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Review Article

A Comprehensive Review on Langya Henipavirus (Layv): A New Zoonotic Threat

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ABSTRACT

Langya henipavirus (Lay V) is an emerging zoonotic pathogen belonging to the Henipavirus genus, closely related to the highly pathogenic Nipah and Hendra viruses. First detected in eastern China in 2022, Lay V has raised global concern due to its ability to cross species barriers and its potential public health impact. Although human-to-human transmission has not yet been documented, its genetic resemblance to other high-fatality henipaviruses necessitates close monitoring. This review provides a detailed account of Lay V's origin, virological properties, clinical manifestations, modes of transmission, and current therapeutic approaches. It also emphasizes the expanding role of pharmacists in areas such as disease surveillance, public education, and outbreak preparedness. In light of the ongoing emergence of zoonotic diseases, Lay V serves as a reminder of the urgent need for integrated healthcare strategies and multidisciplinary readiness.

INTRODUCTION

Emerging zoonotic viruses continue to pose a significant and growing threat to global public health. Over the past two decades, numerous pathogens of animal origin—such as SARS-CoV-2, Ebola, and Nipah virus—have crossed species barriers to infect humans, often with devastating consequences. These events underscore the delicate balance between human activity and the natural world and the urgent need for early detection and preparedness against such threats. Langya henipavirus (LayV) is one of the latest additions to this list of zoonotic pathogens. First identified in 2022 in the eastern Chinese provinces of Shandong and Henan, LayV belongs to the *Henipavirus* genus of the *Paramyxoviridae* family, a group known for its highly pathogenic members like Nipah and Hendra viruses. These related viruses have been associated with severe respiratory and neurological illnesses and high case fatality rates in past outbreaks, raising

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concerns about the potential severity of LayV. Although current evidence suggests that LayV infections are sporadic and relatively mild, its genetic similarity to more dangerous henipaviruses makes it a virus of interest. It is believed to be zoonotic in origin, with shrews identified as the primary natural reservoir. Most human cases so far have involved individuals with occupational exposure to animals, such as farmers, and no confirmed human-to-human transmission has been observed to date. However, the virus's ability to jump from animals to humans—alongside increasing human encroachment into wildlife habitats—suggests that LayV and similar pathogens could become more prominent threats in the future. In the absence of specific antiviral therapies or vaccines, the response to such novel viruses relies heavily on supportive care, surveillance, and public health interventions. Here, the role of pharmacists becomes increasingly important. Pharmacists, particularly those involved in hospital and community settings, can contribute significantly to disease surveillance, patient education, medication management, and public awareness campaigns. Their accessibility and trusted position within healthcare systems make them essential frontline responders in both preventing and managing outbreaks of emerging infectious diseases. Understanding LayV's biology, transmission patterns, clinical manifestations, and current management strategies is vital for the healthcare community. This review explores the virological characteristics, epidemiological trends, and clinical features of Langya virus, and emphasizes the proactive role pharmacists can play in monitoring, preventing, and responding to emerging zoonotic threats like LayV.

Virology and Classification

Langya henipavirus (LayV) is a novel member of the *Henipavirus* genus, within the family *Paramyxoviridae*. This viral family includes several other clinically important human and animal pathogens, such as measles virus, mumps virus, and the parainfluenza viruses. Among the *Henipavirus* members, LayV is closely related to Nipah virus (NiV) and Hendra virus (HeV), both of which are known for causing severe and often fatal infections in humans and animals.

Taxonomic Classification

- Family: Paramyxoviridae
- Genus: Henipavirus
- Virus: Langya henipavirus (LayV)
- Genome Type: Negative-sense, single-stranded RNA (–ssRNA)
- Genome Length: ~18,000 nucleotides (18 kb)

The genome of LayV is non-segmented and consists of a single strand of negative-sense RNA, a characteristic feature of the Mononegavirales order. The virus follows the classical genome organization of other henipaviruses and encodes at least six structural proteins, each responsible for specific functions in viral replication and host interaction.

Genomic Organization and Proteins

The LayV genome encodes the following proteins in the standard order:

- Nucleocapsid protein (N): Encapsulates the RNA genome and forms the nucleocapsid.
- Phosphoprotein (P): Acts as a cofactor for RNA polymerase and is involved in viral transcription and replication.

- Matrix protein (M): Plays a key role in viral assembly and budding.
- Fusion protein (F): Mediates fusion of the viral envelope with host cell membranes.
- Glycoprotein (G): Responsible for host cell attachment.
- Large polymerase protein (L): Functions as the RNA-dependent RNA polymerase for genome replication and mRNA synthesis.
- LayV also encodes accessory proteins (such as C, V, and W proteins) from the P gene, which may be involved in immune evasion and interferon antagonism, as observed in other henipaviruses, though further research is needed to confirm their function in LayV.

Evolutionary and Molecular Features

Phylogenetic analysis shows that LayV is genetically distinct but closely related to Mojiang virus, another rodent-borne henipavirus, and shares moderate genetic identity with Nipah and Hendra viruses. Unlike other henipaviruses that use fruit bats (*Pteropus spp.*) as their primary reservoir, shrews have been identified as the natural host of LayV, indicating a divergent evolutionary pathway within the genus. Currently, no genetic reassortment or recombination events have been detected in LayV, suggesting genomic stability in the early stages of its emergence.

Reservoir and Host Range

- Primary reservoir host: Shrews, particularly *Crocidura lasiura* species, where viral RNA was detected in approximately 27% of the tested population.
- Potential intermediate hosts: Serological evidence of LayV-specific antibodies has been found in:
- Goats (~2%)
- Dogs (~5%)

Epidemiology

Langya henipavirus (LayV) was first identified in 2022 during an active surveillance study of febrile patients with recent animal exposure in eastern China, specifically in the Shandong and Henan provinces. The discovery was reported by Wang et al. in the *New England Journal of Medicine (NEJM)*, marking the first time this virus had been detected in humans.

First Reported Cases

A total of 35 laboratory-confirmed cases were recorded between 2018 and 2021, with the findings published in 2022. These cases were identified through sentinel surveillance for zoonotic infections among patients presenting with unexplained fever.

Demographics:

The majority of infected individuals were middle-aged adults, and none of the cases involved children.

Occupational Risk:

A large proportion of the patients were farmers or rural laborers who had frequent and direct contact with domestic animals or the natural environment, suggesting a strong occupational exposure component.

Transmission Dynamics

Zoonotic Transmission (Animal to Human): Current evidence indicates that LayV is transmitted primarily from animals to humans, likely through direct or indirect contact with infected animal hosts, particularly shrews, which have been identified as the primary reservoir.

Human-to-Human Transmission:

Based on contact tracing of 15 close household contacts and 9 healthcare workers, no evidence of person-to-person transmission has been observed to date. However, the sample size is small, and the potential for future adaptation cannot be ruled out, especially considering the behavior of other henipaviruses like Nipah.

Geographic Distribution

Localized Outbreaks:

So far, all known cases have been geographically restricted to rural areas of China, specifically in the Shandong and Henan provinces.

No International Spread:

As of now, there is no evidence of global or international transmission, and LayV remains a locally contained infection. However, the risk of wider spread remains, especially with increased human-animal interface in agricultural communities.

Reservoir Surveillance

In a related animal surveillance study, LayV RNA was detected in approximately 27% of shrews sampled, confirming their role as the natural reservoir. Additionally, seropositivity in domestic animals such as dogs and goats raises concerns about possible intermediate hosts or vectors that may facilitate spillover into human populations.

Clinical Features

- Fever: Universal (nearly 100%)
- Fatigue/Malaise: ~54%
- Cough: ~50%
- Myalgia (muscle pain)
- Headache
- Nausea/Vomiting
- Leukopenia (low white blood cell count): ~50%
- Thrombocytopenia (low platelet count): ~35%
- Liver dysfunction (transaminase elevation): ~20%
- Typical severity: Mild to moderate in most cases

Diagnosis

1. RT-PCR (Real-Time Reverse Transcription Polymerase Chain Reaction)

Preferred method for acute infection. Highly sensitive and specific for Nipah virus detection in the early phase. qRT-PCR from throat/nasal swabs, blood, urine, or cerebrospinal fluid can yield reliable results within hours. Homegrown assays (SYBR Green, TaqMan) and commercial platforms (e.g., portable Truenat NiV System used in Kerala) support rapid, field-friendly diagnostics. RT-LAMP, an isothermal amplification technique, offers sensitivity 10× greater than standard RT-PCR (detects ~100 pg RNA), with colorimetric or turbidity readouts in ~45 min—ideal for resource-limited settings

2. Serology

ELISA assays for IgM/IgG antibodies become useful during the convalescent phase (~10–14 days post-symptom onset). Typically, IgM appears within 3–7 days, IgG by day 17, and IgG may persist for months. Used primarily for epidemiological surveillance and retrospective diagnosis, serology complements PCR for cases presenting late in illness. Antigens used in ELISA (e.g., recombinant N protein) are immunodominant and standardized for reservoir host testing (e.g., bats)

3. Virus Isolation & Neutralization

Virus culture/neutralization tests remain the gold standard but are restricted to BSL-4 facilities due to high pathogenic risk. Pseudo type neutralization assays may be performed in BSL-2 labs, improving access to specificity testing.

4. Differential Diagnosis

Due to nonspecific early symptoms, it is crucial to rule out other pathogens:

Influenza and common respiratory viruses can yield similar presentations—molecular panels including these are recommended Nipah vs. Nipah-like pathogens: Hemagglutinin tests detect influenza but not NiV; ensure diagnostic assays specifically include Paramyxoviridae. Other viral encephalitides (e.g., Japanese encephalitis, Henipavirus variants) may cross-react; antigen- or sequence-specific RT-PCR reduces this risk

6. Treatment and Prevention

No approved antivirals or vaccines Like other henipaviruses (e.g., Nipah, Hendra), LayV has no specific treatment or vaccine. Standard care is supportive, focusing on rest, hydration, and symptomatic relief (e.g., NSAIDs for fever) Ribavirin (off-label potential) Because LayV belongs to the same family as Nipah and Hendra, ribavirin may be considered despite no conclusive evidence specific to LayV Symptom management OTC medications can alleviate fever, cough, headache, nausea, etc

Prevention

- Avoid animal exposure
- Limit contact with shrews (primary reservoir), goats, dogs, pigs, and their excretions .
- Avoid raw animal products (e.g., date palm sap, uninspected meat)
- Practice strict hygiene
- Frequent hand-washing with soap and water
- Cover your mouth/nose when sneezing or coughing and dispose of tissues promptly
- Prevent human-to-human spread
- No clear evidence of human-to-human transmission has emerged
- Still, avoid contact with bodily fluids of anyone suspected to be infected.
- Surveillance & monitoring
- Ongoing studies include PCR and antibody testing in humans and animals.
- Monitoring transmission dynamics and mutation risk is a public health priority.

Role of Pharmacists

1. Surveillance and Early Detection

Pharmacists often serve as the first point of contact in the healthcare system, positioning them to identify unusual symptom patterns and report potential cases to public health authorities. Their involvement in disease monitoring and surveillance has been instrumental during previous outbreaks, aiding in early detection and response efforts.

2. Patient Education and Combating Misinformation

Pharmacists are trusted sources of health information and can play a significant role in educating the public about emerging viruses. They can dispel myths, provide accurate information about disease transmission and prevention, and promote healthy behaviors. During the COVID-19 pandemic, pharmacists effectively countered misinformation and guided patients on infection control measures.

3. Pharmacovigilance and Medication Management

In the face of new viral threats, pharmacists are crucial in monitoring adverse drug reactions, ensuring the safe use of medications, and managing drug shortages. Their expertise contributes to the evaluation of drug efficacy and safety, particularly when new treatments are being introduced.

4. Outbreak Response and Public Health Support

Pharmacists can assist in outbreak management by participating in contact tracing efforts, supporting infection control measures, and ensuring the continuity of care for patients. Their accessibility and integration into the community make them valuable assets in public health initiatives.

5. Vaccination Campaigns and Immunization Services

Should a vaccine for Langya virus become available, pharmacists are well-positioned to support immunization efforts. They can administer vaccines, manage vaccine storage and inventory, and educate patients about the benefits and safety of vaccination. Pharmacists have been central to vaccine distribution since the COVID-19 pandemic and continue to play a critical role in public health.

6. Research Gaps and Future Directions

Broader Ecological & Reservoir Studies LayV RNA has been detected in small mammals—especially wild shrews (~27%)—and sporadically in goats and dogs. However, these studies are localized (primarily in Shandong and Henan provinces), and there's a need for wider ecological surveillance across regions to identify additional reservoirs, understand spillover dynamics, and assess environmental factors influencing transmission

Investigating Human-to-Human Transmission

So far, no evidence of human-to-human spread has been observed among traced contacts—but the sample sizes remain small (e.g., 9 index cases, 15 contacts). Henipaviruses (like Nipah and Hendra) *can* transmit between humans under certain conditions, so a more robust investigation—through expanded contact tracing, seroprevalence surveys, and monitoring of household clusters—is urgently needed

Vaccine Development & Preclinical Testing

Multiple in silico immunoinformatic studies have proposed promising multi-epitope vaccine candidates targeting LayV's surface glycoproteins (G and F), showing strong antigenicity and stable docking with immune receptors (e.g., TLR3/TLR4/TLR9) However, experimental validation—including in vitro immunogenicity assessments and animal model testing—is still pending. This is the next critical step before any clinical trials can begin.

Clinical Evaluation of Antivirals

There are currently no approved treatments specifically for LayV.

Some evidence from related henipavirus outbreaks suggests potential efficacy of ribavirin and chloroquine, especially in animal models Yet, rigorous preclinical studies and eventually clinical trials are required to evaluate dosing, safety, and therapeutic potential against Langya.

Diagnostic Tools & Surveillance Capacity

Present methods rely on PCR and limited ELISA assays, with no widely available standardized test kits Developing and scaling up rapid, accurate diagnostics is essential for early detection in both human and animal populations. Integrating advanced genomic surveillance (such as metagenomic sequencing or AI-enhanced screening) can help detect mutations, identify outbreaks swiftly, and monitor viral evolution .

CONCLUSION

Langya virus (LayV) is a newly identified zoonotic henipavirus first detected in eastern China, with 35 confirmed human cases between late 2018 and mid-2022, all non-fatal . Genetically, it clusters with highly lethal henipaviruses such as Nipah and Hendra, which carry case-fatality rates up to 70 % . Currently, there is no evidence of human-to-human transmission—each case appears to be an independent spillover, mostly among farmers and animal workers . Investigations have identified shrews as the primary reservoir (approximately 27 % of sampled shrews tested positive), with low-level exposure detected in goats (around 2 %) and dogs (around 5 %) . Infected individuals typically experience mild-to-moderate symptoms—fever, fatigue, cough, loss of appetite, headache, and muscle aches—with some presenting leukopenia, thrombocytopenia, and occasional mild liver or kidney impairment . As an RNA virus, LayV has the capacity to mutate, raising concerns about possible adaptation leading to efficient human transmission or increased virulence . Pharmacists are critical in responding to such emerging threats: they can monitor over-the-counter purchase trends for early outbreak signals, educate high-risk populations on avoiding wild animal contact and practicing hygiene, facilitate referrals for PCR/ELISA testing, counter misinformation, support investigational antiviral use (e.g. ribavirin), and advocate for integrated surveillance under a One-Health approach. Given LayV's pedigree and spillover pattern, sustained vigilance and workforce readiness—including pharmacy professionals—are essential to prevent future outbreaks.

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