before. Three more outbreaks have emerged in Kerala state since then, with the most recent one ending in September 2023.

People in Kerala don't drink date palm sap. It remains unclear exactly how people there are getting infected from bats.

In 1918, a deadly influenza virus emerged in France amongst soldiers fighting in the trenches of World War I. The ensuing pandemic is the reference point for all modern pandemics. The origin of the virus is hotly debated, though the first cases were recorded in Kansas. Scientists suspect infected birds were the original source of the virus, and some even believe it may have incubated in pigs.

By the early 1920s, about a third of the world's population had contracted the influenza strain. It then disappeared, never to be seen again in humans. Up to an estimated fifty million people were dead. The virus, which scientists believe killed around 2.5% of its victims, had ignited one of the deadliest pandemics in human history.

Although Nipah was not noticed for another 81 years, it was likely infecting people around the same time. Nipah is an ancient virus, possibly old enough to have been infecting people in South Asia when the Black Plague decimated Europe in the Middle Ages. The consequences of a virus with a 75% kill rate going global are unimaginable.

We possess countermeasures today we didn't have a century ago. Globalization, as it pertains to viruses, is a double-edged sword. Pathogens can bounce across international ports more easily today, and disease spillovers from animals to humans are becoming more common as we tear down nature that hasn't been so drastically disturbed for millennia. But at the same time, a connected world allows ideas and innovation to share a quick and straightforward path to reaching the most remote areas on our planet.

The international spread of knowledge led virologists to catch Nipah in 1999. It prompted doctors and virologists around the world to risk their lives during the 2014 Ebola response. And it enabled the production of a vaccine for the never-before seen SARS-CoV-2 virus in less than a year in 2020. Can the lessons we've learned from those crises help us prepare for extremely deadly and transmissible pathogens — a so-called doomsday virus?

"Nipah would be that if it were more transmissible," Gurley told me. "The value of the Nipah story is what we've learned and how we've learned it. I think the approach we've used to study

and understand Nipah spillovers can be useful for many of these disease systems that have already flagged themselves to be a potential risk."

Even in the scenario that Nipah doesn't ever threaten larger populations, one of its cousins might. Nobody can predict when the next pandemic will happen, or which pathogen will cause it. But when it comes, we may come to rely on the people preparing now and new advances in medical technology.

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