Epidemiological Trends of Lymphochoriomeningitis Virus Infection

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ABSTRACT

Lymphocytic choriomeningitis virus (LCMV) a member of family Arenaviridae genus Mammarenavirus, discovered in 1933 from a patient with meningoencephalitis, persists as a significant zoonotic threat, primarily harbored by house mice and linked to aseptic meningitis in humans. Its global impact ranges from mild flu-like symptoms to severe neurological complications, particularly perilous in immunocompromised individuals and pregnant women, leading to fetal abnormalities and mortality. Human transmission primarily occurs through contact with rodents or exposure to contaminated aerosols, highlighting house mice (Mus musculus), especially persistently infected ones, as key agents in human infections. M. musculus and Mus domesticus are the natural and reservoir host of LCMV virus. Except for vertical transmission from infected pregnant women to foetus and organ donation, there is no evidence of human-to-human transfer. The LCMV targets the endothelial and lymphatic cells and replicate there or settle down in lymphatic tissues like spleen or lymph nodes and further replicate there leading to viremia to various organs. In the 1950s virus has been detected about 8% of the patients suffering with neuroinvasive disease. Diagnosis remains challenging due to limited diagnostic tools, Serological tests like IFA and EIA target immunoglobulin M and G, RT-PCR, and viral isolation being employed. Therapeutic options, notably ribavirin, show promise but remain limited, while ongoing vaccine research investigates candidates like reverse genetically altered recombinant LCMV and replicating LCMV-based vectors. LCMV's global prevalence, though constrained by diagnostic limitations, underscores its continued public health impact, necessitating sustained research into diagnostics, treatments, and vaccines to mitigate its multifaceted threats.

Keywords: Choriomeningitis; Aseptic Meningitis; Meningioencephalitis; Arenavirus; Encephalitis

CITATION

Fatima K, Kausar R, Afzal Z, Tariq M, Mubashir M, Rizvi F, Adil M, Rani Z, Ali D, Nazir H, Kasli MAF and Khan AMA, 2023. Epidemiological trends of lymphochoriomeningitis virus infection. In: Aguilar-Marcelino L, Zafar MA, Abbas RZ and Khan A (eds), Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan, Vol 3: 589-598. https://doi.org/10.47278/book.zoon/2023.126

CHAPTER HISTORY Received: 08-Jan-2023 Revised: 27-Feb-2023 Accepted: 20-July-2023

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1. INTRODUCTION

Lymphocytic choriomeningitis virus (LCMV) was the first time isolated by Lillie and Armstrong in 1933 from cerebrospinal fluid of a patient suffering with meningoencephalitis (Bonthius 2009). House mouse (*Mus musculus*) recognized as a natural reservoir host of the virus in year 1935 by Traub (Vilibic-Cavlek et al. 2021). In the studies after the discovery of LCMV, it was recognized as the main reason of aseptic meningitis in human beings (Meerburg et al. 2009). Virus was detected in 58 cases out of 713 in the years between 1953 and 1958 from USA. Along with these massive cases were reported from Germany (47 cases) in years between 1968 to1971 and USA (181 cases) in years 1973 to 1974 (Sarute and Ross 2021). LCMV is a neglected rodent-borne zoonotic virus due to limited diagnostic aids. Although cases were reported from round the globe, or the virus was also isolated from the rodents of Americas, Africa, Asia, and Europe. Though the diagnostic tools are limited still the LCMV is an important cause of meningitis in humans (Taniguchi et al. 2020).

Lymphocytic choriomeningitis virus (LCMV) is a member of family *Arenaviridae* genus *Mammarenavirus*. Old-world and new-world arena viruses are the two categories into which *Mammarenaviruses* are separated. In the same way as Lassa virus (LASV), the cause of Lassa fever, belongs to the old-world arena virus group, so does LCMV (Anesi et al. 2019). Two negative-sense single-stranded RNA segments, designated S and L, make up the LCMV genome. A viral nucleoprotein (NP) and glycoprotein precursor are encoded by the S segment, which is about 3.4 kilobases (kb) long. In contrast, the L segment, which is about 7.2 kb long, encodes a viral RNA-dependent RNA polymerase (L) and a polypeptide that contains a tiny zinc finger-domain (Z) (Baker 1998). Noncoding areas are responsible for LCMV's virulence, but they can also be used as targets to encourage viral attenuation for vaccine development (MacNeil et al. 2012).

2. TRANSMISSION

Arena viruses often spread horizontally, however some species of arenavirus can also spread vertically (Mims 1981). Although Wnzhu virus vertical transmission has not yet been experimentally shown, pups and dams were determined to be the source of horizontal transmission (Blasdell et al. 2016). The virus might behave as a possible teratogen, which is referred to as any environmental element that can cause a permanent aberration in form or function, a limitation of growth, or the death of the embryo or foetus, if it infects the embryo or foetus by vertical transmission (Gilbert-Barness 2010).

2.1. SIGNS AND SYMPTOMS

In Humans LCMV causes nausea, flu-like fever, headache, neck stiffness, sometimes photophobia and in severe cases meningitis and encephalitis (Vilibic-Cavlek et al. 2021). LCMV also infect the fetus in the comb of mother leading to its role as an emerging fetal teratogen. In congenital infection it leads to chorioretinitis, Hydrocephalus and periventricular calcifications. Mortality rate in children which are infected congenitally is about 35% and 70% of among them shows long-term neurologic sequelae (Bonthius 2009). In the result of LCMV directly acquired from rodent's leads to a highly fatal hepatitis in captive Callitrichid primates, this kind of hepatitis also occurs as sporadic outbreaks among many species

of tamarins and marmosets (Anesi et al. 2019). In individuals with strong immunity LCMV infection is usually asymptomatic or self-limited febrile disease although it occurs in about one third cases only and recovers in two to three weeks (Jamieson et al. 2006). On the other hand, in patients with compromised immunity like organ transplant recipients, LCMV can leads to a failure of multiple organs with a high fatality rate (Doherty et al. 1992). LCMV also play a role as a teratogen pass on to fetus in the comb of mother transplacentally and leads to ocular or CNS malformation, abortion, or intrauterine death of fetus (Welsh et al. 1991). In immunocompetent patients one third of the patients that acquire LCMV are a symptomatic while from the remaining two-thirds half of the cases shows non-specific febrile condition while the remaining suffer with central nervous system infection and in them symptoms appear about 6 to 20 days after the initial exposure (McLay et al. 2013).

LCMV shows a biphasic course in infected individuals starting from nonspecific conditions like nausea, headache, vomiting, malaise, and myalgia. While in the second phase main target is nervous system showing nervous signs like nuchal rigidity, photophobia, and headache and in some cases may leads to serious outcome like myelitis hydrocephalus or encephalitis or in rare cases LCMV can also leads to orchitis, parotitis, pneumonitis and, myocarditis. In acquired cases the rate of mortality is as low as 1%. On the other hand, immunocompromised patients are on higher risk (McLay et al. 2013).

LCMV can be transferred from infected person to non-infected through organ transplant. Cases of LCMV have been reported from the patients that received liver and kidney from the infected individual. But LCMV did not develop in patients that received cornea from infected individuals (Louten 2016). LCMV leads to multiple organ failure in recipients in terminal stages, at early stages after the transplant symptoms like flu, fever leukocytosis, abdominal pain, coagulopathy has been noted. It leads to a high mortality rate in patients up to about 71%. The patient that survived required ventriculoperitoneal shunt placement (Welsh et al. 1991).

In congenitally infected LCMV, leads to abortion in early first trimester of age. In about 88% of the PI cases it leads to hydrocephalus, neonatal meningitis, chorioretenitis and periventricular calcification (Anesi et al. 2019). Usually, Persistent infection occurs during the viremic stage of the disease when the virus is present in huge amount in the blood of the mother and cross the placental barrier to infect the fetus (19). High mortality rate up to 35% has been noted in persistently infected infants while the survivors suffer with neurological disorders for a long period (Blasdell et al. 2016).

3. LCM VIRAL PROTEINS AND THEIR FUNCTION:

With a bisegmented RNA genome that encodes two proteins on each segment in an ambisense orientation L polymerase protein and the small matrix protein Z on the L segment and glycoprotein GPC and nucleoprotein NP on the S segment arena viruses are a diverse family of negative-strand enveloped RNA viruses (Buchmeier 2007). Humans can contract a wide range of illnesses from arena viruses, but there are few preventative or curative measures available (McLay et al. 2013; Zapata and Salvato 2013). Neurologic illnesses can be brought on by the lymphocytic choriomeningitis virus (LCMV) (Bonthius). Organ transplant recipients who passed away from a febrile illness had the Dandenong virus (DANV) isolated from them (Palacios et al. 2008). Arena viruses that cause hemorrhagic fever (HF), including the Lassa virus (LASV), the Lujo virus (LUJV), the Junin virus (JUNV), the Machupo virus (MACV), the Sabia virus (SABV), the Guanarito virus (GTOV), and the Chapare virus (CHPV), can result in multisystem organ failure and death. In several West African nations, LASV is an endemic illness that results in 500,000 infections and 5,000 yearly fatalities (McCormick et al. 1987). There isn't a licensed vaccine for human use now, except for Candid#1, which is used as the JUNV vaccine in Argentina. There aren't many therapeutic choices, thus supportive care is generally used. A broad-spectrum antiviral drug called ribavirin has only

been proven to be somewhat effective when given at the insidious early stages of viral infection (McCormick et al. 1986). Argentine HF (AHF), which is caused by the JUNV, has been treated with moderate effectiveness by immune plasma transfusion (Enria et al. 2008) but not hemorrhagic fever from Lassa. Other arena viruses, such as Mobala virus (MOBV), Mopeia virus (MOPV), Ippy virus (IPPYV), Amapari virus (AMAV), and Pichinde virus (PICV), have been isolated from the same host species and belong to the same serogroups as the other arenaviral pathogens. However, it is unknown why these viruses are not linked to human diseases (Zapata and Salvato 2013).

The 15-kDa arenavirus Z protein serves a variety of purposes (Kleinschmidt-DeMasters and Beckham 2015), including helping to create the virions' matrix layer (Salvato et al. 1992; Neuman et al. 2005), mediating virus budding (Perez et al. 2003; Strecker et al. 2003), and regulating viral genome replication and transcription (Cornu and de la Torre 2002; Kranzusch and Whelan 2011). According to studies, the Z protein of New World (NW) pathogenic arenaviruses, such as MACV, JUNV, SABV, and GTOV, but not of Old World (OW) pathogenic ones (LASV and LCMV), can bind RIG-i and reduce the generation of IFN (Fan et al. 2010). Here, we provide a unique finding: all known human arenavirus infections' Z proteins, but not those of nonpathogens, suppress RLRs by binding to RLRs and preventing RLR-MAVS interactions. The N-terminal domain (NTD) of pathogenic Z proteins has been identified as the key regulator of RLR binding and inhibition. When a pathogenic Z NTD is switched out for a nonpathogenic Pichinde virus (PICV) genome, viral proliferation in Vero cells is unaffected, but type I IFN responses are markedly suppressed, and viral replication in primary human macrophages is increased. Our study identifies a universal innate immune-system suppressive mechanism shared by all pathogenic arenaviruses, which may shed light on arenavirus pathogenesis.

3.1. SOURCES OF INFECTION

Common house mice serve as both the reservoir and the LCMV's primary rodent host. In persistently infected mice that fails to develop immune response again the virus during the intrauterine period leads to long lasting asymptomatic infection ad results in the shedding of large amount of virus in all body secretions and excretions like in nasal secretion, milk, semen, saliva, and urine (Blasdell et al. 2016).

Human beings exposed to infection through the exposure of mucosa to rodents dropping contaminated aerosols or through the direct contact with rodents just like in case of rodent bite or licking. Pets rodents also play a role in the spread of infection to humans. Many out breaks were directly linked with the exposure to PI pet hamsters (Kleinschmidt-DeMasters and Beckham 2015).

Except for vertical transmission from infected pregnant women to foetus and organ donation, there is no evidence of human-to-human transfer. When exposed to the bodily fluids of infected house mice (*Mus musculus*), which serve as the virus's natural reservoir, humans may get infected with LCMV (Zapata and Salvato 2013).

4. PATHOGENESIS

Rodents are the targets of LCMV, especially hamsters and common house mice. The virus gets entry into the human body through direct contact with rodents like licking or biting or indirectly by inhaling the virus that is present in rat excretions and secretions (Taniguchi et al. 2020). After the entry into the human body, the virus targets the endothelial and lymphatic cells and replicate there or settle down in lymphatic tissues like spleen or lymph nodes and further replicate there (Kleinschmidt-DeMasters and Beckham 2015).

In response to targeting macrophages and lymphatic cells body immune system leads to the activation of innate immune response and body makes interferons or pro inflammatory cytokines against the virus (Blasdell et al. 2016).
In viremia, virus spreads to multiple organs like liver, spleen, lungs, kidney but the main tropism is towards the cell of CNS, where they target almost all types of nervous cells including neurons or microglia (McCormick et al. 1986).
In immunocompetent patient's virus leads to an asymptomatic disease, while in the immunocompromised patients it may leads to serious outcomes. The main signs of the disease are due to body own immune response against the virus that may leads to inflammation or excessive tissue damage (Djavani et al. 2000). Natural killer or cytotoxic T lymphocytes are the main player that leads to the clearance of virus from the body but also affect body own tissues (Kleinschmidt-DeMasters and Beckham 2015).
In immunocompetent patient's virus just show flu like symptoms while in compromised patients leads to serious nervous signs like meningoencephalitis, encephalitis or aseptic meningitis or involvement of multiple organs of the body. In pregnant mother's virus can infect the fetus and play a role as a teratogen or may leads to abortion in first trimester. Signs and symptoms vary from a no serious flu like condition to seizures, blindness neurologic deficits, hepatitis, or hemorrhagic fever (Djavani et al. 2000).

4.1. EPIDEMIOLOGY OF LCMV

M. musculus and *Mus domesticus* are the natural and reservoir host of LCMV virus. Persistently infected mice (infected in the comb of mother) fail to develop immune resonse against LCMV and become a a-symptomatic, chronic carrier, and shed virus during whole life through natural secretions or excretions. Hamsters and pets' mice also work as a carrier of virus. Human-beings directly gets the infection from rodent bites or mucosal exposure of infected secretions of rodents. Large number of outbreaks of LCMV have been reported that are directly linked with the exposure of infected hamsters. As human-to-human transmission is not documented except through organ transplantation or through the uterus of infected dam.
Rodents are the targets of LCMV specially hamsters and common house mice. The virus get entry into the human body through the direct contact with rodents like licking or biting or indirectly through the inhalation of the virus present in the secretions and excretions of rodents.

4.2. LCMV PREVALENCE IN HUMANS

As the reservoir host for LCMV is distributed worldwide, the virus has been reported from worldwide, but due to lack of diagnostic facilities, some mild or asymptomatic infection, true picture remains un-known. In the 1950s virus has been detected about 8% of the patients suffering with neuroinvasive disease and these cases mostly reported in winter season when the interaction of rodents with human beings increased.
A study during the last decade shows that in Finland 5% of the cases suffering with neroinvasive disease were screened positive for the IgG of LCMV. In these studies, they noticed that the virus infect humans irrespective of gender, with the 5-10 years age group being infected more than any other. Additionally, 5.1% of cerebrospinal fluid (CSF) samples taken from individuals with neuroinvasive illness in southern Iraq (Nasiriyah region, 2012–2013) contained virus. On more investigation from the same area reveals the prevalence of the virus in neurologically infected or healthy individuals both. About 12.2% seroprevlance was recorded in healthy groups. A seroprevalence investigation was conducted in overall population that shows that up to 15% of population is infected with the virus.
Cases of LCMV were also reported from Argentina with2.3%, Canada with 4%, Albama with 5.1%, spain with 1.7% and in Argentina with the 3.3% of seroprevalance. Although limited data available on the

seropervalence of the virus in the pregnant women, 1.6% of pregnant women were found positive in Argentina and 3.9% Croatian women, but in both scenario IgM antibodies were not found suggwsting a history of past infection. According to studies, the number of instances among humans who had intimate contact with rats is greater. According to an Austrian study, 13% of the personnel at the Vienna Zoo were LCMV seropositive.

4.3. DIAGNOSTIC AIDS

We can isolate virus from the nasopharyngeal secretions and blood during the early stage of disease. There is a time restriction in finding virus form the nasopharyngeal secretions as the virus is present for a short period of time. We can detect the virus by growing the sample in different cell lines like vero cells, L-929 or BHK-21.
LCMV can also be detected by the inoculation of CSF or blood of infected individual into newborn mice, if it leads to development of convulsive disease during a short duration of a week is pathognomonic for the virus. For further confirmation RT-PCR or IFA can be performed on the brain of mice. By the help of RT-PCR viral RNA can be detected from the sample of blood or CSF fluid. Serological tests like IFA and EIA target immunoglobulin M and G, but these facilities are limited.
Congenitally infected children have a difficult time being diagnosed with LCMV since most newborns were free of the virus when they were born, making diagnosis difficult. In these circumstances, the mother and foetus' IgG and IgM titers should be evaluated.

4.4. THERAPY OF LCMV INFECTION

There are limited therapeutic options for LCMV in humans. In majority of the cases main line of treatment is symptomatic or the use of already available options for viral treatment. Ribavirin is among the first purposed anti-viral for LCMV infected patients. Ribavirin has a complex mechanism of action that directly leads to inhibition of virus growth by inhibiting inosine monophosphate dehydrogenase that will ultimately leads to the depletion of GTP, it’s an analogue of guanosine. Ribavirin also acts as immunomodulatory drugs that will help in differentiation of of native CD4 T-cells to helper T cells that increses the antiviral activity. Ribavirin can be given through oral or intravenous route to the patients.
In addition to ribavirin, favipravir that inhibit the growth of various RNA viruses by inhibiting the growth of RdRp, also being used to treat LCMV infected patients on trial basis. This drus is clinically approved by japnese government for the treatment of influenza infection or currently being used to treat the COVID patients. Lab trials on acute disseminated LCMV infected mice, shows excellent results of drug. In less severe cases of animals infected with LCMV, it leads to permanent inhibition of virus growth with complete protection from mortality.
Currently umifenovir is being used for the treatment of influenza infected patients, is also being studied for the treatment of covid-19. It works by inhibiting various lifecycle stages of the viruses by interacting with virion lipids or protein. Umifenovir, according to Herring et al. (2021), can reduce the proliferation of numerous arenaviruses, including LCMV, in vitro, opening the door for future use of this medication to treat LCMV-infected individuals.

5. VACCINE RESEARCH IN LCMV

Reverse genetically altered recombinant LCMV (rLCMV), in addition to serving as a significant research model in immunology, is a significant potential for the creation of vector-based vaccines. In immunosuppressed mice, who are deficient in a functioning type I IFN receptor, Krolik et al. (2021)

recently published the findings of a safety and effectiveness examination of a non-replicating rLCMV vector producing ovalbumin as a model antigen. When mice was immunised, this resulted in the development of multifunctional cytotoxic CD8+ T-cells and memory T-cells, which cleared the rLCMV-ovalbumin vector 7 days after vaccination (Krolik et al. 2021). Non-replicating rLCMV-based vectors appear to be a good choice for vaccine development due to the rLCMV viral vector's outstanding safety profile and retained effectiveness in immunocompromised animals.

Replicating LCMV-based vectors have been investigated as potential therapeutic cancer vaccines with the goal of eliciting antitumor T-cell mediated immunity and long-term tumour control. A novel vaccine called TT1-E7E6 was developed by Schmidt et al. (2020) using replicating attenuated LCMV that encoded a non-oncogenic form of the oncoproteins E7 and E6 of human papillomavirus type 16 (HPV-16). The mouse model used to evaluate TT1-E7E6 demonstrated vector clearance, induction of CD8+ T cells specific for HPV-16, and tumour reduction, indicating that the LCMV-based TT1-E7E6 vaccine would represent a great prospect for the immunotherapy of HPV-16-positive malignancies (Schmidt et al. 2020).

6. VACCINATION OF LCMV

6.1. APATHOGENIC ARENAVIRUSES AS LIVE VACCINES

With the introduction of the vaccinia virus for the prevention of smallpox or the 17D strain of the yellow fever virus, the use of live-attenuated strains or similar apathogenic viruses for immunisation has a long history (Riedel ; Frierson 2010). Both successfully target cellular adaptive immunity as well as a potent immune response that produces neutralising antibodies against the chemical (Wrammert et al. 2009).

6.2. REASSORTMENT OF LASV AND MOPV

Promising outcomes were obtained when a plaque-purified clone (ML29) was used as a LASV vaccination (Lukashevich et al. 2005). Only animals that had received the MOPV vaccine, which was likewise protective, did not exhibit a brief rise of liver enzymes in plasma following LASV exposure.

6.3. INACTIVATED OR DEAD VACCINES

After transiently transfecting expression plasmids into HEK-293T cells, virus-like particles comprising GP1, GP2, NP, and Z were created. ELISA was used to measure the binding antibodies that were elicited. In order to determine whether or not this strategy will be effective, further functional trials will be required (Branco et al. 2010).

6.4. MUCOSAL VACCINATION

Additionally, oral administration requires little to no physical exertion, making immunisation campaigns possible. To express LASV NP and LCMV NP, S. typhimurium and the vaccinia virus underwent genetic modification. Recombinant vector-injected mice displayed LASV NP-specific IgA and particularly reactive splenocytes, and the results were good (Djavani et al. 2000).

6.5. RECOMBINANT VIRUSES EXPRESSING ARENAVIRUS PROTEINS

Since the early 1980s, recombinant viral vectors have been in use. They are a great tool and have a number of benefits over other vaccination platforms when used as vaccine vectors for the expression of foreign antigens (Thummel et al. 1981; Mackett et al. 1992)

6.6. DNA VACCINE

Target genes can be expressed and delivered into the host using plasmid DNA to stimulate immunity. Plasmid DNA is taken up by antigen-presenting cells and other body cells, and the subsequent protein synthesis from the plasmid DNA results in the presentation of peptides encoded by the plasmid DNA by MHC I and II (Huygen 2005). In addition to their considerable work on LCMV, Whitton et al. have also studied the extremely pathogenic LASV. After giving mice plasmid DNA expressing LASV or LCMV NP, the immune response and protective capacity in response to LCMV or Pichinde virus (PICV) challenge were evaluated (Rodriguez-Carreno et al. 2005).

7. CONCLUSION

The lack of commercially accessible serologic tests has contributed to the fall in the percentage of meningitis cases attributable to LCMV, yet this virus continues to be a significant cause of meningitis in humans. However, there is little clinical interest in the condition, and LCMV hasn't been used very much. The discovery of fatal LCMV infections in multiple groups of solid organ transplant recipients who got organs from donors who passed away from causes that appeared to be unrelated to infection further demonstrated the pathogenic potential and clinical importance of this underappreciated human pathogen. LCMV should also be regarded as a developing teratogen in pregnancy. Obstetricians should be aware of the increasing role of LCMV as a TORCH agent that can affect maternal, foetal, and neonatal health even though only 82 cases of congenital LCMV infection have been documented so far.

REFERENCES

Anesi JA et al., 2019. Arenaviruses and West Nile virus in solid organ transplant recipients: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clinical Transplantation 33(9): e13576.

Aly GS et al., 2017. Congenital Viral Infections. Viral Infections in Children 1: 1-46.

Baker DG, 1998. Natural pathogens of laboratory mice, rats, and rabbits and their effects on research. Clinical Microbiology Reviews 11(2): 231-266.

Bonthius DJ, 2009. Lymphocytic choriomeningitis virus: a prenatal and postnatal threat. Advances in Pediatrics 56(1): 75-86.

Bonthius DJ, 2012. Lymphocytic choriomeningitis virus: an underrecognized cause of neurologic disease in the fetus, child and adult. Seminars in Pediatric Neurology 19(3): 89-95.

Blasdell KR et al., 2016. Evidence of human infection by a new mammarenavirus endemic to Southeastern Asia. Elife 5: e13135.

Branco LM et al., 2010. Lassa virus-like particles displaying all major immunological determinants as a vaccine candidate for Lassa hemorrhagic fever. Virology Journal 7(1): 1-19.

Buchmeier MJ, 2007. Arenaviridae: the viruses and their replication. Fields Virology 1792-1827.

Cornu TI and de la Torre JC, 2002. Characterization of the arenavirus RING finger Z protein regions required for Z-mediated inhibition of viral RNA synthesis. Journal of Virology 76(13): 6678-6688.

Djavani M et al., 2000. Murine immune responses to mucosally delivered Salmonella expressing Lassa fever virus nucleoprotein. Vaccine 18(15): 1543-1554.

Doherty PC et al., 1992. Roles of alphabeta and gammadelta T cell subsets in viral immunity. Annual Review of Immunology 10(1): 123-151.

Enria DA et al., 2008. Treatment of Argentine hemorrhagic fever. Antiviral Research 78(1): 132-139.

Fan L et al., 2010. Z proteins of New World arenaviruses bind RIG-I and interfere with type I interferon induction. Journal of Virology 84(4): 1785-1791.

Frierson JG, 2010. The yellow fever vaccine: a history. The Yale Journal of Biology and Medicine 83(2): 77.

Field KJ ad Sibold AL, 1998. The laboratory hamster and gerbil, CRC Press.
Gilbert-Barness E, 2010. Teratogenic causes of malformations. Annals of Clinical & Laboratory Science 40(2): 99-114.
Huygen K, 2005. Plasmid DNA vaccination. Microbes and Infection 7(5-6): 932-938.
Jamieson DJ et al., 2006. Lymphocytic choriomeningitis virus: an emerging obstetric pathogen? American Journal of Obstetrics and Gynecology 194(6): 1532-1536.
Kranzusch PJ and Whelan SPJ, 2011. Arenavirus Z protein controls viral RNA synthesis by locking a polymerase–promoter complex. Proceedings of the National Academy of Sciences 108(49): 19743-19748.
Krolik M et al., 2021. Recombinant lymphocytic choriomeningitis virus-based vaccine vector protects type I interferon receptor deficient mice from viral challenge. Vaccine 39(8): 1257-1264.
Kleinschmidt-DeMasters BK and Beckham JD, 2015. West Nile Virus Encephalitis 16 Years Later. Brain Pathology 25(5): 625-633.
Lukashevich IS et al., 2005. A live attenuated vaccine for Lassa fever made by reassortment of Lassa and Mopeia viruses. Journal of Virology 79(22): 13934-13942.
Lapošová K et al., 2013. Lymphocytic choriomeningitis virus: invisible but not innocent. Acta Virologica 57(2): 160-70.
Louten J, 2016. Virus transmission and epidemiology. Essential Human Virology 71.
Meerburg BG et al., 2009. Rodent-borne diseases and their risks for public health. Critical Reviews in Microbiology 35(3): 221-270.
Mätz-Rensing K and Bleyer M, 2019. Viral diseases of common marmosets. The Common Marmoset in Captivity and Biomedical Research 2019: 251-264.
MacNeil A et al., 2012. Solid organ transplant–associated lymphocytic choriomeningitis, United States, 2011. Emerging Infectious Diseases 18(8): 1256.
McNab F et al., 2015. Type I interferons in infectious disease. Nature Reviews Immunology 15(2): 87-103.
Mackett M et al., 1992. Vaccinia virus: a selectable eukaryotic cloning and expression vector. 1982. Biotechnology (Reading, Mass.) 24: 495-499.
McCormick JB et al., 1986. Lassa fever. New England Journal of Medicine 314(1): 20-26.
McCormick JB et al., 1987. A prospective study of the epidemiology and ecology of Lassa fever. Journal of Infectious Diseases 155(3): 437-444.
McLay L et al., 2013. Targeting virulence mechanisms for the prevention and therapy of arenaviral hemorrhagic fever. Antiviral Research 97(2): 81-92.
Mims CA, 1981. Vertical transmission of viruses. Microbiological Reviews 45(2): 267-286.
Neuman BW et al., 2005. Complementarity in the supramolecular design of arenaviruses and retroviruses revealed by electron cryomicroscopy and image analysis. Journal of Virology 79(6): 3822-3830.
Palacios G et al., 2008. A new arenavirus in a cluster of fatal transplant-associated diseases. New England Journal of Medicine 358(10): 991-998.
Perez M et al., 2003. The small RING finger protein Z drives arenavirus budding: implications for antiviral strategies. Proceedings of the National Academy of Sciences 100(22): 12978-12983.
Romero JR and Newland JG, 2003. Viral meningitis and encephalitis: traditional and emerging viral agents. Seminars in Pediatric Infectious Diseases 14(2): 72-82.
Riedel S, 2010. Edward Jenner and the history of smallpox and vaccinationp. In: Fleshman JW, editor. Baylor University medical center proceedings: Taylor and Francis; pp: 21-25
Rodriguez-Carreno MP et al., 2005. Evaluating the immunogenicity and protective efficacy of a DNA vaccine encoding Lassa virus nucleoprotein. Virology 335(1): 87-98.
Sarute N and Ross SR, 2021. The board is set, the pieces are moving: Modulation of New World arenavirus entry by host proteins. PLoS Pathogens 17(6): e1009605.
Salvato MS et al., 1992. Biochemical and immunological evidence that the 11 kDa zinc-binding protein of lymphocytic choriomeningitis virus is a structural component of the virus. Virus Research 22(3): 185-198.
Schmidt S et al., 2020. Live-attenuated lymphocytic choriomeningitis virus-based vaccines for active immunotherapy of HPV16-positive cancer. Oncoimmunology 9(1): 1809960.
Strecker T et al., 2003. Lassa virus Z protein is a matrix protein sufficient for the release of virus-like particles. Journal of Virology 77(19): 10700-10705.

Taniguchi S et al., 2020. Analysis of the function of the lymphocytic Choriomeningitis virus S segment untranslated region on growth capacity in vitro and on virulence in vivo. Viruses 12(8): 896.

Thummel C et al., 1981. Expression of SV40 T antigen under control of adenovirus promoters. Cell 23(3): 825-836.

Vilibic-Cavlek T et al., 2021. Lymphocytic Choriomeningitis—emerging trends of a neglected Virus: A narrative review. Tropical Medicine and Infectious Disease 6(2): 88.

Welsh RM et al., 1991. Natural killer (NK) cell response to virus infections in mice with severe combined immunodeficiency. The stimulation of NK cells and the NK cell-dependent control of virus infections occur independently of T and B cell function. The Journal of Experimental Medicine 173(5): 1053-1063.

Wrammert J et al., 2009. Human immune memory to yellow fever and smallpox vaccination. Journal of Clinical Immunology 29: 151-157.

Zapata JC and Salvato MS, 2013. Arenavirus variations due to host-specific adaptation. Viruses 5(1): 241-278.