





Emerging RNA Viruses: Epidemiology, Pathogenesis, and Challenges for Vaccine Development: Review

Zahraa Hussein Obaid^{1,*} , Ahmed Saleem Abbas^{2,3} , Lubna Abd Almuttalib Al-Shalah⁴ , Ghazi Mohamad Ramadan^{5,6} 

^{1,4} Environmental Research & Study Center, University of Babylon, Babylon 51002, Iraq.

² Software Department, College of Information Technology, University of Babylon, Babylon 51002, Iraq.

³ College of Science, University of Al-Hilla, Babylon 51001, Iraq.

⁵ Syrian Fertility Center, Al-Hamrat Street No. 1, Tartus 2200, Syria, Department of Anaesthesia Techniques and Intensive Care.

⁶ Al Taff University College, Karbala 56001, Iraq.

Corresponding Author Email:

zahraa.almamory@uobabylon.edu.iq

Received: 10 January 2026,

Revised: 1 February 2026,

Accepted: 12 March 2026,

DOI: [10.57238/jbb.2026.7432.1163](https://doi.org/10.57238/jbb.2026.7432.1163)



Access this article online

Copyright: ©2026 The authors. This article is published by Nabea Al-Ajyal Foundation Press and is licensed under the CC BY 4.0 license(<http://creativecommons.org/licenses/by/4.0/>).

ABSTRACT

"For decades, emerging RNA viruses have continued to multiply and diversify constantly for humanity. Many regulations have been issued regarding different strains of coronavirus to combat human infection, and they do not cause the deaths of millions of people around the world.". Emerging RNA viruses, including coronaviruses, flaviviruses, and filoviruses, have demonstrated the ability to cause pandemics and outbreaks with devastating health and economic impacts.

Their high mutation rates and zoonotic potential complicate public health responses. This review provides a detailed overview of the epidemiological trends of major emerging RNA viruses, their mechanisms of host infection and immune evasion, and the current challenges in vaccine development. Key obstacles include antigenic variability, cross-species transmission, and limited duration of immune protection. Advances in mRNA vaccine technology, vector-based vaccines, and universal vaccine strategies are also discussed. Proactive surveillance, rapid vaccine platforms, and global collaboration are emphasized as critical components for future preparedness.

Keywords: Emerging viruses, RNA viruses, vaccine development, epidemiology, zoonosis.

1. Introduction

RNA viruses are important emerging pathogens that are responsible for numerous disease outbreaks of global concern. Many RNA viruses have caused severe disease in large populations and posed a serious threat to world health and security. For example, West Nile virus emerged in North America in 1999, resulting in thousands of cases of neuroinvasive disease. Middle East Respiratory Syndrome Coronavirus emerged in 2012, causing severe respiratory disease outbreaks in the Middle Eastern countries. In 2014, Ebola virus re-emerged in West Africa, resulting in the largest outbreak

recorded with thousands of infected cases [1].

Several characteristics that emerging viral pathogens usually share include the following: they are genetically diverse and incur high mutation rates; they are initially non-human viruses and jump from animal reservoirs to humans; as a result, they are novel to the human host and encounter no pre-existing immunity; they disseminate globally via air or other transport mediums; and they possess pathogenic mechanisms that allow extensive replication and spread in humans while also enabling evasion from innate immunity and killing of host cells [2]. The immense human and natural reservoirs of the pathogenic viruses can serve as a constant source for novel emerging viruses. Therefore, owing to the genetic and biological diversity of RNA viruses and the close ecological relationship between animals and humans, it is expected that there will be more emerging infectious agents in the future [3].

Emerging infectious diseases are major threats to the health and welfare of humans, livestock, and wildlife. Among the emerging pathogens, the hope virus will be RNA virus. Undoubtedly, the most effective approach in preventing viral diseases is vaccination. However, for numerous viral diseases that are a threat to human health, agriculture, and wildlife, vaccines are not currently available. Vaccine development for such viral diseases not only has the potential to avert human tragedies but also offers considerable economic benefits [4]. Vaccine development against these highly pathogenic and emerging viruses is a daunting challenge. Immediate research goals include improving biosafety, improving immunogenicity, and understanding viral pathogenesis. Emerging infectious diseases caused by viruses, especially RNA viruses, are a constant threat to global public health [5]. Further research on the virulence mechanism of emerging viruses is crucial, considering both vaccine development and the prevention of emerging infectious diseases.

2. Overview of RNA Viruses

RNA viruses are unicellular organisms composed of either positive or negative stranded RNA. A significant portion of newly emerging viruses are RNA viruses. Unlike DNA viruses, RNA viruses replicate in the cytoplasm of the host cell and use host as well as their own encoded proteins for replication. Thus, host factors essential for the replication of RNA viruses are actively involved in diverse cellular processes. Viruses hijack these cellular factors by encasing viral genetic material along with the proteins that enable its replication.

Viral proteins either overpower host factors or work together in concert as a functional complex with viral RNA as substrate [6]. The genome of RNA viruses mutates faster than chromosomal DNA because of low fidelity or highly error-prone RNA-dependent RNA polymerases (RdRP). They have smaller sizes and variable structures as compared to DNA viruses. RNA viruses arise from materials akin to RNA, i.e., Ribozyme or Z-RNA, the latter inherent to NE structure [7]. They do not have a place to grow in this state, and thus have to host their reproduction cycle on some cell including cells that have chromosomal genome [1].

This triangle best explains co-evolution of DNA and RNA viruses with chromosomal genome in selecting RNA viruses as emerging ones. The rate of co-evolving of Dengue virus and business associated with global warming and displacement of species from the tropics to the temperate regions or extreme weather events causing floods amplify the threatening fortunes of RNA viruses (RFV). Using the CaMV and TMV [8], the first model of RNA virus co-evolution was put forward with hints along the path for their arithmetic and kinetics analysis. 21 years later, RNAs of established viruses (sRNA) integrated into chromosomes of their cellular hosts providing RNA viruses with new tools for co-evolution with upper genomes. Further along this path, it may be suggested that mutational RNA viruses are the ones responsible for the emergence of a new genome from pregenome because of the latter polishes its errors just as elite sportsmen [9].

2.1. Classification of RNA Viruses

Despite being ecologically diverse, RNA viruses can be broadly classified into two groups based on their genome organization, genome size, mode of replication, and other properties. The first group contains the segmented RNA viruses, which have their RNA genome divided into two or more parts. These segments are individually packaged into particles, a property termed “segmentation.” Examples of viruses in this group include influenza virus, sendai virus, Northern and Southern segmented bark beetle viruses, and sinbis virus.

Segmented RNA viruses tend to have a smaller genome size (less than 15 kb) than their non-segmented relatives [10]. The reason for such small genomes is the need to fit all the segments into viral particles, which are usually tightly packed. Consequently, these viruses have a number of stringent constraints, both biological and physical, that do not apply to the non-segmented RNA viruses. In contrast, the second group contains RNA viruses with non-segmented genomes, where all of the RNA is contained in a single particle.

These viruses can further be subdivided into three main groups conditions. The first group contains viruses that possess immunological properties similar to picornaviruses. Examples include polio virus, cytopathic intestinal echo virus, and many animal-infecting viruses such as foot and mouth disease virus. These viruses are able to find the appropriate receptor in human tissues and can circumvent the barrier of intestinal immunity or transmit asymptotically. After reaching the central nervous system, they replicate extensively in the cell bodies of motor neurons, killing the host by shutting down the synthesis of cellular macromolecules and the spreading of the neurotoxic poliovirus protease [11,12].

2.2. Characteristics of RNA Viral Genomes

RNA viruses are the most genetically diverse forms of life, displaying great adaptability and rapid evolution of new variants. These features give a large range of infection foci, allowing virus to infect a wide range of hosts. With the increasing number of sequenced viruses, it has become evident that although viruses are considered to be simple organisms encoding an average of 10 proteins, their overall genetic and phenotypic complexity is great.

On the one hand, the genomes of different RNA viruses differ significantly in size, structure, and genome/sequence compression ratios. On the other hand, an extreme variability in the genome of different isolates of the same RNA virus exists. The drastic differences in genome structures and encoded proteins are the result of different evolutionary pathways with various selective pressures [13]. However, many features are broadly shared among RNA viruses, which in conjunction allow for a great diversity and adaptability within the virosphere (a sociological term that refers to the community of viruses). One of the prerequisites of successful adaptation to a rapidly and drastically changing environment is the ability to efficiently introduce genetic change in a short amount of time [5].

Table 1. Application

Application Area	Description	Impact
Surveillance Systems	Strengthening global monitoring of emerging RNA viruses	Early detection of outbreaks, rapid response
Vaccine Research and Development	Developing vaccines for rapidly mutating RNA	Accelerates creation of adaptable vaccine platforms

	viruses	
Public Health Policy	Formulating policies for virus containment and prevention	Improves pandemic preparedness and response
Diagnostic Advancements	Creating fast, sensitive tests for RNA virus identification	Enhances early diagnosis and treatment
Therapeutic Innovations	Designing antiviral therapies targeting RNA virus replication mechanisms	Expands treatment options beyond vaccines
International Collaboration	Sharing data and resources across countries	Global coordination in fighting viral threats
Education and Awareness	Public campaigns about emerging viruses and prevention measures	Reduces spread through informed behavior

This replication error, coupled with the level of virulence and propagation speed, leads to the emergence of mutants in a population and, consequently, phenomena such as a change in virulence or host tropism. Since it acts as an evolutionary machinery, understanding the principles and mechanisms of RNA virus evolution and the relative contributions of individual agents to change in genetic and phenotypic characteristics is necessary for predicting potential emergence and probable future evolutionary pathways. The knowledge of the emergence foci and stocks and of temporal and spatial evolutionary pathways is crucial for local, national, and international planning in several domains [14].

3. Epidemiology of Emerging RNA Viruses

Emerging diseases have been recognized since ancient times, notably the black plague, which devastated Europe during the fourteenth century, the influenza A virus pandemic of [18], Hantavirus pulmonary syndrome in the United States in the early 1990s, and the extreme acute respiratory syndrome outbreak in late 2002 [15].

The term “emerging disease” is used to describe the arrival of a previously unrecognized infection in a given host species, or a recognized infection that is newly found in a host not previously known to have it, and/or has expanded into a new ecological niche or geographical zone, sometimes accompanied by a significant change in pathogenicity. Most emerging diseases tend to be infections, and many are zoonotic, affecting humans or domestic animals originally infected in the wild. For example, there has been intense concern about the crossing of H5N1 avian influenza virus into humans, which began occurring in 1995, and the outbreak of Ebola virus in Guinea, which in 2014 spread to a number of countries previously free of the infection [1].

More recently, Zika virus was brought to public attention as an emerging pathogen causing a very different clinical manifestation and significant morbidity in Polynesia and South America than previously seen in Africa. Infants born with congenital Zika syndrome, a condition including microcephaly, have prompted the World Health Organization to declare it a Public Health Emergency of International Concern in February 2016. Thus, although not new for the planet as a whole, emerging viruses have recently become an extreme threat to human health. Current estimates are that there are at least 1,400 pathogens of humans.

More than 60% of these are of animal origin, which involve viruses, viruses or prions in feces, viruses

or fungi infecting the aberra. Nearly 300 of the 840 pathogens have been recognized as having emerged since 1940, coinciding with large-scale developments in agriculture, transportation systems and urbanization. Agro-ecological changes facilitated sapronoses such as salmonellosis, cholera, schistosomiasis, and *Cryptosporidium*, whereas peri-urban areas supported the emergence of arenic diseases like leptospirosis, yellow fever and viral hemorrhagic fevers.

It was calculated that about one emerging agent per year is identified (around 56% to be RNA viruses). Such zoonotic agents are more likely to be RNA viruses, and they involve arboviruses, filoviruses, bunyaviruses, paramyxoviruses and coronaviruses, which are associated with human respiratory diseases, and pegiviruses, gypsy viruses, hepatitis E viruses and astroviruses, which cause hepatitis or gastro-enteritis. The advent of high-throughput sequencing has opened doors to the rapid identification of previously unrecognized viruses. The priority viruses have posed significant risks to public health [17].

Table 2. Methodology

Step	Description	Techniques/Tools Used
Literature Review	Collection of global data on emerging RNA viruses	Scientific databases (PubMed, WHO reports)
Epidemiological Data Analysis	Analysis of outbreak patterns, transmission dynamics	Statistical modeling, GIS mapping
Pathogenesis Study	Investigation of viral entry, replication, immune evasion	In vitro cell culture, animal models, histology
Genomic Sequencing	Identification of viral mutations and variants	Next-generation sequencing (NGS), bioinformatics
Vaccine Development Assessment	Review and evaluation of current and experimental vaccines	Preclinical and clinical trial data analysis
Challenge Identification	Recognizing hurdles in vaccine development (e.g., mutation rates)	Expert consultations, systematic reviews
Data Synthesis	Integrating findings to propose solutions and future directions	Comparative analysis, meta-analysis

3.1. Global Surveillance and Reporting

Emerging infectious diseases are an ongoing occurrence, continue to appear with an increasing frequency in humans, and are responsible for substantial morbidity and mortality even in the absence of heightened public awareness. However, governments' recent heightened attention to biosecurity and bioterrorism has raised awareness of the potential for the same techniques used to gather basic information on infectious agents to be deliberately misused [18]. The majority of human infections by new infectious agents are the result of interaction with wildlife.

Health systems must be prepared for the unexpected appearance of a new agent in a human population. Despite the ubiquity of alerts, distressing pictures, and a wealth of fantasy and misinformation, the overwhelming majority of infectious disease outbreaks pose little or no risk of

worldwide spread. Surveillance of reported clusters, syndromic surveillance, and reporting of unusual clusters are the responsibilities of all healthcare professionals. Education is critical as much of the health workforce and systems in the developing world are nevertheless of limited capacity compared with those for whom the alert system was developed. Emerging infectious diseases have the potential for epidemic spread within the interconnected global industrial system and are thus of an entirely different order of magnitude than those more common, but more localized diseases that they would displace from the public health radar [19].

New infectious diseases have emerged since the dawn of history. Surveillance of these reports must be of high standard. Alerts are sent around the world warning of the genuine emergence of a new disease in a human population that has not previously been exposed. Enforcement of stringent infection control measures, isolation, and travel restrictions has led to the virtual elimination of some causes of major outbreaks.

The reduction of biodiversity consequent upon economic development is likely to lead to outbreaks of diseases that spillover from wildlife into domestic animals or previously unaffected human populations. Efforts are now underway with the support of WHO to prepare countries for high consequence emerging diseases that will nevertheless arise. In addition to the specific measures that should be pursued to develop these capabilities, the knowledge and support of the general population and of healthcare workers in particular are essential for them to be mobilized when needed [20].

3.2. Risk Factors for Emergence

Not too long ago the world witnessed the emergence of a new deadly virus: H1N1, responsible for the epidemic of influenza A zoonosis. Viral infections that can jump the species barrier can have serious implications. These so-called emerging viruses have recently come to dominate the public health agenda [21]. Epidemiological data show an unprecedented increase in the number of viral zoonosis outbreaks in the last two decades. Recently, the emergence of Nipah virus (NiV), a bat-derived deadly pathogen that spilled over from fruit bats to humans through an intermediate host in Malaysia, showed that viruses can evolve quickly and jump species barriers. More generally, bats harboured a wealth of new viruses, including new strains of the above-mentioned H1N1 virus [22]. The threat of viral emergence is now greater than ever. Since so much is still unknown, researchers have turned to the host. Indeed, the ecology and evolutionary history of a pathogen and its native host can provide clues to understanding why certain pathogens are predisposed to emerge in novel hosts [23].

The emergence of a zoonotic virus requires that numerous key transitions occur from wildlife reservoir species to human hosts. During these successive transitions, the virus is simultaneously posed with shifting selection pressures arising from changes to its interaction with new cell types and tissues, the immune system, and the ecological and social context of a new host. It is plausible that many of the early transitions during the emergence process are gradual and erratic, resulting in a patient virus that is successfully maintained in a spillover host.

Recent studies suggest that emergent zoonotic viruses arise from wildlife reservoirs with pre-existing biological properties of concern for public health. The recent emergence of a series of deadly viruses, coupled with the growing recognition of the public health threat posed by zoonosis, have drawn our attention to the question of why certain viruses are predisposed to spillover infections and disease emergence in humans [24].

3.3. Case Studies of Recent Outbreaks

Three case studies illustrate viral outbreaks that have been poorly characterized and for which vaccines are needed.

3.3.1. Ebola Virus Ebola

Debuted in 1976 when outbreaks were noted in Zaire and Sudan. In the first outbreak in Zaire, 318 cases were reported, with an initial mortality of 88%. After several years of quiet, filoviruses such as Ebola and Marburg reemerged in outbreaks throughout Africa. An outbreak began in Western Africa in 2014, initially in Guinea. The virus spread to countries such as Sierra Leone and Liberia and later Senegal and Nigeria, infecting thousands and causing a mortality risk of 60%–70%. Before the outbreak, there was a lack of knowledge and understanding of the virus and what steps could be taken to begin effective mitigation efforts.

When the outbreak first started, there was little in the way of containment procedures, meaning the Ebola virus spread rapidly [1]. Fortunately, a combination of efforts including extensive collaboration of multiple international organizations, the development of effective treatment cocktails, and the availability of a limited number of experimental vaccines allowed the eventual control of the situation [25].

3.3.2. Chikungunya Virus Chikungunya

An arbovirus transmitted primarily by *Aedes* mosquitoes, spent most of the 20th century as an obscure threat limited to Africa and parts of Asia. Athenian Grecian-influenced viruses and the reunification and re-emergence of the East and Central African genotypes stranded in India and similar locales resulted in localized epidemics. Once thought limited to Africa and Asia, cases in the Americas were reported in late 2013. The virus rapidly spread through the entire continent once introduced to the Caribbean to Southern and South America. Although mostly not locally transmitted outside Central and Southern America, cases were imported to Italy.

Symptoms of infection include fever, headache, joint pain with a likelihood of chronic side effects. Public health recommendations center on mosquito control, specifically *Aedes*-oriented methods. Unfortunately, licensed vaccines do not exist. Prioritized development must be carried out to fill the biomedical gap. Attempts at prevention and treatment begin with recombinant VLPs, purified live-attenuated viruses, and subunit protein vaccines. To prevent reinfections, the development of monoclonal antibody cocktails has been pursued [26].

Table 3. results

RNA Virus	Epidemiological Trends	Pathogenesis Highlights	Vaccine Development Status
SARS-CoV-2	Global pandemic, multiple variants emerged	Severe respiratory disease, cytokine storm	Approved mRNA and vector-based vaccines
Ebola virus	Sporadic outbreaks in Africa	Hemorrhagic fever, high mortality	Approved recombinant vector vaccine (rVSV-ZEBOV)
Zika virus	Rapid spread in Americas	Neurological defects (microcephaly in infants)	Vaccines under development, no widespread approval yet
Dengue virus	Endemic in tropical regions	Hemorrhagic fever, antibody-dependent	Several vaccines approved (e.g.,

		enhancement	Dengvaxia)
Influenza virus (H1N1)	Seasonal and pandemic outbreaks	Respiratory illness, antigenic shift and drift	Annual updated vaccines available
Nipah virus	Sporadic outbreaks in South Asia	Severe encephalitis and respiratory symptoms	Vaccines in early stages of clinical trials

4. Pathogenesis of RNA Viruses

The emergence of a new RNA virus is a complicated process. Firstly, an RNA virus with a new receptor will infect a new host or spread from one animal to a new species. This step usually involves the mutation of envelope proteins to permit cell entry. For many RNA viruses, this is already a considerable challenge. However, prior evolution events/prerequisite factors can enhance the fitness of the new factor in the new host. Commonly, RNA viruses do not have their own polymerases and rely on host cellular polymerases. New viruses may need to switch host polymerases or re-adapt to recipient cell polymerases. This adaptation includes recognizing new promoters, dNTP supply, or even the complete suite for the other species-preferable functions [1]. Another adaptation is counteracting host defense mechanisms. It is a race against time, and either an offense (initial stages) or defense mechanism (later stage) can be detrimental, resulting in unbalanced pathogenicity [27].

Clear safeguards of pre-formed and activation-induced pathways “translate” into variations in pathogens. Viral evasion mechanisms exerted after detection can be barely understood. Vaccine development, clinical therapies or outbreak control need to understand these mechanisms in order to be effective. Whether an RNA virus infects a new species and causes an endemic, epidemic, or pandemic is largely determined by the interactions among virus, host immunity, and environment [28]. The most important consideration is whether humans are the target.

This facet is believed by some to determine if a zoonosis is a chicken- or pig-driven pandemic. Based on experience and hypotheses, there are various combinations of virus, host immunity, and environment that can allow successful emergence and mass infection. Mine includes elucidation of hosts, tactics, and environmental changes. Resistance mechanisms of those who escaped a pandemic might include innate immunity, pre-exposure herd immunity, and even co-infection. New infectious diseases may emerge in unexpected animal species and human populations.

4.1. Mechanisms of Viral Entry

Viruses infect host cells and take over the host cellular machinery to replicate their genome and express viral proteins for progeny production. Therefore viruses have to ensure their entry into host cells and delivery of their genome to the correct cytoplasmic compartment for ensuing replication. In general, at least six steps are involved in the viral entry process: virus receptor recognition, virus-receptor interaction, virus internalization, cytoplasmic escape of the genome, genome replication, and migration of progeny viral genome to the nuclear compartment for transcription.

The recent progress in understanding mechanisms of entry of emerging RNA viruses using different cellular receptors is discussed below. This discussion is intended to emphasize that emerging viruses utilize multiple cellular receptors with unique virus and host specificity to activate diverse entry pathways and deliver their genome to respective cytoplasmic compartments for replication [29].

Immuno-suppressive viruses such as human immunodeficiency virus type 1 (HIV-1), Marek’s disease

virus (MDV), and various human tumor viruses maintain the tumor state [29]. Emerging viruses such as H5N1 and H1N1 influenza A viruses can jump from one host species to another and cause pandemics. Some emerging viruses are designated as category A, B, or C biological agents and accounted as potential bioterrorism agents.

Category A viruses that can be easily disseminated via airborne or water-borne routes to infect the general population include variola major, Bacillus anthracis, Francisella tularensis, Yersinia pestis, Ebola virus, and Marburg virus. For bioterrorism agents it is preferable to use dry powdered form of the agent that can travel with jet stream and stay airborne for hours for 50 km.

Thus bioterrorism viruses should either be airborne or have to be engineered with the use of natural reservoirs such as rodents, monkeys, or arthropods for delivery. Moreover, aerosolized viruses or viruses delivered by infected vectors should be virulent and with no vaccine or medications. Numerous viruses such as avian and human influenzas, West Nile, Ebola, and Marburg are candidates for bioterrorism [30].

4.2. Host Immune Response

The mammalian host immune system comprises two main recognition and defense systems: the innate immune system that detects non-evolutionary conserved and broadly expressed core microbial molecules, and the adaptive immune system that recognizes pathogen-specific and evolutionarily newly acquired antigens for better protection upon repeated infections. The antiviral host defense is mounted with the fearsome innate immune system first. After evolving to have highly effective antiviral cytokines and pathways, mammalian hosts rely on this potent weapon, like other hosts, to rapidly recognize the special microbial hallmark features of the emerging RNA viruses and combat them [31].

An array of cellular sensors that detect the invasion of RNA viruses has been identified. While host pattern recognition receptors (PRRs) for fungus have evolved into membrane-spanning Toll-like receptors (TLRs) that each recognizes a specific signature, the evolution of RNA virus-specific host detection systems is more complicated and defensive. PRRs to detect RNA viruses can be a large, membrane-spanning, and poorly preserved type such as TLR3 and TLR7, but the more recently evolved PRRs for these viruses are mostly cytosolic, smaller, and better conserved.

The greatest challenge in the development of vaccines against emerging viruses is not only that they have much higher rates of mutation and recombination than DNA and other viruses, but also that most emerging viruses have very few or no human-hosted viruses. The epitope and engineered immunogenicity may be less reliable. However, considerable hope and efforts for the changed vaccine development road have emerged as information on the virus or vaccine more universally recognizable by mammalian hosts and engineering technology have mostly built up [32].

The innate immune system is the first line of defense against infection. Following the detection of WNV by host cellular sensors, the IFN signaling pathway is initiated, leading to the production of and establishment of an anti-viral environment. In response to WNV infection, a substantial amount of IFN is produced from the astrocytes or other infectious host cells surrounding the infection locus. The detected IFN can be transmitted to non-infected distal nervous cells, such as neurons, to protect them from WNV infection. In addition, it can also backact on the infected cells. There are also cyber-immune invasions leading to the widespread expansion of viruses.

Defensive adaptive immune system activation occurs after WNV replication and lasts longer than that of the innate immune response. The activation of the adaptive immune system is initiated by effector B or T cells that are directly stimulated by the recognition of antigens in the draining lymph nodes. Specific IgM from plasma cells targeted to the WNV surface protein E is produced to neutralize extracellular WNV or virion and prevent productive cellular internalization. The activated CD4+ T cells stimulate B and CD8+ T cells to expand as well as to directly kill WNV infected neurons, respectively [33].

4.3. Viral Replication and Spread

Following the initial viral entry into host cells, viral replication is mediated in the cytoplasm via the action of viral proteins and RNA. Positive-strand RNA viruses utilize the viral-encoded RNA-dependent RNA polymerase to generate negative-strand RNA (template for replication) and replicate positive-strand RNA. In contrast, the genome of negative-strand RNA viruses must be transcribed to generate mRNA for translation, while progeny positive-strand RNA is replicated. Double-stranded RNA viruses replicate in membrane-bound vesicles which provide structural confinement for the virus and may act as a site for immunity evasion. Viral replication compartments are generated that modulate host cell processes, thus aiding in viral replication and genome spread [34].

RNA viruses often exhibit a high mutation rate due to absence of proofreading activity by their RNA-dependent RNA polymerases. This fickleness and genetic plasticity of RNA viruses allow for the quick evolution of efficient replication strategies in heterogeneous ecosystems. Survival of RNA viruses depends on the ability to maintain fitness, to replicate and spread in diverse environments, and to adapt following host jumps. The robust “solution” of diverse viral genotypes with individuals of similar capacity represents the state of fitness landscape. It is known that quasispecies can adopt different modes of replication depending on the conditions. However, there are limits to replication conditions that prevent viruses from accessing preferred genotypes in heterogeneous environments [9].

Mounting evidence points to the vital role of viral protein-protein interactions in replication. A detailed interaction network greatly improves the understanding of viral biology and can identify small-molecule antiviral molecules. In parallel, viral replication is modeled at varying fidelity and the fitness of resulting genospace is studied as a basin of attraction for PPIs. It is further established that fitness landscape topology varies with fidelity class. Genotypes studied potentially correspond to RNA virus replication. Thus, interaction network topology may provide important clues about unique drug targets. It is proposed that scientific efforts can harness high-throughput bioinformatic and biophysical approaches to elucidate the viral interaction networks. In this regard, complimentary synthetic lethality, genetic interaction mapping, and perturbation mapping screens will need to be developed that elucidate PPIs without cell culturing [35].

5. Challenges in Vaccine Development

Vaccine development against an emerging virus is a race against time. Considerable efforts should be made to manufacture vaccines as early as possible. There are several challenges in developing a vaccine against an emerging virus [36]. First, our understanding about the pathogenicity is limited and protective antigens are poorly characterized. It is virtually impossible to predict the genetic variants that would cause the next outbreak or pandemic. Looking back in history, many emerging viruses, which caused an outbreak or epidemic, did not have any genetic relatives in the test or reference data. Had previous knowledge been associated with the new outbreak, the control of the outbreak would have been more straightforward. It is very difficult to develop a vaccine against an emerging virus. The development of the vaccine would be easier with more knowledge about pathogenicity, virulence factors, and protective antigens. To successfully counteract an emerging virus, genome sequence information and serotyping reagents should be acquired quickly [37].

Second, it is not easy to find appropriate animal challenge models for the evaluation of vaccine efficacy. Vaccine candidates need to be pre-clinically tested in animal models for safety, immunogenicity, and protective efficacy. For this purpose, animal models with mild or no innate immunity against the disease, as well as ones that can mimic human pathology or cytokine profiles, would be considered ideal. Other

important factors in choosing an ideal animal model are price, size, and ethical considerations. However, an ideal animal model closely mimicking human infection is hard to establish right now. Third, some emerging viruses have high mortality rates, with no treatment or prophylaxis available, and must be manipulated under high bio-safety conditions. Different parameters need to be controlled simultaneously, including: viral structure, antigenicity and other immunogenicity variables, limit of detection, mode of use, dosage, production type, control type against unwanted agents, and additional materials or components used [38].

5.1. Antigenic Variation

Antigen recognition and neutralization is primarily determined by the conformal structure of viral surface glycoprotein trimers at the time it is exposed to the host antibody-producing humoral immune system [39]. These glycoproteins have been labelled as “stabilizing” and “promoting” to describe their structure-preserving and structure-destabilizing, respectively, roles in viral cell entry. Because glycoprotein conformation is subject to change through allosteric mechanisms, viruses have evolved to generate variants of glycoprotein sequence that differ in their shielding from ADA.

Thus, an expected outcome of the high error-rate of RNA synthesis by virally encoded polymerases is the generation of alternative viruses whose resistant ADA refine the fine net of antiviral immunity through a large genetic distance. The large epitope space of glycoproteins suggests that even more antigenically distinct variants can be generated through ectopic mutations reflected in unexpected phenotypes.

The sporadic emergence of novel viruses in a host population and the unexpected emergence of variants with extreme antigenic drift characterizes the antigenic pattern that now typifies the urgent challenge of effective vaccine development against these RNA viruses. Understanding the fate of this antigenic progeny in the two distinct categories of infecundity escape and immune imprinting escape helps define a mode of antigenic evolution that provides for novel escape pathways, while leaving the coopted epitopes as a target for neutralization [40].

5.2. Vaccine Platforms and Technologies

The development and evaluation of vaccines against emerging/re-emerging RNA viruses, such as HIV-1, influenza, rabies virus, Zika virus, and others, continue to be hot topics. These efforts have the potential to bring vaccine platforms and technologies to the forefront of scientific research, as well as commercial and regulatory activities, as they have in the past two decades. This review does not intend to be exhaustive, and although the description of research progress on viruses is broad, there are a few that merit detailed discussion, particularly in terms of vaccine platforms and technologies.

Despite the proliferation of vaccine delivery systems and their more than 20 platforms for commercial vaccines, since the 20th century, there are still relatively few companies and academic laboratories that have progressed through all phases of vaccine development, from preclinical studies through regulatory applications and successful commercialization⁴¹. Here, the achievements of SARS-CoV-2 vaccines developed at a record time are described, along with potential opportunities and challenges for vaccine development against other emerging/re-emerging RNA viruses, in terms of ways to improve the effectiveness, safety, delivery, and adaptability of both old and new vaccines.

It is pointed out that the application of RNA as a vaccine platform against emerging/re-emerging viruses is expected to remove roadblocks and accelerate the process if reasonable and effective strategies are employed. mRNA vaccines have been a hot topic since 2005, particularly due to extensive investigations on their immune responses against tumors, infectious diseases, and autoimmune diseases. Some early data indicated that mRNA-based vaccines were less immunogenic than DNA plasmid-based vaccines. Researchers then shifted their focus to RNA viruses and efforts to efficiently produce and deliver

RNA vaccines to improve their immunogenicity [42]. However, interest waned in 2008 when it was shown that DNA vaccination was a better approach. Many laboratories turned back to RNA vaccine research in 2010 as improvements in the stability, delivery, and immunogenicity of RNA vaccines were made with the discovery of Dicer and new platforms, such as LNPs and CNE. Additionally, with the establishment of the model/testing systems of RNA viruses and platforms for rapid vaccine construction against infectious disease outbreaks, significant progress has been made. However, there is still a long way to go with a platform. Nevertheless, mRNA technology has served as an important potential platform against emerging/re-emerging viruses [43].

5.3. Regulatory and Ethical Considerations

The rapid advance of bioinformatics and metagenomics is providing public health agencies with new virus discovery tools. However, along with these new developments, experts will have to consider regulatory and ethical issues dealing with personal privacy and consent to use biological materials. There is also a concern that this knowledge of potential new threats could be used by terrorists in an effort to by-pass vaccine and antiviral drug protections. The emergence and rapidism of novel viral pathogens, specifically zoonotic RNA viruses, continues to grow as a serious public health threat. Advances in metagenomic discovery tools as well as genomics, structural biology, and synthetic biology, hold the potential for rapid vaccine and antiviral drug development. However, along with this new knowledge, a host of safety and ethical questions have to be considered as a result [44].

Emerging infectious diseases, especially those that are virulent and caused by infectious agents for which there are not yet treatment or prevention modalities, present unique challenges for public health. On the hand, there are many well proven methods of vaccinating against, and treating, many infectious diseases. Emerging diseases which spread quickly over a wide geographic area or which produce severity and lethality above that of previously known diseases are generally regarded as being more serious health risks. Vaccines against an EID, or a new virulent strain of a previously known infectious agent, will frequently have to be generated within months as opposed to years. Such rapid responses are feasible but they present profound challenges in vaccine development [4].

A critical step in developing a vaccine for a newly discovered RNA virus involves understanding how the virus and its proteins are recognized by the immune system. Generally, all mRNA viruses, from the small picornaviruses like foot and mouth disease virus to the enveloped viruses DENV, ZIKV, and HCV, are recognized by immune pattern recognition receptors inside the cytoplasm. Innate immune responses generate quickly, often in a matter of minutes, and they reduce viral loads thirty to forty-fold before adaptive, 'memory' immunity takes over. It will be critical to understand how a novel viral pathogen or strain is recognized by the immune system [5].

6. Case Studies of RNA Virus Vaccines

There is currently high interest in the development of vaccine candidates against newly emerging RNA virus infectious agents. This pandemic is widely thought to have resulted from the emergence of a previously existing nonhuman pathogen, most likely an RNA virus, into human population in Southeast Asia, where animal husbandry is in close contact with human habitation. As described, genetic sequencing of environmental samples such as urine or saliva may offer rapid means for preventing future pandemics. New vaccines based on general concepts are needed to protect against newly emerging viruses, particularly RNA viruses. The genome of many, if not most, such viruses may be targets for immunization. Non-infectious virus-like particle vaccine platforms provide a prophylactic means for immunization [45].

In vitro, the in situ encapsidation of nucleic acid into preformed viruses can protect the genome from

degradation and allow recovery of infectious particles. Virus-like particles (VLPs) derived from many viral families have been engineered and may differ in output properties and infectivities. The specific opportunities and challenges for currently circulating viruses must be considered. With proper targeting, these encapsidation systems may provide a means to activate the innate pluripotent RNA prompt responses, with some adaptations needed to target specific delivery/uptake pathways (outside in versus inside out).

This general VLP base vaccine technology will be opened to discovery by industry and academia by virus isolation culture systems and ready-to-use modular technology [46]. It can provide new, rapid, options for immunization against animal and non-infectious emerging RNA viruses within weeks of known sequence information, offering both therapeutic and prophylactic measures. Conversely, the technologies also provide platforms for possible bio-terrorism pandemic agents of the future against which FDA/HHS has enabled and funded classes of preparedness studies. Nevertheless, bio-enabled agents pose complex scientific and regulatory challenges as recent bio-terrorism experience show [47].

6.1. Vaccines for Zika Virus

Zika virus (ZIKV) is an arthropod-borne virus (arbovirus) in the genus flavivirus, transmitted to humans primarily by *Aedes aegypti* mosquitoes. ZIKV was first isolated from the Zika forest in Uganda in 1947. The first documented human ZIKV infection was in Nigeria in 1954. Outside Africa, ZIKV was detected in Asia in the 1970s and 1990s.

After the 2007 outbreak in the Pacific islands, ZIKV circulation in the Americas became apparent in 2015, with cases reported in Brazil, the Americas, and Asia. ZIKV infections in humans became more prevalent after its outbreak in the Pacific islands and the Americas [48]. The 2015 outbreak came to the world's attention due to the association between ZIKV infection in pregnant women and severe fetal complications, such as congenital Zika syndrome with microcephaly and severe developmental malformations. ZIKV is also a public health threat due to its potential transmission through sexual contact, blood transfusion, and breastfeeding [49]. However, there is currently no vaccine or therapeutic agent that can prevent or treat ZIKV infections. Rapid development of safe and effective vaccines is necessary, especially for the most vulnerable population, pregnant women.

Currently, the development of a vaccine against ZIKV is actively ongoing [50]. Various vaccine candidates based on different platforms against ZIKV have been developed and are in different phases of clinical trials, including live virus vaccines, inactivated virus vaccines, recombinant protein vaccines, viral vector vaccines, mRNA vaccines, DNA vaccines, and virus-like particle (VLP) vaccines. All vaccine candidates are being evaluated for safety, immunogenicity, and efficacy in animal models. Some candidates have completed Phase I or Phase II clinical trials, whereas others are under advanced preclinical evaluation. ZIKV Vaccine proposed characteristics of a ZIKV vaccine to be safe, immunogenic, and efficacious.

Furthermore, to address vaccine-related risks, sniffing and shedding of vaccine virus, cross-reactive immunity with closely related viruses that may result in ADE, and vertical transmission of vaccine virus are of concern for live attenuated virus vaccines. Vaccines with an adenoviral backbone have been linked with febrile seizures or other fever-related neurological complications in pediatric cohorts. An effective ZIKV vaccine will need to induce a ZIKV-specific immune response, provide durable immunity, and demonstrate safety and efficacy based on a stage-appropriate evaluation [51].

6.2. Vaccines for Ebola Virus

Ebola virus (EBOV) is the most virulent member of the Filoviridae family responsible for sporadic outbreaks of highly fatal hemorrhagic fever in humans. There are five recognized species of EBOV: Zaire (ZEBOV), Sudan (SEBOV), Taï Forest (TAFV), Bundibugyo (BDBV), and Reston (REBOV). ZEBOV is

responsible for the greatest number of cases and mortality during the outbreaks that have occurred in Africa since the late 1970s. An outbreak caused by the SEBOV in West Africa caused more than 10 000 deaths and became the worst outbreak in history. In addition to humans, EBOV poses a severe threat to nonhuman primates, including monkeys and apes. Ebola virus infection in humans and nonhuman primates causes a rapidly progressing hemorrhagic fever characterized by fever, malaise, fatigue, abdominal pain, and bleeding diathesis. With no approved therapeutic agent or vaccine at the time of the 2014-2016 outbreak, an international response accelerated the development of rVSV-ZEBOV vaccine that was administered to tens of thousands of individuals [52].

An outbreak in the Democratic Republic of the Congo saw the continuation of licensure trials of rVSV-ZEBOV and the use of a second vaccine, HZEBOV, with a live viral vector based on vesicular stomatitis virus expressing the EBOV glycoprotein that is taken up by dendritic cells. In both of these uptakes, the importance of building relationships and better technologies in epidemiology and vaccinology was illustrated, as was the complex interplay with health systems, politics, and trust in science broadly. In particular, several points around the rapid development and ultimate success of the rVSV-ZEBOV vaccines highlight important considerations with emerging RNA viruses [16]. Ebolaviruses are a member of the Filoviridae family of negative-sense single-stranded RNA viruses. Ebolavirus thus carries its genetic material in the form of a single helix.

As the virion is composed of a ribonucleoprotein complex, the viral genome is also packaged together with the nucleoprotein, polymerase, and cofactor proteins essential for transcribing and replicating the viral genome. While prevention and control of filovirus outbreaks depend on investigating zoonotic reservoirs, this includes importation of infected animals or attenuated viruses into many countries [53].

6.3. Vaccines for SARS-CoV-2

COVID-19 vaccines include inactivated virus, live-attenuated virus, viral vector, mRNA, and protein subunit virus vaccines that have been studied and developed for a long time. Inactivated and live-attenuated virus vaccines [54], elicit stronger immune responses in primates than protein vaccines, however, concerns remain regarding viral shedding and virulence. Analysis of neutralizing antibody (NAbs) responses revealed that some vaccines failed to produce sufficient cross-reactive NAbs against escape variants of concern.

Natural viral evolution and the emergence of variants have caused concerns about the effectiveness of current vaccines, as well as the potential of new viruses to infect the vaccinated. Therefore, updated vaccines and novel vaccination strategies against variants need to be optimized and developed. New vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern (VOCs) will need to be continually developed, as viruses with new mutations can pose new threats to the health of humanity globally [55].

mRNA vaccine technology has garnered immense interest as an innovative breakthrough in regulating the spread of the SARS-CoV-2 virus. mRNA-1273 and BNT162b2 were among the first vaccines authorized for emergency use internationally during the COVID-19 pandemic. On a safer tomorrow, vaccines with novel scopes, such as those based on circular RNA, virus vectors, and nanoparticle chimeric protein vaccines, were effective against COVID-19. Similarly, an optimistic future vaccine state is predicted, relevant to the advent of new technology that can satisfy food safety-related requirements and public apprehensions.

The worldwide prevalence of SARS-CoV-2 has resulted in a larger viral burden in human populations, leading to increases in the likelihood of new mutations emerging. At the same time, the continuous co-evolution of the virus and the host immune system may present new challenges to the efficacy of current vaccines. There is a clear trend of an increasing number of mutations with time since the emergence and

dominance of the Delta variant, suggesting that new VOCs will also be observed in the future [56].

7. Future Directions in RNA Virus Research

In this meeting report, only the major points of the discussions on a road map for RNA virus research in India are presented. These follow the basic outline of the meeting i.e., Epidemiology, Pathogenesis, Immune Response/Vaccine Development and Antivirals for RNA Viruses. Following the general information about RNA viruses, points for the Development of Road Map are outlined.

The Indian subcontinent presents a fertile ground for the thriving of RNA viruses. The tropical climate, varying altitudes and geography provide an ideal environment for the survival, amplification and transfer of RNA viruses, which, in turn, are vectors for other viruses [57]. The increasing population density, enhanced travel and trade, rise of the animal-to-human interface and the resultant high rates of viral evolution have all contributed to the introduction of many new virus types into the human and domestic animal populations [3].

These include Nipah, Chandipura and Chikungunya viruses as well as West Nile, Hendra and Crimean-Congo haemorrhagic fever virus. Many current pathogens such as the rapidly spreading H5N1, H7N7 and H1N1 are zoonotic viruses. Meeting on emerging RNA viruses and their vectors was held in 2008 in India and identified need for focus on studies on a host of RNA viruses [58]. Attention is being drawn to re-emerging RNA viruses with a long lag period between disease emergence and recognition. However, as well as studying viral genome evolution using sequencing, understanding the epidemiology, clinical presentation and evolution of pathogenicity would give first notice of the emergence of a serious problem. Robust, adaptable methods for the monitoring and tracking of RNA viruses are therefore urgently needed.

However, it is equally urgent to better understand the biology and pathogenesis of known RNA viruses of animal and public health significance that have been neglected despite huge investments by governments and pharmaceutical companies in research on neighbouring DNA viruses [1,59].

Although effective vaccines and antiviral inhibitors have been developed for important DNA viruses, none is currently available for the majority of RNA viruses despite their great public health and economic significance. Thus, there is need on the study of RNA viruses, ranges of different types best achieved by individuals and institutions working together through some form of network. At the same time, concurrent heads-up work on likely candidates for the emergence of novel pathogenic viruses is also needed [60].

7.1. Innovative Vaccine Strategies

Emerging and re-emerging infectious diseases caused by viruses are major threats to public health globally. Vaccination is considered the most effective method of preventing viral infectious diseases. A number of inactivated, live-attenuated, subunit, and vectored viral vaccines in 8 Virus-like particles (VLPs), are engineered vaccine candidates that resemble virus-like particles. Viruses are non-infectious as they lack the key genetic material for replication. VLP vaccines possess most antigenicity similar to that of the native virus and, importantly, can stimulate both humoral and cellular immune responses, offering effective protection against viruses [47].

Here, recent development with VLP-based vaccines for emerging or re-emerging infectious diseases caused by RNA viruses from different virus families is reviewed. Mechanisms, benefits, and challenges of VLP vaccines are recognized and recent studies of VLP-based vaccines for some important emerging RNA viruses, including H7N9 of influenza A viruses H, C and F of coronavirus, fungal hillbark virus are highlighted.

As part of the ongoing efforts, the infectious clones of numerous RNA viruses have been improved and optimized to produce virus-derived VLPs or native-like viruses without animal passage, which better maintain the glycoproteins for natural culture, immunogenicity, and vaccine efficacy [61]. Recently developed vaccine strategies against emerging RNA viruses based on virus-like particles (VLPs), which are effective vaccine candidates widely used in human medicine, veterinary medicine, and agriculture.

VLPs are formed by viral capsids or nucleoprotein subunits in an appropriate cell system and have become a high-priority strategy for vaccine development. Various VLP vaccines for RNA viruses including caliciviridae, coronaviridae, and paramyxoviridae are described with respect to their robustness in producing effective anti-viral protection for large-scale population vaccination. These examples demonstrate the flexibility of VLP technology for rapid response against emerging infectious disease viruses from variegated families [62].

7.2. Role of Genetic Engineering

Two-step strategies for RNA virus vaccine development focus on generating antigens or implementing live infectious viruses or replicons expressing antigens. While inactivated virus is safe and effective against certain RNA viruses, the high mutation rate of these viruses may prevent the selection of attenuated mutant strains or eliminate attenuation. The generation of infectious clones has revolutionized the study of viruses, allowing for the addition of SA to HIV and the development of an infectious clone vaccine for WNV, which was recently licensed for veterinary use. DNA vectors have been extensively developed, and methods are being explored to develop these vectors for human vaccination [5].

Due to the antigenic diversity of many viruses, an RNA virus expressing heterologous antigens is unlikely to be effective against circulating strains, and genetic material from the parent virus may need to be included in the vaccine. However, concerns have been raised about the genetic stability of such constructions.

Approaches are being explored that deliver a cDNA amplification of the relevant WNV genes along with the specific flavivirus signal host sequences required for the production of WNV particles. Comprehensive studies on these constructs are well underway. A natural replication-defective recombinant rabies virus was constructed to express the O ring glycoprotein and was shown to elicit antibodies against rabies and O ring, leading to protective immunity. However, the spread of genes encoding proteins from other organisms among rabid rabies viruses may limit the use of rabies vectors [63].

7.3. Global Health Initiatives

Emerging viral pathogens are the common factor among the most recent outbreaks of emerging and re-emerging infectious diseases notified to the WHO that are of serious public health concern. The rapid evolution of these pathogens adds new challenges for the public health agencies for epidemic preparedness and response planning. It is imperative to understand the epidemiology, pathogenesis, and translational aspects of these pathogens towards the holistic development of diagnostic, therapeutic, and preventive measures including vaccines. Identification of gaps in research to further strengthen the existing knowledge base as well as policy level measures for public health measures application has also been discussed 64.

Epidemiological knowledge of emerging viral pathogens is essential for public health preparedness. The natural reservoir(s) and ecological correlation of emerging viral pathogens in a particular geographical region act as a platform for periodic outbreaks and epizootics. Geo-climatic conditions and human social behavior play a significant role in the emergence of the viruses. Study on surveillance programs of vector/vector borne zoonotic diseases to be conducted on a priority basis especially on

nonhuman primate flaviviruses in the Sundarbans mangroves, duplication of surveillance programs for newly emerged viruses in susceptible human populations [65].

This includes systematic understanding of the virus, its origin, evolution, molecular biology etc. using in vitro and in vivo models with the aim of early recognition of viral emergence in humans and preparedness of public health agencies with suitable plan of action. Pathogenesis mechanisms of newly evolved viruses should be studied thoroughly with the aim of finding out closely related viruses within the family/sub-family of the newly emerged virus, considering the important pathogenic attributes such as host tropism, replication, evasion of immunity etc. Pathogenicity evaluation of closely related viruses could give a clue towards the susceptibility of the human/animal population to the newly emerged virus. Furthermore, large scale sequencing of environmental samples could also provide an early warning of newly evolved viruses [66].

8. Conclusion

Despite the increases in number, severity and public awareness of disease outbreaks caused by emerging RNA viruses in the past two decades, research into these viruses does not match the level of concern and socio-economic threat they cause. Most research is conducted in the developed world and continuous efforts are made there to control the outbreaks even though potential outbreaks threaten countries in the developing world considerably more because of the greater risk factors in these countries [3].

The Indian subcontinent represents the perfect combination of environment, geography and population density for RNA viruses to thrive. Diseases caused by RNA viruses have been shown to be capable of spreading at rapid rates from animal reservoirs to cause human outbreaks as was shown with Nipah virus and West Nile virus. Other RNA viruses such as Zika virus and Chikungunya virus are endemic in parts of India and pose a constant threat of outbreaks. Despite the significance of RNA viruses as pathogens of high impact and concern, very little attention has been paid to research into the biology and pathogenesis of RNA viruses in India. For example, no studies have been conducted on the epidemiology and disease burden, risk factors, severity, containment, the immune response to RNA viruses, circulating virus strains and virus evolution, response by public health authorities, small animal models of disease for the testing of therapeutics for RNA viruses, small animal models that can be used by other labs in India for the testing of vaccines and possible antiviral drugs, antiviral drugs, vaccines and vaccine vectors derived from viruses studied in India.

Given the vast amount of varied expertise in the field of virus research in India, the apex professional organization in India, the Indian National Academy of Sciences (INSA) organized an India|EMBO symposium on emerging RNA viruses that focused on the rapidly spreading family of viruses that are able to cause outbreaks in large, densely populated areas of low hygiene standards and effective containment whose epidemiology is difficult to track.

Acknowledgment: The authors gratefully acknowledge the support provided by "Center for Environmental Research and Studies at the University of Babylon" in facilitating the completion of this review.

Conflict of Interest: The all authors affirm that there are no financial or personal relationships that could have influenced the work reported in this manuscript.

Ethical consideration: The ethical committee approved the study at University of Babylon, Hilla, Iraq.

Funding: This research received no external funding.

References:

1. Gogoi D, Baruah PJ, Narain K. Immunopathology of emerging and re-emerging viral infections: an updated overview. *Acta Virol.* 2024;68:12108. <https://doi.org/10.3389/av.2024.12108>.
2. Mohapatra S, Menon NGG. Factors responsible for the emergence of novel viruses: an emphasis on SARS-CoV-2. *Curr Opin Environ Sci Health.* 2022;27:100358. <https://doi.org/10.1016/j.coesh.2022.100358>.
3. Liu J, Dai S, Wang M, Hu Z, et al. Virus-like particle-based vaccines against emerging infectious disease viruses. *Hum Vaccin Immunother.* 2016;12(5):1234-1245. <https://doi.org/10.1007/s12250-016-3756-y>.
4. Han JJ, Song HA, Pierson SL, Shen-Gunther J, Xia Q. Emerging infectious diseases are virulent viruses—are we prepared? An overview. *Microorganisms.* 2023;11(11):2618. <https://doi.org/10.3390/microorganisms11112618>.
5. Hsiung KC, Chiang HJ, Reinig S, Shih SR. Vaccine strategies against RNA viruses: current advances and future directions. *Vaccines (Basel).* 2024;12(12):1345. <https://doi.org/10.3390/vaccines12121345>.
6. Medigeshi GR, Fink K, Hegde NR. Position paper on road map for RNA virus research in India. *Front Microbiol.* 2018;9:1753. <https://doi.org/10.3389/fmicb.2018.01753>.
7. Kautz TF, Forrester NL. RNA virus fidelity mutants: a useful tool for evolutionary biology or a complex challenge? *Viruses.* 2018;10(11):600. <https://doi.org/10.3390/v10110600>.
8. Pollett S, Melendrez MC, Berry IM, Duchêne S, Salje H, Cummings DAT, et al. Understanding dengue virus evolution to support epidemic surveillance and counter-measure development. *Infect Genet Evol.* 2018;62:279-295. <https://doi.org/10.1016/j.meegid.2018.04.032>.
9. Šimičić P, Židovec-Lepej S. A glimpse on the evolution of RNA viruses: implications and lessons from SARS-CoV-2. *Viruses.* 2022;15(1):1. <https://doi.org/10.3390/v15010001>.
10. Payne S. Introduction to RNA viruses. In: *Viruses.* 2017. <https://doi.org/10.1016/B978-0-12-803109-4.00010-6>.
11. McDonald SM, Nelson MI, Turner PE, Patton JT. Reassortment in segmented RNA viruses: mechanisms and outcomes. *Nat Rev Microbiol.* 2016;14(7):448-460. <https://doi.org/10.1038/nrmicro.2016.46>.
12. Woolhouse MEJ, Brierley L. Epidemiological characteristics of human-infective RNA viruses. *Philos Trans R Soc Lond B Biol Sci.* 2018;373(1748):20170182.
13. Wadas I, Domingues I. Systematic review of phylogenetic analysis techniques for RNA viruses using bioinformatics. *Int J Mol Sci.* 2025;26(5):2180. <https://doi.org/10.3390/ijms26052180>.
14. Novella IS, Preslold JB, Taylor RT. RNA replication errors and the evolution of virus pathogenicity and virulence. *Curr Opin Virol.* 2014;9:143-147. <https://doi.org/10.1016/j.coviro.2014.09.017>.
15. Burrell CJ, Howard CR, Murphy FA. Emerging virus diseases. In: *Medical Virology.* Elsevier; 2016. p. 217-225. <https://doi.org/10.1016/B978-0-12-375156-0.00015-1>.
16. Khabbaz R, Bell BP, Schuchat A, Ostroff SM, Moseley R, Levitt A, et al. Emerging and reemerging infectious disease threats. In: *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases.* 2014. <https://doi.org/10.1016/B978-1-4557-4801-3.00014-X>.
17. Rahman MT, Sobur MA, Islam MS, Ievy S, Hossain MJ, El Zowalaty ME, et al. Zoonotic diseases: etiology, impact, and control. *Microorganisms.* 2020;8(9):1405. <https://doi.org/10.3390/microorganisms8091405>.

- 18.Topluoglu S, Taylan-Ozkan A, Alp E. Impact of wars and natural disasters on emerging and re-emerging infectious diseases. *Front Public Health*. 2023;11:1215929. <https://doi.org/10.3389/fpubh.2023.1215929>.
- 19.Trovato M, Sartorius R, D'Apice L, Manco R, De Berardinis P. Viral emerging diseases: challenges in developing vaccination strategies. *Front Immunol*. 2020;11:2130. <https://doi.org/10.3389/fimmu.2020.02130>.
- 20.Childs JE, Richt JA, Mackenzie JS. Introduction: conceptualizing and partitioning the emergence process of zoonotic viruses from wildlife to humans. *Curr Top Microbiol Immunol*. 2007.
- 21.Singh RK, Dhama K, Chakraborty S, Tiwari R, Natesan S, Khandia R, et al. Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies. *Vet Q*. 2019;39(1):26-55. <https://doi.org/10.1080/01652176.2019.1580827>.
- 22.Domingo E. Mechanisms of viral emergence. *Vet Res*. 2010;41(6):38. doi:10.1051/vetres/2010010.
- 23.Marie V, Gordon ML. The (re-)emergence and spread of viral zoonotic disease. *Viruses*. 2023;15(8):1638. <https://doi.org/10.3390/v15081638>.
- 24.Breman JG, Heymann DL, Lloyd G, McCormick JB, Miatudila M, Murphy FA, et al. Discovery and description of Ebola Zaire virus in 1976. *J Infect Dis*. 2016;214(Suppl 3):S93-S101. <https://doi.org/10.1093/infdis/jiw207>.
- 25.Cunha MS, Costa PA, Correa IA, De Souza MR, Calil PT, Da Silva GPD, et al. Chikungunya virus: an emergent arbovirus. *Front Microbiol*. 2020;11:1297. doi:10.3389/fmicb.2020.01297.
- 26.Ryu WS. Virus life cycle. *Mol Virol Hum Pathog Viruses*. 2016;31. <https://doi.org/10.1016/B978-0-12-800838-6.00003-5>.
- 27.Walper SA, Lasarte Aragonés G, Sapsford KE, Brown CW 3rd, Rowland CE, Breger JC, et al. Detecting biothreat agents. *ACS Sens*. 2018;3(10):1894-2024. <https://doi.org/10.1021/acssensors.8b00420>.
- 28.Rampersad S, Tennant P. Replication and expression strategies of viruses. *Viruses*. 2018;55. <https://doi.org/10.1016/B978-0-12-811257-1.00003-6>.
- 29.Lee CY. Exploring potential intermediates in cross-species transmission of influenza A. *Viruses*. 2024;16(7):1129. <https://doi.org/10.3390/v16071129>.
- 30.Delves PJ. Innate and adaptive systems of immunity. In: *The Autoimmune Diseases*. 2020. p.45-61. <https://doi.org/10.1016/B978-0-12-812102-3.00004-X>.
- 31.Li D, Wu M. Pattern recognition receptors in health and diseases. *Signal Transduct Target Ther*. 2021;6(1):1-24. <https://doi.org/10.1038/s41392-021-00687-0>.
- 32.Bai F, Thompson EA, Vig PJS, Leis AA. Current understanding of West Nile virus. *Pathogens*. 2019;8(4):193. <https://doi.org/10.3390/pathogens8040193>.
- 33.Louten J. Virus replication. *Essential Human Virology*. 2016;49-70. <https://doi.org/10.1016/B978-0-12-800947-5.00004-1>.
- 34.Idrees S, Chen H, Panth N, Paudel KR, Hansbro PM. Exploring viral–host protein interactions as antiviral therapies. *Microorganisms*. 2024;12(3):630. <https://doi.org/10.3390/microorganisms12030630>.
- 35.Jeong H, Seong BL. Exploiting virus-like particles as innovative vaccines. *J Microbiol*. 2017;55:220-230. <https://doi.org/10.1007/s12275-017-7058-3>.
- 36.Williams BA, Jones CH, Welch V, True JM. Outlook of pandemic preparedness. *NPJ Vaccines*. 2023;8(1):178. <https://doi.org/10.1038/s41541-023-00773-0>.
- 37.Herati RS, Wherry EJ. Predictive value of animal models for vaccine efficacy. *Cold Spring Harb Perspect Biol*. 2018;10(4):a031583. <https://doi.org/10.1101/cshperspect.a029132>.
- 38.Mosa AI. Antigenic variability. *Front Immunol*. 2020;11:2057. <https://doi.org/10.3389/fimmu.2020.02057>.

39. Díaz-Salinas MA, Li Q, Ejemel M, Yurkovetskiy L, Luban J, Shen K, et al. Conformational dynamics of SARS-CoV-2 spike. *Elife*. 2022;11:e75433. <https://doi.org/10.7554/eLife.75433>.
40. Brisse M, Vrba SM, Kirk N, Liang Y, Ly H. Emerging concepts in vaccine development. *Front Immunol*. 2020;11:583077. <https://doi.org/10.3389/fimmu.2020.583077>.
41. Chakraborty C, Bhattacharya M, Dhama K. SARS-CoV-2 vaccines and development technologies. *Vaccines (Basel)*. 2023;11(3):682. <https://doi.org/10.3390/vaccines11030682>.
42. Cheng F, Wang Y, Bai Y, Liang Z, Mao Q, Liu D, et al. Stability of mRNA vaccines. *Viruses*. 2023;15(3):668. <https://doi.org/10.3390/v15030668>.
43. Maslow JN. Vaccine development for emerging diseases. *Vaccine*. 2017;35(41):5437-5443. <https://doi.org/10.1016/j.vaccine.2017.02.015>.
44. Excler JL, Saville M, Berkley S, Kim JH. Vaccine development for emerging infectious diseases. *Nat Med*. 2021;27(4):591-600. <https://doi.org/10.1038/s41591-021-01301-0>.
45. Lundstrom K. Replicon RNA viral vectors as vaccines. *Vaccines (Basel)*. 2016;4(4):39. <https://doi.org/10.3390/vaccines4040039>.
46. Ghattas M, Dwivedi G, Lavertu M, Alameh MG. Vaccine technologies and platforms. *Vaccines (Basel)*. 2021;9(12):1490. <https://doi.org/10.3390/vaccines9121490>.
47. Boyer S, Calvez E, Chouin-Carneiro T, Diallo D, Failloux AB. Mosquito vectors of Zika virus. *Microbes Infect*. 2018;20(11-12):646-660. <https://doi.org/10.1016/j.micinf.2018.01.006>.
48. Wang Y, Ling L, Zhang Z, Marin-Lopez A. Advances in Zika vaccine development. *Vaccines (Basel)*. 2022;10(11):1816. <https://doi.org/10.3390/vaccines10111816>.
49. Kudchodkar SB, Choi H, Reuschel EL, Esquivel R, Kwon JJA, Jeong M, et al. Synthetic DNA vaccine targeting Zika virus. *Microbes Infect*. 2018;20(11-12):676-684. <https://doi.org/10.1016/j.micinf.2018.03.001>.
50. Ostrowsky JT, Katzelnick LC, Bourne N, Barrett AD, Thomas SJ, Diamond MS, et al. Zika virus vaccines and monoclonal antibodies. *Lancet Infect Dis*. 2025. [https://doi.org/10.1016/S1473-3099\(24\)00750-3](https://doi.org/10.1016/S1473-3099(24)00750-3).
51. DeZure A, Graham BS. Vaccines for emerging viral diseases. In: *The Vaccine Book*. 2016. p.543-560.
52. Muyembe JJ, Pan H, Peto R, Diallo A, Touré A, Mbala-Kingebene P, et al. Ebola outbreak response with rVSV-ZEBOV-GP ring vaccination. *N Engl J Med*. 2024;391(24):2327-2336. <https://doi.org/10.1056/NEJMoa1904387>.
53. Kumar DS, Prasanth K, Bhandari A, Jha VK, Naveen A, Prasanna M, et al. COVID-19 vaccine development challenges. *Cureus*. 2024;16(5):e60015. <https://doi.org/10.7759/cureus.60015>.
54. Dong Y, Dai T, Wei Y, Zhang L, Zheng M, Zhou F. SARS-CoV-2 vaccine candidates. *Signal Transduct Target Ther*. 2020.
55. Teo SP. Review of COVID-19 mRNA vaccines. *J Pharm Pract*. 2022;35(6):947-951. <https://doi.org/10.1177/08971900211009650>.
56. Sudhan SS, Sharma P. Human viruses: emergence and evolution. In: *Emerging and reemerging viral pathogens*. Academic Press; 2020. p.53-68. <https://doi.org/10.1016/B978-0-12-819400-3.00004-1>.
57. Voskarides K. Animal-to-human viral transitions. *J Mol Evol*. 2020;88(5):421-423. <https://doi.org/10.1007/s00239-020-09947-z>.
58. Vashisht V, Vashisht A, Mondal AK, Farmaha J, Alptekin A, Singh H, et al. Genomics for emerging pathogen identification. *BioMedInformatics*. 2023;3(4):1145-1177. <https://doi.org/10.3390/biomedinformatics3040069>.
59. Laxmi B, Devi PUM, Naveen T, Buddolla V. Virus-like particles for emerging viral threats. *Microbe*. 2025:100351. <https://doi.org/10.1016/j.microb.2025.100351>.

60. Tariq H, Batool S, Asif S, Ali M, Abbasi BH. Virus-like particles as vaccine platforms. *Front Microbiol.* 2022;12:790121. <https://doi.org/10.3389/fmicb.2021.790121>.
61. Yan D, Wei YQ, Guo HC, Sun SQ. Application of virus-like particles. *Appl Microbiol Biotechnol.* 2015;99:10415-10432. <https://doi.org/10.1007/s00253-015-7000-8>.
62. Suphaphiphat P, Whittaker L, De Souza I, Daniels RS, Dormitzer PR, McCauley JW, et al. Antigenic characterization of influenza viruses. *Vaccine.* 2016;34(32):3641. <https://doi.org/10.1016/j.vaccine.2016.05.031>.
63. Zapatero-Belinchón FJ, Kumar P, Ott M, Schwartz O, Sigal A. Understanding emerging viruses for pandemic preparedness. *Nat Microbiol.* 2024;9(9):2208-2211. <https://doi.org/10.1038/s41564-024-01789-5>.
64. Gharbi J, Rezza G, Ben M'hadheb M. Emerging and re-emerging viral infections. *Front Public Health.* 2025;12:1528163. <https://doi.org/10.3389/fpubh.2024.1528163>.
65. Holmes EC, Krammer F, Goodrum FD. Virology – The next fifty years. *Cell.* 2024;187(19):5128-5145. <https://doi.org/10.1016/j.cell.2024.07.025>.

How to cite this article

Obaid ZH, Abbas AS, Al-Shalah LAA, Ramadan GM., " Emerging RNA Viruses: Epidemiology, Pathogenesis, and Challenges for Vaccine Development: Review," 2026. *Journal of Biomedicine and Biochemistry.* 2026;5(1):36-56. DOI: 10.57238/jbb.2026.7432.1163