Review Article

Journal of Advanced Veterinary Research
(2025) Volume 15, Issue 4, 535-546

Camelpox: The hidden threat to camel farming

M. Gandul A. Yuliani[1*], Aswin R. Khairullah[2], Nanik Hidayatik[1], Arindita N. Novianti[1], Bantari W.K. Wardhani[3], Ikechukwu B. Moses[4], Andi T. Khalisa[5], Sheila M. Yanestria[6], Dea Anita A. Kurniasih[7], Ima Fauziah[2], Kartika A. Fauzia[8], Muhammad K.J. Kusala[2], Syahputra Wibowo[9], Abdul H. Furqoni[10], Bima P. Pratama[11], Arif N.M. Ansori[12,13,14]

[1]*Division of Basic Veterinary Medicine, Faculty of Veterinary Medicine, Universitas Airlangga, Kampus C Mulyorejo, Jl. Dr. Ir. H. Soekarno, Surabaya, East Java, 60115, Indonesia.*
[2]*Research Center for Veterinary Science, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*
[3]*Research Center for Pharmaceutical Ingredients and Traditional Medicine, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*
[4]*Department of Applied Microbiology, Faculty of Science, Ebonyi State University, Abakaliki Rd, Abakaliki, Ebonyi, 481101, Nigeria.*
[5]*Faculty of Military Pharmacy, Universitas Pertahanan, Kawasan IPSC Sentul, Sukahati, Bogor, West Java, 16810, Indonesia.*
[6]*Laboratory of Veterinary Public Health, Faculty of Veterinary Medicine, Universitas Wijaya Kusuma Surabaya, Jl. Dukuh Kupang XXV No. 54, Surabaya, East Java, 60225, Indonesia.*
[7]*Research Center for Public Health and Nutrition, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*
[8]*Research Center for Preclinical and Clinical Medicine, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*
[9]*Eijkman Research Center for Molecular Biology, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*
[10]*Center for Biomedical Research, National Research and Innovation Agency (BRIN), Jl. Raya Bogor Km. 46 Cibinong, Bogor, West Java, 16911, Indonesia.*
[11]*Research Center for Process Technology, National Research and Innovation Agency (BRIN), KST BJ Habibie, Serpong, South Tangerang, Banten, 15314, Indonesia.*
[12]*Postgraduate School, Universitas Airlangga, Kampus B Dharmawangsa, Jl. Airlangga 4-6, Surabaya, East Java, 60286, Indonesia.*
[13]*Uttaranchal Institute of Pharmaceutical Sciences, Uttaranchal University, Chakrata Rd, Dehradun, Uttarakhand, 248007, India.*
[14]*Medical Biotechnology Research Group, Virtual Research Center for Bioinformatics and Biotechnology, Jl. Gunung Anyar Kidul No. 33, Surabaya, East Java, 60493, Indonesia.*

ARTICLE INFO

Recieved: 23 July 2025

Accepted: 27 August 2025

*Correspondence:

Corresponding author: M. Gandul Atik Yuliani
E-mail address: m-gandul-a-y@fkh.unair.ac.id

Keywords:

Camelpox, CMLV, Lesion, Public health, Virus.

ABSTRACT

Camelpox is an infectious disease brought on by the camelpox virus (CMLV), a member of the *Poxviridae* family's Orthopoxvirus (OPV) genus. In 1909, camelpox was initially identified in India. It is believed that CMLV only spontaneously infects camels from the Old World. Since camels are utilized for transportation, racing, nomadic herding, and the production of milk, wool, and meat, camelpox is found in camel-breeding regions of Africa, the Middle East, and Asia north of the equator. The skin is typically where CMLV enters the body. The virus travels to local lymph nodes after local replication and the development of primary cutaneous lesions, resulting in leukocyte-associated viremia, which may be accompanied by fever. Genes that control or circumvent host immune responses, host cell apoptosis, and cell or tissue tropism are found in the CMLV genome. Postmortem examination of camels that died of a severe camelpox illness revealed several smallpox-like lesions on the mouth, respiratory (particularly the trachea and lungs), and digestive tract mucous membranes. One to three days after the fever starts, skin lesions such as erythematous macules, papules, vesicles, pustules, and crusts from ruptured pustules start to show up. For the diagnosis of camelpox, transmission electron microscopy (TEM), cell culture isolation, conventional polymerase chain reaction (PCR) tests, immunohistochemistry, and the presence of neutralizing antibodies are some of the suggested tests. Three ways exist for CMLV to spread: direct contact, indirect contact, and insect vectors. As an alternative treatment, antiviral medications might be used, particularly for young camels. A preventative method to stop the spread of camelpox in enzootic nations is the camelpox vaccine.

Introduction

Camelpox is an infectious disease brought on by the camelpox virus (CMLV), a member of the *Poxviridae* family's Orthopoxvirus (OPV) genus (Balamurugan *et al*., 2013). Although human cases have also been documented, camels are the primary victims of this disease (Fashina *et al*., 2022). Enzootic transmission of camelpox occurs in nearly every camel-breeding zone, with the exception of Australia (Eckstein *et al*., 2022). In 1909, camelpox was initially detected in India; however, in 1972, a new strain of the camelpox virus was obtained and named orthopox virus (AL-Eitan *et al*., 2024). In 1975, reports of experimental infection and particular CMLV characteristics were published (Shchelkunova and Shchelkunov, 2022). Camelpox only affects camel farms, particularly in underdeveloped nations, and has a negative economic impact because it causes large losses in terms of camel weight loss, illness, death, and milk output (Balamurugan *et al*., 2013).

Most often affecting young camels between the ages of two and three, camelpox disease outbreaks in herds are frequently linked to weaning or inadequate nutrition, and in extreme cases, it can be lethal (Zhu *et al*., 2019). There are morbidity, mortality, and case fatality rates (CFR) of 30–90%, 1–15%, and 25%, respectively, associated with the disease (Prabhu *et al*., 2015). Animals that recover develop a lifetime immunity to reinfection. Camelpox is spread by direct contact with diseased animals, either via aerosols or skin abrasions (Bulatov *et al*., 2024). Water can become a source of infection when the virus is dispersed into the environment by the scabs, saliva, and secretions of sick camels (Narnaware *et al*., 2021).

Mild local infections to serious systemic infections are among the clinical symptoms. The symptoms of this illness include skin lesions, enlarged lymph nodes, and fever (Arog *et al*., 2024). Skin lesions start as erythematous macules, develop into papules and vesicles, and finally turn into pustules one to three days after the fever starts (Alkharusi *et al*., 2023). These lesions initially show up on the nose, earlobes, eyelids, and head. Skin lesions may later extend to the perineum, genitalia, mammary glands, neck, and limbs (Ayelet *et al*., 2013). Lesions from smallpox can spread throughout the body in its local form. Healing takes four to six weeks. The mucous membranes of the mouth, respiratory system, and digestive system are linked to smallpox lesions in the systemic form (Narnaware *et al*., 2021).

A differential diagnosis by laboratory testing is necessary since camelpox can be tentatively diagnosed based on clinical signs and smallpox lesions, but it will be mistaken for other viral disorders such infectious ecthyma (parapoxvirus) and papillomatosis (papillomavirus) (Aregawi and Feyissa, 2016). For the diagnosis of camelpox, a number of procedures are advised, including immunohistochemistry, conventional PCR assays, cell culture isolation, transmission electron microscopy (TEM), and the presence of neutralizing antibodies (Pfeffer *et al*., 1998a). Until recently, a CMLV-based vaccine was the only way to prevent camelpox, but this method was not commonly applied (Gieryńska *et al*., 2023). Treatment of diseased animals may also benefit from having access to antivirals (Dahiya *et al*., 2016).

Understanding camelpox is crucial for preventing financial losses in

ISSN: 2090-6277/2090-6269/

camel-farming regions as well as for managing the disease holistically and logistically to prevent its spread to neighboring areas (Duraffour *et al*., 2011a). Camels are prized as migratory animals that may be farmed, processed into animal feed, racehorses, milk, wool, and meat; therefore, the spread of camelpox among herds has a significant economic impact (Greger, 2007). The purpose of writing a review article on camelpox is to present the latest and comprehensive information about camelpox disease, including causes, symptoms, transmission, diagnosis, and prevention and control efforts.

Etiology

The epitheliotropic DNA virus is the cause of camelpox illness in camels (Joseph *et al*., 2021). This virus belongs to the family *Poxviridae* and the subfamily *Chordopoxvirinae* of the Orthopoxvirus (OPV) genus (Duraffour *et al*., 2011a). Brick-shaped virions are 265–295 nm in size and have an outer membrane made up of tubular proteins that are organized erratically (Bayisa, 2019). Numerous virus-encoded enzymes that are linked within the virion are carried by CMLV, which is replicated in the cytoplasm. CMLV is sensitive to chloroform and resistant to ether (Kandeel and Al-Mubarak, 2022). CMLV was heat resistant at 56°C for an hour and unaffected by pH values between 3 and 8.5, but after 30 minutes, its infectivity was eliminated at 70°C (Mambetaliyev *et al*., 2024).

The CMLV genome is made up of 211 putative genes and is a single linear double-stranded DNA molecule that is 205,719 bp long. The CMLV genome is made up of identical inverted terminal repeats that are about 7 kbp long and encircle the core region (Yousif and Al-Naeem, 2012). Despite having structural and functional similarities to other OPVs, the CMLV genome has a distinct 3 kbp region that codes for three ORFs (CMLV185, CMLV186, and CMLV187) that are not found in other OPVs (Afonso *et al*., 2002). The genes that encode proteins involved in host tropism, pathogenicity, or immunomodulation are changeable at the ends of the orthopoxvirus genome, whereas the genes in the middle are conserved (Gubser and Smith, 2002).

Nucleotide sequence study indicates that CMLV and variola virus (VARV) are most closely related. The protein that CMLV-CMSITR encodes is 650 bp from the minus end, just like the VARV (Gubser *et al*., 2007a). CMLV and VAR are 96.6–98.6% identical at the nucleotide level (Shchelkunov *et al*., 2000). Additionally, the DNA distance matrix revealed that CMLV and VAR had smaller genetic distances than CMLV and vaccinia virus (Gubser and Smith, 2002). CMLV is more closely related to VAR than to other viruses, as evidenced by the proportion of amino acid identity between CMLV and other poxviruses. The genome of camelpox contains a unique *Hind III* restriction map and is composed of 66.9% A + T (Gubser and Smith, 2002). There are currently over 45 known CMLV serotypes. Three of them, CMLV1, CMLV2, and CMLV-Hyd 06, are more prevalent in the Indian subcontinent, whereas serotypes 19 and 16 are more prevalent in the Middle East and Africa (Bhanuprakash *et al*., 2010a). These strains express themselves differently in different cells and in chicken eggs that have not yet developed, and they have varied physicochemical characteristics (Duraffour *et al*., 2011a).

Camelpox is a disease in camels caused by a DNA virus that exhibits epitheliotropic behavior (Joseph *et al*., 2021). This pathogen is classified under the *Poxviridae* family and specifically within the *Chordopoxvirinae* subfamily of the Orthopoxvirus genus (Duraffour *et al*., 2011a). The virus particles are brick-like in shape, measuring approximately 265–295 nanometers, and feature a disorganized outer membrane made of tubular proteins (Bayisa, 2019). Camelpox virus (CMLV) replicates in the cytoplasm and carries multiple enzymes within its structure. It is known to be chloroform-sensitive yet resistant to ether (Kandeel and Al-Mubarak, 2022). The virus withstands heat at 56°C for up to one hour and remains stable in pH levels ranging from 3 to 8.5; however, its infectivity is fully lost when exposed to 70°C for 30 minutes (Mambetaliyev *et al*., 2024).

CMLV's genome comprises a single, linear double-stranded DNA of 205,719 base pairs, containing 211 predicted genes. This genome includes symmetrical inverted terminal repeats of about 7 kilobases flanking a central core region (Yousif and Al-Naeem, 2012). Although it shares a conserved structure and function with other *Orthopoxviruses*, CMLV contains a distinct 3 kbp segment encoding three unique open reading frames (ORFs): CMLV185, CMLV186, and CMLV187, which are absent in related viruses (Afonso *et al*., 2002). While the central region of the genome holds conserved genes, those located near the termini are more variable and often associated with host range, virulence, or immune evasion mechanisms (Gubser and Smith, 2002).

Genomic analyses have demonstrated that CMLV is most closely related to the variola virus (VARV), with a specific encoded protein located 650 bp from the negative strand's end—a position also noted in VARV (Gubser *et al*., 2007a). The nucleotide sequence similarity between CMLV and VARV ranges from 96.6% to 98.6% (Shchelkunov *et al*., 2000). Furthermore, phylogenetic distance analysis confirms that CMLV is genetically closer to VARV than to the vaccinia virus (Gubser and Smith, 2002). The proportion of amino acid similarities further supports the close evolutionary link between CMLV and VARV. The camelpox genome is uniquely characterized by its *Hind III* restriction profile and exhibits a high A + T content of approximately 66.9% (Gubser and Smith, 2002). Presently, more than 45 CMLV serotypes have been identified. Among these, CMLV1, CMLV2, and CMLV-Hyd 06 are mainly observed in the Indian subcontinent, whereas serotypes 19 and 16 are predominantly found in Middle Eastern and African regions (Bhanuprakash *et al*., 2010a). These viral strains display distinct biological behavior depending on the host cells and embryonated chicken eggs they infect, with differing physical and chemical profiles (Duraffour *et al*., 2011a).

Virus Life Cycle

Poxviruses, in contrast to other DNA viruses, primarily rely on proteins encoded by the virus to replicate in the cytoplasm (Aryaloka *et al*., 2024). A model of the vaccinia virus in mammalian cells has been used to infer the majority of the knowledge on poxvirus replication (Pei *et al*., 2023). Mature virions can enter by merging with the host cell through interactions with the endosomal membrane or glycosaminoglycans on the cell surface (Villanueva *et al*., 2005). Poxviruses need 11–12 proteins for their post-attachment entrance, even though single-receptor-mediated absorption into cells has not been documented (Moss, 2012).

Extracellular enveloped virions (EEV/EV) are released when CMLV merges with the host cell membrane (Lorenzo *et al*., 2000). Poxvirus shedding starts with the release of lipids and proteins from the virion, which is followed by the loss of the core membrane (Kao *et al*., 2023). There have been reports of uncoating being inhibited by transcriptional or translational suppression, suggesting that uncoating requires either the protein encoded by the virus or the virus-induced protein (Najarro *et al*., 2001). The core of the virus, which contains DNA, enzymes encoded by the virus, and early transcription factors, enters the cytoplasm, where it caps and polyadenylates around half of the transcripts (Moss, 2013). DNA is made available for replication by virus-encoded DNA polymerase, thymidine kinase, and thymidylate kinase (Caillat *et al*., 2008).

Viral growth factors and complement-binding proteins, which are encoded by the Vaccinia virus, control its spread and, by binding to C4b, block the conventional complement pathway, respectively (Albarnaz *et al*., 2018). Poxvirus replication takes place at certain sites called viroplasms in the cytoplasm (Evans, 2022). Poxvirus-infected cells have a high rate of recombination, which propels the development and acquisition of advantageous traits that enable their growth and spread without endangering the host too soon (Yao and Evans, 2003). Classes of mRNA and intermediate and final protein synthesis come after DNA replication (Liu *et al*., 2018).

The virus is packaged and released either as an enveloped virion (WV) with a triple membrane or as a mature virion (MV) with a single ex-

terior membrane following the expression of its last genes (Moss, 2012). It is thought that EVs mediate dissemination within hosts, whereas MVs enhance spread between hosts (Beerli *et al*., 2019). Viral particles may leave by the Golgi apparatus or the microvilli, depending on the poxvirus and the affected cell (Perdiguero and Blasco, 2006). Poxviruses can obtain their envelope from vacuoles and exit the cell either by type-A inclusion bodies or non-membrane-bound vacuoles (Villanueva *et al*., 2005).

The 211 putative genes that CMLV encodes encode a variety of proteins with lengths ranging from 53 to 1869 amino acids. Proteins linked to the virion core, intracellular mature virus (IMV), enzymes involved in protein modification, DNA packaging, and the release of external enveloped virions (EEV) are among the proteins that CMLV expresses that are comparable to those of other *Orthopoxviruses* (Afonso *et al*., 2002).

Unlike most DNA viruses, poxviruses carry out replication primarily in the cytoplasm using their own viral-encoded proteins (Aryaloka *et al*., 2024). Much of the current understanding of poxvirus replication stems from research using the vaccinia virus as a model in mammalian systems (Pei *et al*., 2023). Entry of mature virions into host cells occurs through fusion with the host's endosomal membrane or interaction with glycosaminoglycans present on the cell surface (Villanueva *et al*., 2005). Although no single receptor has been definitively identified, poxviruses depend on 11 to 12 specific proteins to facilitate post-binding entry into the cell (Moss, 2012).

When camelpox virus (CMLV) fuses with the host plasma membrane, it results in the release of extracellular enveloped virions (EV or EEV) (Lorenzo *et al*., 2000). This process begins with the shedding of the virion's lipid and protein components, followed by disintegration of the core membrane (Kao *et al*., 2023). Inhibition of viral uncoating by blocking transcription or translation suggests that this stage necessitates either a virus-derived protein or one synthesized under viral influence (Najarro *et al*., 2001). Once uncoated, the viral core—containing genetic material, enzymes, and early transcription factors—enters the cytoplasm, where approximately half of its transcripts undergo capping and polyadenylation (Moss, 2013). DNA replication is facilitated by viral enzymes such as DNA polymerase, thymidine kinase, and thymidylate kinase (Caillat *et al*., 2008).

To support its proliferation and immune evasion, the Vaccinia virus encodes various proteins, including viral growth factors and proteins that bind complement components like C4b, thus inhibiting the classical complement pathway (Albarnaz *et al*., 2018). Poxvirus replication occurs in specialized cytoplasmic sites termed "viroplasms" (Evans, 2022). These viruses exhibit high recombination rates within host cells, which likely aid in adaptation and the development of favorable traits without causing rapid host mortality (Yao and Evans, 2003). Following DNA synthesis, intermediate and late stages of protein production are initiated, resulting in a complete set of viral proteins (Liu *et al*., 2018).

In the final stages, the virus is assembled and released as either a mature virion (MV) with a single membrane or as a wrapped virion (WV) enclosed in a triple membrane structure (Moss, 2012). MVs are believed to facilitate host-to-host transmission, while EVs are more involved in spreading within the host (Beerli *et al*., 2019). The route of egress can vary depending on the poxvirus species and host cell type, with viral particles exiting via microvilli or the Golgi apparatus (Perdiguero and Blasco, 2006). Poxviruses may derive their envelope from intracellular vacuoles and exit cells through inclusion bodies or vacuole-mediated mechanisms (Villanueva *et al*., 2005).

CMLV encodes 211 predicted genes that translate into a diverse set of proteins, ranging from 53 to 1869 amino acids in length. These include structural proteins of the virion core, components of the intracellular mature virus (IMV), enzymes for protein post-translational modification, DNA packaging machinery, and proteins involved in the release of external enveloped virions, many of which are homologous to proteins found in other *Orthopoxviruses* (Afonso *et al*., 2002).

History

In the early 1970s, camelpox gained a lot of attention, even though outbreaks had previously been documented, initially from India (Lesse, 1909). Since then, numerous nations have consistently reported cases of illness. The illness was long referred to as common camelpox, and in 1970 the causal virus (CMLV) was discovered for the first time by culture in chicken embryos (Sadykov, 1970). Then, in 1972, CMLV was also isolated in tissue culture (Ramyar and Hessami, 1972). CMLV was regarded as a "smallpox-like" member of the Orthopoxvirus genus in the late 1970s because of its resemblance to VARV in terms of serological cross-reactivity, limited host range, and culture features (Baxby, 1972; Baxby *et al*., 1975; Davies *et al*., 1975). Further evidence for the resemblance between CMLV and VARV comes from in vivo trials where an infectious dose of CMLV prevented attack on camels infected with the VARV EA8 strain (Baxby *et al*., 1975). Those working on the global smallpox eradication campaign were extremely concerned about this. Twenty years later, however, genome characterization investigations utilizing the HindIII enzyme and restriction fragment length polymorphism analysis verified that CMLV is a distinct member of the OPV genus (Pfeffer *et al*., 1996; Renner-Müller *et al*., 1995). Furthermore, the full genome sequence of CMLV strains shows that CMLV and VARV are most closely related. They may have a common ancestor and share several genes relevant to basic replication and host-associated functions (Afonso *et al*., 2002; Gubser *et al*., 2007a).

Host Range

One of the most prevalent infectious Orthopoxvirus (OPV) infections affecting both Old World (*Camellus dromedarius* and *C. bactrianus*) and New World camels is camelpox (Joseph *et al*., 2021). Whereas Old World camels are from Asia and Africa, New World camels are from South America (Burger *et al*., 2019). Camels from the New World include the vicuña, guanaco, alpaca, and llama (Khalafalla *et al*., 2024). It is believed that only Old World camels are naturally infected by CMLV (Haller *et al*., 2014). The host range of CMLV strains is generally quite small. The virus has not been successfully injected intradermally into guinea pigs, lambs, goats, and rabbits (Al-Bayati *et al*., 2022; Baky *et al*., 2006; Duraffour *et al*., 2011b; Mambetaliyev *et al*., 2024). Only infant rats and monkeys have been successfully infected, aside from camels (Baxby, 1974; Duraffour *et al*., 2011b). Sheep and cattle that come into close touch with infected camels stay healthy even in spontaneous infections, suggesting that CMLV is primarily host specific (Maikhin *et al*., 2023). However, chickens were able to develop local pox lesions due to the CMLV CP/Nw/92/2 isolate from Sudan (Khalafalla *et al*., 1998).

Epidemiology

Since camels are utilized for transportation, racing, nomadic herding, and the production of milk, wool, and meat, camelpox is found in camel-breeding regions of Africa, the Middle East, and Asia north of the equator (Balamurugan *et al*., 2013). CMLV infections are frequently detected in semidesert areas in herds that are migratory (Bulatov *et al*., 2024). The disease occurs in almost every country where camel farming is carried out, except the introduced dromedary camel in Australia and the tylopods (llamas and related species) in South America (Balamurugan *et al*., 2013). This illness was first documented in India's Punjab and Rajaputana, and subsequently in numerous other nations (Bhanuprakash *et al*., 2010b). The disease is endemic in Africa (Algeria (Renner-Müller *et al*., 1995), Egypt (Bassiouny *et al*., 2014), Kenya (Davies *et al*., 1975), Mauritania (Zhugunissov *et al*., 2021), Nigeria (Adedeji *et al*., 2018), Somalia (Kriz, 1982), Morocco, Ethiopia (Ayelet *et al*., 2013), Oman (Alkharusi *et al*., 2023), and Sudan (Khalafalla *et al*., 1998)), Asia (India (Bera *et al*., 2011), Afghanistan (Balamurugan *et al*., 2013), and Pakistan (Pfeffer *et al*., 1998a)), the Middle East (Iran (Mosadeghhesari *et al*., 2014), Iraq (Al-Baya-

ti *et al*., 2022), Saudi Arabia (Elzein *et al*., 1999), United Arab Emirates (UAE) (Joseph *et al*., 2021), and Yemen (Aregawi and Feyissa, 2016)), and the southern parts of the former Soviet Union. In two Syrian provinces, Hama and Duma, the first camelpox outbreak was recently documented (Al-Zi'abi *et al*., 2007). The geographical distribution of camel pox across Africa and Asia is depicted in Figure 1, highlighting regions identified as hotspots, areas experiencing virus reemergence, and countries reporting emerging zoonotic cases.

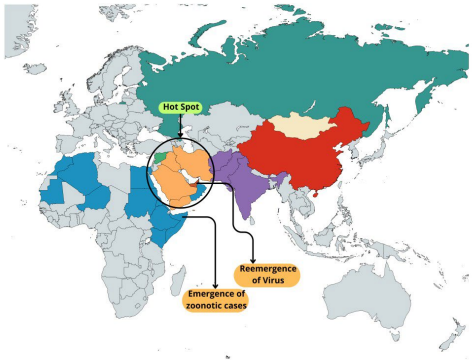

Figure 1. Geographical distribution of camelpox across Africa and Asia: Hotspot regions, reemergence zones, and areas with emerging zoonotic cases.

This disease is socio-economically significant as it causes huge losses in terms of morbidity, mortality, weight loss and reduced milk production (Prabhu *et al*., 2015). Young calves between the ages of two and three are typically affected by this disease in herds. Its severe lethal variant, known as the generalized type, can occasionally result in significant mortality because acquired immunity fades after five to eight months (Moussatché *et al*., 2008). Numerous studies have demonstrated that while lesser forms of camelpox occur during the dry season, more severe forms of the illness emerge during the rainy season, increasing the prevalence of outbreaks (Arog *et al*., 2024; Narnaware *et al*., 2021). Male camels had a greater incidence and case fatality rate (CFR) than female camels (Zhugunissov *et al*., 2021). Young animals have a mortality rate of 25–100%, while mature animals have a mortality rate of 10–28% (Tadesse *et al*., 2018). Additionally, the existence of coexisting illnesses (such trypanosomosis), stress, age, the animal's nutritional state, and virus virulence all affect mortality (Dahiya *et al*., 2016). Since camels migrate about to drink and graze, outbreaks are frequently short-lived and can lead to herd mixing and the introduction of new camels (Mohammadpour *et al*., 2020).

In a recent study of a CMLV outbreak in Eastern Saudi Arabia, live CMLV was found in AMPL homogenates, and 42.9% of convalescent camels (8.8% of the herd) had atypical tiny, pockmarked skin lesions (AMPL) for almost a year after the onset of clinical symptoms (Yousif and Al-Naeem, 2012). They got to the conclusion that a significant persistence mechanism in previously infected camel herds during the inter-epizootic period may be the modest and frequently overlooked AMPL in infected animals or the persistent survival of CMLV in skin lesions. There have also been reports of a high incidence of CMLV antibodies in camels. There is no chronic carrier status in recovered animals, and they are permanently resistant to reinfection (Dahiya *et al*., 2016). The prevailing CMLV strains, which differ in virulence, age, and sex can all affect the course and result of camelpox disease (Joseph *et al*., 2021). Therefore, the average age of the animals (4 years), the rainy season, the addition of new camels to the herd, and the same water supply are risk factors linked to a higher frequency of camelpox disease (Bulatov *et al*., 2024).

Camelpox predominantly affects regions across Africa, the Middle East, and parts of Asia situated north of the equator—areas where camels are widely used for purposes such as transportation, racing, nomadic herding, as well as for milk, wool, and meat production (Balamurugan *et al*., 2013). Infections caused by camelpox virus (CMLV) are commonly observed in migratory camel populations inhabiting semi-arid zones (Bulatov *et al*., 2024). This viral disease has been reported in nearly all countries with active camel husbandry, except for Australia-where dromedary camels are introduced species—and South America, where camelids like llamas are present but unaffected (Balamurugan *et al*., 2013). The initial documentation of camelpox emerged from the Punjab and Rajaputana regions in India and was later identified in various other nations (Bhanuprakash *et al*., 2010b). It is now considered endemic in several African nations including Algeria (Renner-Müller *et al*., 1995), Egypt (Bassiouny *et al*., 2014), Kenya (Davies *et al*., 1975), Mauritania (Zhugunissov *et al*., 2021), Nigeria (Adedeji *et al*., 2018), Somalia (Kriz, 1982), Morocco, Ethiopia (Ayelet *et al*., 2013), Oman (Alkharusi *et al*., 2023), and Sudan (Khalafalla *et al*., 1998). Endemicity also extends to countries in Asia such as India (Bera *et al*., 2011), Afghanistan (Balamurugan *et al*., 2013), and Pakistan (Pfeffer *et al*., 1998a), as well as the Middle East including Iran (Mosadeghhesari *et al*., 2014), Iraq (Al-Bayati *et al*., 2022), Saudi Arabia (Elzein *et al*., 1999), UAE (Joseph *et al*., 2021), and Yemen (Aregawi and Feyissa, 2016), and the southern territories of the former USSR. In Syria, camelpox was first confirmed in the provinces of Hama and Duma (Al-Zi'abi *et al*., 2007).

Economically, camelpox imposes significant burdens due to high morbidity and mortality rates, reduced weight, and a decline in milk productivity (Prabhu *et al*., 2015). Calves between two and three years of age are especially vulnerable. The more severe form, known as the generalized type, may lead to substantial fatalities, particularly because acquired immunity may only last for five to eight months (Moussatché *et al*., 2008). Studies have shown that while milder forms of the disease are more common during dry seasons, severe outbreaks tend to rise during rainy periods (Arog *et al*., 2024; Narnaware *et al*., 2021). Male camels are more frequently and severely affected compared to females (Zhugunissov *et al*., 2021). Young animals exhibit mortality rates ranging from 25% to 100%, while adults have lower, yet notable, rates of 10% to 28% (Tadesse *et al*., 2018). Additional risk factors influencing disease severity and fatality include co-infections (e.g., trypanosomosis), stress levels, age, nutritional status, and viral strain virulence (Dahiya *et al*., 2016). Because camels often move in search of water and pasture, outbreaks are typically brief but may lead to herd mixing and viral spread through the introduction of new animals (Mohammadpour *et al*., 2020).

A recent investigation in Eastern Saudi Arabia found that CMLV remained viable in AMPL (atypical minute pock-like lesion) homogenates. Approximately 42.9% of the convalescent camels (equivalent to 8.8% of the herd) displayed persistent skin lesions for up to a year post-infection (Yousif and Al-Naeem, 2012). The study suggested that these minor but persistent lesions may serve as a reservoir during inter-epidemic periods, maintaining viral circulation in herds. Although antibodies against CMLV are frequently detected, animals that recover do not become chronic carriers and develop lifelong immunity (Dahiya *et al*., 2016). Differences in virus strain, along with variables like age and sex of the host, influence the manifestation and outcome of infection (Joseph *et al*., 2021). Consequently, key risk factors associated with increased disease incidence include the average age of the camels (typically around four years), rainy weather, shared water sources, and the introduction of new animals into herds (Bulatov *et al*., 2024).

Pathogenesis

The skin is typically where CMLV enters the body. On the other hand, oro-nasal infections have also been documented (Balamurugan *et al*., 2013). The virus travels to local lymph nodes after local replication and the development of primary cutaneous lesions, resulting in leukocyte-associated viremia, which may be accompanied by fever (Obermeier *et al*., 2024). The virus can be isolated from a variety of tissues at this time, such as the skin, lungs, turbinates, and lymphoid organs (Bhanuprakash *et al*., 2010b). After a few days, widespread secondary skin lesions start to emerge, and fresh lesions keep popping up for two to three days before

the viremia goes away (Tadesse *et al*., 2018). One host species is afflicted by both CMLV and VARV, and the two viruses are distinct from one another. Human illness is uncommonly caused by CMLV. Similarly, whereas camels immunized with VARV are immune to CMLV infection in the future, VARV cannot infect camels (AL-Eitan *et al*., 2024). Additionally, it was discovered that when this virus was administered intradermally, it did not cause any harm to sheep, goats, rabbits, guinea pigs, rats, hamsters, or mice (Haller *et al*., 2014). Cattle, sheep, and goats are among the other animal species that are not infected by CMLV since it is host specific (Al-Zi'abi *et al*., 2007).

Since camelpox can result in serious illness, it is possible that CMLV will affect how the host reacts to the infection. Similar to other OPVs, CMLV encodes a number of genes that interfere with the host's response to interferon (IFN), key pro-inflammatory cytokines (such as interleukin-IL-1b, IL-18, and tumor necrosis factor (TNF), chemokines, and complement, hence inhibiting or influencing the host's antiviral immune response (Duraffour *et al*., 2011a). Numerous viral immune-disrupting techniques have been thoroughly examined (Perdiguero and Esteban, 2009). Genes that encode particular proteins found in CMLV have the ability to alter or circumvent host immunological responses, host cell apoptosis, and cell or tissue tropism. They are TNF receptor II crmB, complement binding protein, protein kinase inhibitor, chemokine binding protein, CD47-like protein, IL-1/Toll-like receptor inhibitor (Bowie *et al*., 2000), IFN inhibitor (Perdiguero and Esteban, 2009), IFN-c receptor (Balamurugan *et al*., 2013), IFN-a/b binding protein (Moss and Shisler, 2001), and signal transducer and activator of transcription (STAT) 1-inhibitor (Najarro *et al*., 2001). Similarly, CMLV encodes homologs of myxoma, rabbit fibroma, and vaccinia poxvirus proteins, which are known to affect host range or pathogenicity (Haller *et al*., 2014). Serpins that exhibit antifusion or antiapoptotic action and are implicated in inflammation are similar to the proteins encoded by open reading frames (ORFs) 31L, 188R, and 200R (Turner *et al*., 1995). ORFs 32L and 55L encode proteins that are comparable to the VAVC proteins K3L and E3L that mediate IFN resistance (Smith *et al*., 1998). Protein 6L may control apoptosis in CMLV-infected cells and shares a tight relationship with an unidentified human protein of the UPF0005 family (Duraffour *et al*., 2011b). The 201R protein binds to cell surface integrins by the action of a signal peptide called the RGD motif (Alcami *et al*., 1998). Soluble interferon gamma receptors (IFN-gR), which have broad species specificity and inhibit cytokine activity, are encoded by VARV, CPXV, and CMLV. This new characteristic of IFN-gR might facilitate the multispecies replication of all these OPVs (Alcami and Smith, 1995). It has recently been demonstrated that CMLV expresses a novel virulence factor, schlafen-like protein 176R-(v-slfn-57 kDa), and a novel protein that inhibits apoptosis, v-GAAP. These proteins are expressed both early and late in infection and are involved in regulating the pathogen's innate and adaptive immune responses (Gubser *et al*., 2007b). CMLV can modify or inhibit the host immune response in a number of ways. Through in vitro simulation of the in vivo environment, this mechanism has been clarified (Duraffour *et al*., 2011a).

The most common entry point for camelpox virus (CMLV) is through the skin, although infections via the oral and nasal routes have also been reported (Balamurugan *et al*., 2013). Following initial replication at the site of entry and formation of primary skin lesions, the virus moves to nearby lymph nodes, leading to leukocyte-associated viremia, which may present with fever (Obermeier *et al*., 2024). At this systemic stage, CMLV can be detected in multiple tissues including the lungs, nasal turbinates, skin, and lymphoid organs (Bhanuprakash *et al*., 2010b). A few days after the onset of primary symptoms, secondary skin eruptions become apparent and continue to appear for two to three days until the viremia subsides (Tadesse *et al*., 2018).

Despite similarities in host range with the variola virus (VARV), CMLV remains distinct. It rarely causes disease in humans, and while camels vaccinated with VARV exhibit immunity to CMLV, VARV itself cannot infect camels (AL-Eitan *et al*., 2024). Experimental studies indicate that CMLV introduced intradermally into other animals such as goats, sheep, rabbits, guinea pigs, rodents, and mice does not result in infection, reaffirming its high host specificity (Haller *et al*., 2014). Domestic livestock like cattle, sheep, and goats are not susceptible to the virus either (Al-Zi'abi *et al*., 2007).

Given the potential severity of camelpox, the virus can significantly affect host's immune function. Like other *Orthopoxviruses*, CMLV encodes numerous genes that interact with the host's immune mechanisms by modulating responses to interferons (IFNs), inflammatory cytokines (such as IL-1β, IL-18, and TNF), chemokines, and the complement cascade, ultimately disrupting antiviral defenses (Duraffour *et al*., 2011a). A wide range of viral immune evasion strategies has been documented (Perdiguero and Esteban, 2009). Several specific proteins encoded by CMLV are responsible for inhibiting immune responses, regulating apoptosis, and defining tissue or host specificity. These include tumor necrosis factor receptor II crmB, complement-regulating proteins, inhibitors of protein kinases and chemokines, CD47-like proteins, Toll-like receptor antagonists, and various IFN inhibitors (Bowie *et al*., 2000; Perdiguero and Esteban, 2009; Balamurugan *et al*., 2013; Moss and Shisler, 2001; Najarro *et al*., 2001).

Additionally, CMLV contains gene homologs similar to those found in myxoma, rabbit fibroma, and vaccinia viruses, which influence host range and virulence (Haller *et al*., 2014). It also produces serpin proteins involved in inflammation and cell survival, such as those encoded by ORFs 31L, 188R, and 200R (Turner *et al*., 1995). The viral genes ORFs 32L and 55L encode proteins that mimic vaccinia K3L and E3L, both of which counteract IFN-mediated responses (Smith *et al*., 1998). Another CMLV protein, 6L, appears to regulate apoptosis and shares similarity with an uncharacterized human UPF0005 protein (Duraffour *et al*., 2011b). The 201R protein uses an RGD motif to bind host cell integrins, enhancing viral entry (Alcami *et al*., 1998).

Furthermore, CMLV, along with other *Orthopoxviruses* like VARV and CPXV, encodes soluble IFN-γ receptors (IFN-gR), which can block cytokine signaling across species, possibly supporting cross-species infectivity (Alcami and Smith, 1995). Recently, two novel immunomodulatory proteins were identified in CMLV: the schlafen-like protein 176R (v-slfn, ~57 kDa) and the apoptosis inhibitor v-GAAP. These proteins are expressed in both early and late stages of infection and contribute to modulating host immune responses (Gubser *et al*., 2007b). Laboratory simulations have helped elucidate how CMLV suppresses innate and adaptive immune pathways, mirroring in vivo infection dynamics (Duraffour *et al*., 2011a).

Immune Response

The genes in the CMLV genome control or circumvent host cell apoptosis, cell or tissue tropism, and host immunological responses (Taylor and Barry, 2006). A number of viral proteins, such as the 35-kDa chemokine-binding protein homolog, complement-binding protein, TNF-II crmB, dsRNA-dependent protein kinase inhibitor, IL-1/Toll-like receptor inhibitor, IFN-g receptor, serine proteinase inhibitor, CD47-like protein, Stat1 inhibitor, and IFN-a/b binding protein, are implicated immune evasion (Najarro *et al*., 2001; Bowie *et al*., 2000; Moss and Shisler, 2001). Likewise, CMLV encodes poxviral protein homologs that affect host range or viral pathogenicity. These include the myxoma viral virulence protein M-T4, a homolog of the rabbit fibroma virus N1R protein, the ectromelia virus host range factor p28, and homologs of the VACV host range proteins C7L, N1L, and A14.5L virulence proteins (Barry *et al*., 1997; Betakova *et al*., 2000; Kotwal *et al*., 1989; Perkus *et al*., 1990; Senkevich *et al*., 1995). In addition, CMLV encodes a special set of 12 ankyrin repeat proteins linked to the virus's host range and defense against infection-induced death (Mossman *et al*., 1996). CMLV006, which is unique to CMLV and cowpox virus (CPXV), is thought to behave as a glutamate-binding subunit that can generate l-glutamate-activated ion channels of cellular NMDA receptors (Bhanuprakash *et al*., 2010a). It is a homologue of human CPXV S1R

and CGI-119. Some CMLV ORFs linked to virulence and host range may or may not encode functional proteins because of the development of fragmented or truncated genes. Among the ORFs are the VACV K1L host range protein, semaphorin-like proteins, guanylate kinase, the VACV B7R virulence protein, the TNF-R crmE homologous area, and many portions of the VACV B16R IL-1 binding protein (Afonso *et al*., 2002).

CMLV ORFs like 181R, 196R, 1L/206R, and 2L/205R are believed to encode soluble proteins that bind TNF, CC chemokines, IFN-g, and IFN-a/b (Alcam *et al*., 1999; Alcami and Smith, 1995; Alcami *et al*., 1998; Symons *et al*., 1995). Furthermore, proteins that are very similar to VACV epidermal growth factor and soluble complement inhibitor are encoded by ORFs 11R and 23L (Blomquist *et al*., 1984; Kotwal *et al*., 1990). Serpins with antifusion or antiapoptotic properties are similar to the proteins encoded by ORF 31L, 188R, and 200R (Turner *et al*., 1995). ORFs 32L and 55L encode proteins that are comparable to the VAVC proteins K3L and E3L that mediate IFN resistance (Smith *et al*., 1998). Furthermore, it has been suggested that ORFs 201R, 176R, and 6L may have host range or immunomodulatory roles (Gubser and Smith, 2002). The 6L protein may control apoptosis in CMLV-infected cells and shares strong kinship with human proteins of the UPF0005 family, mouse glutamate-binding proteins, and the antiapoptotic integral membrane protein family Bax inhibitor-1 (BI-1) (Kawai *et al*., 1999; Kumar *et al*., 1991; Walter *et al*., 1995; Xu and Reed, 1998). The 57 kDa cytoplasmic Schlafen-like protein (slfn) (v-slfn), which is related to the murine Schlafen protein (m-slfn) and helps regulate both innate and adaptive immune responses to infections, is linked to virulence and anti-host immunity in the undisturbed CMLV 176R gene (Eskra *et al*., 2003; Geserick *et al*., 2004; Shchelkunov *et al*., 1998; Schwarz *et al*., 1998). ORF 201R facilitates the binding of a secreted protein to cell surface integrins, which allows the protein to connect with either infected or uninfected cells. The protein shares amino acid similarities with the OPXV TNF receptors CrmB and CrmD (Alcami *et al*., 1998). The soluble IFN-g receptor (IFN-g R), which is encoded by VACV, CPXV, and CMLV, is another significant host immune evasion mechanism created by OPXV. By blocking interaction with cellular receptors and consequent host-induced antiviral effects, this receptor counteracts the activity of IFN-g cytokines with broad species specificity (Alcami and Smith, 1995).

Several genes encoded within the camelpox virus (CMLV) genome play vital roles in modulating or bypassing host cell apoptosis, determining tissue or cell specificity (tropism), and suppressing immune system responses (Taylor and Barry, 2006). Various viral proteins are implicated in immune evasion strategies, including homologs of chemokine-binding proteins (35 kDa), complement regulatory proteins, TNF receptor type II (crmB), inhibitors of double-stranded RNA-dependent protein kinases, Toll/IL-1 receptor blockers, interferon gamma (IFN-γ) and alpha/beta (IFN-α/β) binding proteins, STAT1 inhibitors, and proteins resembling CD47 and serine protease inhibitors (Najarro *et al*., 2001; Bowie *et al*., 2000; Moss and Shisler, 2001). Moreover, CMLV produces orthologs of poxviral proteins known to influence host specificity or viral virulence. These include analogs of the myxoma virus M-T4 protein, the rabbit fibroma virus N1R protein, ectromelia virus host range factor p28, and several vaccinia virus proteins such as C7L, N1L, and A14.5L (Barry *et al*., 1997; Betakova *et al*., 2000; Kotwal *et al*., 1989; Perkus *et al*., 1990; Senkevich *et al*., 1995).

CMLV also encodes a distinctive set of 12 ankyrin repeat proteins associated with its ability to expand host range and avoid cell death due to infection (Mossman *et al*., 1996). Among its unique features is the CMLV006 gene, which is shared with cowpox virus (CPXV) and potentially functions as a glutamate-binding subunit capable of generating NMDA-like ion channels. This gene shares homology with human S1R and CGI-119 proteins (Bhanuprakash *et al*., 2010a). Some genes related to host range and virulence appear as fragmented or truncated open reading frames (ORFs), raising questions about their protein-coding potential. These include orthologs to VACV genes such as K1L (host range protein), semaphorin-like proteins, guanylate kinase, virulence gene B7R, TNF-R homolog crmE, and parts of the IL-1 binding protein B16R (Afonso *et al*., 2002).

Specific ORFs—181R, 196R, 1L/206R, and 2L/205R—are predicted to encode soluble proteins that interact with key immune mediators like TNF, CC-chemokines, IFN-γ, and IFN-α/β (Alcam *et al*., 1999; Alcami and Smith, 1995; Alcami *et al*., 1998; Symons *et al*., 1995). Additionally, ORFs such as 11R and 23L are believed to encode proteins closely resembling the VACV epidermal growth factor and complement regulatory proteins (Blomquist *et al*., 1984; Kotwal *et al*., 1990). Proteins expressed from ORFs 31L, 188R, and 200R are classified as serpins and contribute to antiapoptotic and antifusion processes during infection (Turner *et al*., 1995). Similarly, proteins from ORFs 32L and 55L resemble the VACV proteins K3L and E3L, which help the virus resist interferon-mediated antiviral mechanisms (Smith *et al*., 1998).

ORFs 201R, 176R, and 6L may influence host range and immune modulation (Gubser and Smith, 2002). The protein expressed from gene 6L has potential antiapoptotic activity and demonstrates structural similarities with human UPF0005 proteins, mouse glutamate-binding proteins, and Bax inhibitor-1 (BI-1), a known antiapoptotic transmembrane protein (Kawai *et al*., 1999; Kumar *et al*., 1991; Walter *et al*., 1995; Xu and Reed, 1998). The CMLV gene 176R encodes a ~57 kDa cytoplasmic schlafen-like protein (v-slfn) that plays a dual role in modulating both innate and adaptive immune responses. It shares similarities with the murine schlafen (m-slfn) gene and is considered crucial to CMLV virulence and immune evasion (Eskra *et al*., 2003; Geserick *et al*., 2004; Shchelkunov *et al*., 1998; Schwarz *et al*., 1998).

The product of ORF 201R, a secreted protein that binds cell surface integrins, enables interactions with both infected and uninfected host cells. This protein has sequence similarity to the OPXV TNF receptor analogs CrmB and CrmD (Alcami *et al*., 1998). Another important immune evasion strategy employed by CMLV—also seen in VACV and CPXV—is the expression of a soluble IFN-γ receptor (IFN-γR). This protein blocks host IFN-γ cytokines by preventing their binding to cellular receptors, thereby dampening the host antiviral response across various species (Alcami and Smith, 1995).

Pathology

There is little information available on camelpox pathology. On postmortem examination, several smallpox-like lesions were seen on the mucous membranes of the mouth, respiratory tract (particularly the trachea and lungs), and digestive tract of camels that had died from a severe camelpox infection (Narnaware *et al*., 2021). Lesions in the lungs can range in size from 0.5 to 1.3 cm in diameter, and occasionally they can be as large as 4-5 cm (Bhanuprakash *et al*., 2010a). The lung surface may have a central hemorrhagic center in smaller lesions. Furthermore, the deadly variant of camelpox infection has also been linked to liver and heart illnesses (Pfeffer *et al*., 1998a).

Histopathology of skin lesions reveals classic vacuolization, cytoplasmic swelling, and keratinocyte enlargement of the epidermis' outer stratum spinosum (Al-Bayati *et al*., 2022). These cells rupture, causing vesicles and local edema linked to neutrophil, eosinophil, and mononuclear cell perivascular binding (Alkharusi *et al*., 2023). The borders of cutaneous lesions may also exhibit significant epithelial hyperplasia (Obermeier *et al*., 2024). Typically, lung diseases are characterized by hydropic degeneration, fibrosis and necrosis, which obliterate the normal architecture, and proliferation of bronchial epithelial cells linked to proliferative alveolitis, and bronchiolitis invaded by macrophages (Kinne *et al*., 1998).

Clinical Symptoms

The illness is typified by 9–13 days incubation phase during which the temperature rises initially, followed by skin lesions, swollen lymph nodes, and prostrations (Alkharusi *et al*., 2023). Depending on the type of

CMLV causing the infection, camelpox might present with moderate local symptoms or severe systemic disease (Arog *et al*., 2024). All phases of lesion development, including the formation of macules, pustules, vesicles, scabs, and papules on the labia, are present in a normal skin lesion or rash (Bhanuprakash *et al*., 2010a). One to three days after the fever starts, skin lesions such as erythematous macules, papules, vesicles, pustules, and crusts from ruptured pustules start to show up (Kachhawaha *et al*., 2014). Lesions often heal in 4–6 weeks. Although skin lesions are often confined, they can occasionally spread to other areas of the body. The latter type is frequently observed in herds of young animals that are 2-3 years old and are linked to poor nutrition and weaning (Dahiya *et al*., 2016). The eruption primarily affects the mucous membranes of the mouth, nose, and eyelids, as well as the head, nostrils, and ear margins. The lesions may later spread to the genitalia, legs, neck, scrotum, perineum, and mammary glands (Al-Zi'abi *et al*., 2007). The prognosis is more likely to be fatal in the generalized form, where the lesions may spread throughout the body, particularly on the head and limbs, with sporadic swelling in the neck and abdomen. Some lesions that resemble smallpox may also appear on the mucous membranes of the mouth, respiratory, and digestive tracts (Al-Salihi, 2018). Animals that are affected may show signs of diarrhea, mucopurulent nasal discharge, lacrimation, anorexia, and salivation (Aregawi and Feyissa, 2016). Septicemia brought on by secondary bacterial infections like Staphylococcus aureus can induce miscarriages in pregnant animals as well as death in those animals (Balamurugan *et al*., 2013). Camels with severe disease also develop proliferative poxvirus lesions in the bronchi and lungs, unlike smallpox, which mainly causes pustules on the skin and squamous epithelium of the oropharynx (Kinne *et al*., 1998).

Camelpox infection generally follows an incubation period of 9 to 13 days, beginning with a febrile phase, followed by cutaneous eruptions, enlargement of lymph nodes, and sometimes extreme fatigue (Alkharusi *et al*., 2023). The clinical severity of the disease varies depending on the CMLV strain, ranging from mild localized infections to serious systemic conditions (Arog *et al*., 2024). The cutaneous manifestations typically progress through all lesion stages—macules, papules, vesicles, pustules, crusts, and scabs—which may initially appear on the lips and genital areas (Bhanuprakash *et al*., 2010a). Around one to three days after fever onset, erythematous macules begin to appear, followed by progressive development into papules and pustules, and eventually forming crusts as pustules rupture (Kachhawaha *et al*., 2014). Healing usually occurs within four to six weeks.

While the majority of skin lesions remain localized, in some cases—especially among young, poorly nourished, or recently weaned animals—lesions may disseminate more extensively (Dahiya *et al*., 2016). Common sites of lesion development include mucous membranes of the mouth, nasal cavity, eyelids, and peripheral regions such as the head, nostrils, and ears. Further progression may involve the genitalia, legs, neck, scrotum, perineum, and mammary tissue (Al-Zi'abi *et al*., 2007). The generalized form, characterized by widespread lesions, is more frequently fatal and often involves swelling of the neck and abdomen. Occasionally, lesions resembling smallpox may occur in the respiratory or digestive tracts (Al-Salihi, 2018). Clinical signs can also include diarrhea, nasal discharge, eye tearing, inappetence, and excessive salivation (Aregawi and Feyissa, 2016). Secondary infections, particularly by Staphylococcus aureus, may cause septicemia, fetal loss in pregnant camels, or death (Balamurugan *et al*., 2013). In severe cases, proliferative poxvirus lesions are also found in the bronchi and lungs, unlike smallpox, which is usually restricted to the skin and oral mucosa (Kinne *et al*., 1998).

Diagnosis

Tissue samples (skin or organ biopsy) are most helpful in determining the infectious agent after clinical symptoms of the disease have appeared (Duraffour *et al*., 2011a). A differential diagnosis may be required since camelpox in camels can be mistaken for other viral illnesses such infectious ecthyma (parapoxvirus) and papillomatosis (papillomavirus) (Essbauer *et al*., 2010). The diagnosis of camelpox is frequently made using cellular and molecular assays, pathological findings, and clinical indicators. For the diagnosis of camelpox, five complimentary methods could be proposed: immunohistochemistry, conventional PCR assays, cell culture isolation, transmission electron microscopy (TEM), and the demonstration of neutralizing antibodies. A thorough explanation of sample preparation, storage, and test procedures has already been published for each of these methods (Pfeffer *et al*., 1998a; Elliot and Tuppurainen, 2008). TEM is a quick and accurate way to show that OPV is present in tissue samples or scabs, although it needs comparatively large virus concentrations in the sample (Gelderblom and Madeley, 2018). This method makes it possible to distinguish between the brick-shaped OPV and the egg-shaped parapoxvirus (Ayelet *et al*., 2013). It is important to treat tissue samples that are appropriate for TEM as stated (Elliot and Tuppurainen, 2008).

Virus isolation in cell culture should be started in accordance with TEM. It is possible to infect cell cultures using homogenized blood, serum, and tissue materials (Aregawi and Feyissa, 2016). Cultures should be observed for ten to twelve days. However, cytopathic consequences, such as the development of multinucleated syncytia, may manifest as early as one day after infection, contingent on the viral concentration. Although CMLV development can also be achieved across the chorioallantoic membrane (CAM), it is crucial to keep in mind that the pitting generated by VARV and CMLV in this system is identical (Baxby, 1972). TEM, PCR, or sequencing must be used to determine that the causal agent is CMLV (Elliot and Tuppurainen, 2008).

Numerous commercial kits are available for the extraction of DNA from clinical materials and cell culture samples. CMLV DNA may now be extracted from skin samples using a two-step extraction process that is both dependable and reasonably priced (Yousif *et al*., 2010). CMLV can be detected by PCR assays that look for sequences encoding DNA polymerase (DNA pol), hemagglutinin (HA), ankyrin repeat protein (C18L), or type A inclusion bodies (ATI) (Khalafalla *et al*., 2015). ATI gene-based PCR was carried out using a set of primers that produce amplicons of varying sizes, enabling OPV species differentiation. The viral species can subsequently be identified with certainty thanks to a further step that involves restriction digestion using BglII or XbaI (Meyer *et al*., 1994). Although OPV species can be distinguished using restriction fragment length polymorphism (RFLP) of HA-PCR TaqI amplicons, species-specific primers in the OPV HA open reading frame have also been identified (Ropp *et al*., 1995). Recently, C18L single-plex and C18L duplex DNA pol PCR were created to distinguish CMLV from other OPVs, capripoxviruses, and parapoxviruses (Balamurugan *et al*., 2009). One benefit of this test is that it does not require the extra step of restriction analysis. SYBR Green quantitative PCR was used by the same authors, but only to measure CMLV and assess the effectiveness of the traditional single-plex or duplex PCR described above. There is currently no known real-time quantitative PCR method for the precise diagnosis of CMLV.

Diagnosis is most reliable when tissue biopsies from lesions or internal organs are analyzed after the appearance of clinical symptoms (Duraffour *et al*., 2011a). Because camelpox shares similar symptoms with other viral skin diseases—such as contagious ecthyma (parapoxvirus) and papillomatosis (papillomavirus)—differential diagnosis is necessary (Essbauer *et al*., 2010). Clinical observation, supported by histopathology and molecular tests, is typically used to confirm CMLV infection. Five primary diagnostic methods are commonly employed: immunohistochemistry, conventional PCR, virus isolation in cell culture, transmission electron microscopy (TEM), and serological detection of neutralizing antibodies. Detailed protocols for sample handling and assay execution have been published (Pfeffer *et al*., 1998a; Elliot and Tuppurainen, 2008).

TEM is a rapid and reliable tool to identify orthopoxvirus morphology in lesion material, although it requires high viral concentrations for effective detection (Gelderblom and Madeley, 2018). The technique is partic-

ularly useful for distinguishing the brick-like structure of *Orthopoxviruses* from the ovoid form of parapoxviruses (Ayelet *et al.*, 2013). Specimen handling for TEM must follow strict guidelines (Elliot and Tuppurainen, 2008).

Virus isolation should follow the initial detection of viral particles by TEM. Blood, serum, or organ suspensions can be used to infect cell lines, which are monitored over a 10–12 day period. Cytopathic effects—such as syncytium formation—may appear as early as the first day, depending on viral load (Aregawi and Feyissa, 2016). Although virus propagation using the chorioallantoic membrane (CAM) is possible, CMLV and VARV produce similar lesion patterns, necessitating confirmatory testing via PCR or sequencing (Baxby, 1972; Elliot and Tuppurainen, 2008).

Several commercial kits are available to extract viral DNA from clinical or cultured samples. A reliable, cost-effective two-step extraction method has been established for skin samples (Yousif *et al.*, 2010). Molecular detection of CMLV commonly targets specific gene regions such as DNA polymerase (DNA pol), hemagglutinin (HA), ankyrin repeat protein (C18L), and type A inclusion body (ATI) genes (Khalafalla *et al.*, 2015). PCR targeting the ATI gene produces amplicons of distinct sizes, enabling identification of different *Orthopoxviruses*. The use of restriction enzymes such as BglII or XbaI further aids in species confirmation (Meyer *et al.*, 1994). Additional tools like RFLP analysis of HA-PCR products using TaqI and species-specific primers have also been validated (Ropp *et al.*, 1995).

To improve specificity and avoid restriction digestion steps, newer assays such as C18L single-plex and duplex PCRs have been developed, capable of distinguishing CMLV from capripoxviruses and parapoxviruses (Balamurugan *et al.*, 2009). While SYBR Green-based real-time PCR has been used for relative quantification, a standardized real-time PCR protocol for specific CMLV detection is not yet available.

Transmission

Three primary routes exist for CMLV to spread: direct contact, indirect contact, and insect vectors. Figure 2 illustrates the major pathways involved in the transmission of CMLV among camels and its zoonotic potential to humans. Contact with ill animals can result in direct virus transmission through skin abrasion or inhalation (Fashina *et al.*, 2022). Camels contract the disease indirectly when they come into contact with a contaminated environment (Gieryńska *et al.*, 2023). The virus is released into the environment by infected camels through scab material and secretions such milk, saliva, and secretions from the eyes and nose (Arog *et al.*, 2024). Dried scabs contain virus particles that can contaminate the environment for up to four months (Elliot and Tuppurainen, 2008). Subsequently, susceptible animals can contract the virus from the contaminated environment (Diaz, 2021). There have also been suspicions of disease spread through arthropod vectors.

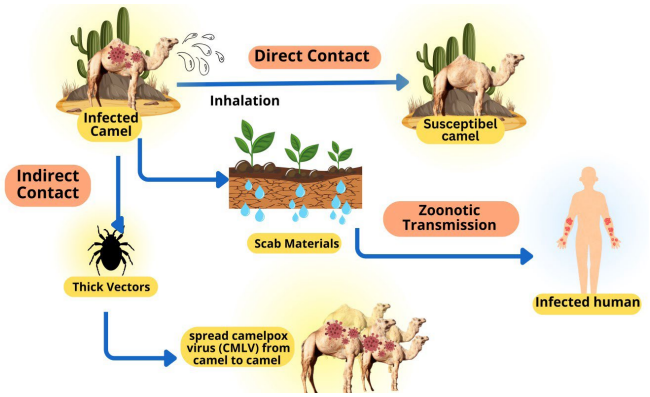

Figure 2. Transmission pathways of camelpox virus: role of direct contact, indirect vectors, and zoonotic spillover.

Camel ticks (*Hyalomma dromedarii*) collected from animals infected with common camelpox have been found to harbor CMLV (Bulatov *et al.*, 2024). Therefore, it is believed that ticks could contribute to the disease transmission between camels. The results of research that demonstrate that the incidence of camelpox infection rises right after intense rains, when the camel louse population also rapidly grows, lend further credence to this notion (Wernery *et al.*, 1997). However, it is currently unknown if ticks spread disease mechanically or physiologically. The role of arthropods in CMLV transmission requires more investigation.

Conclusive evidence of CMLV transmission to non-natural hosts, including humans, was also obtained from Sudan in 2014 and India in 2009 (Bera *et al.*, 2011; Khalafalla and Abdelazim, 2017). In Sudan, camel herders had lesions on their arms, hands, feet, back, and abdomen, while in India, camel herders had skin diseases limited to their hands and fingers. No additional instances have been confirmed, despite the fact that there have been a number of human cases linked to camelpox infection in the past (Khalafalla, 2023). It is believed that direct contact between sick camels and those who manage them is how CMLV is spread to people.

Risk Factors

Outbreaks of camelpox in susceptible camel populations around the world are caused by a number of risk factors. New animals being added to the herd, sharing water, coming into touch with the same animal handler, the age of the animals (the prevalence is higher in animals under 4 years old), and the rainy season are the main risk factors for disease infections (Khalafalla and Ali, 2007). Moreover, disease transmission is aided by the migration of animal herds. The disease is mainly spread by direct contact between susceptible animals and sick animals or indirectly through a polluted environment (Narnaware *et al.*, 2021). Usually, skin abrasions or aerosols inhaled through the respiratory system cause infection (Wernery and Kaaden, 2002). Animals that are fed prickly plants may develop skin abrasions, which make it easier for viruses to enter and cause infection (Al-Bayati *et al.*, 2022). Furthermore, immunological immaturity in young animals, inadequate nutrition, and a lack of maternal antibodies lead to increased infection and mortality rates (Zhu *et al.*, 2019). The virus is said to spread to the majority of bodily secretions, including milk, saliva, and secretions from the nose and eyes, after first proliferating locally (Gubser and Smith, 2002). Scab-containing habitats are especially dangerous for animals which are sensitive since the virus can survive in dried scabs for at least four months (Bera *et al.*, 2011). There is a seasonal tendency to this disease, with a higher occurrence during the rainy season. This could be due to increased activity of the arthropod vectors that carry the sickness (Balamurugan *et al.*, 2013). This assertion is further supported by the isolation of CMLV from the tick *Hyalomma dromedarii* (Pfeffer *et al.*, 1998a). CMLV has a narrow host range, and while antibodies to the virus have been found in sheep (6%) and goats (10%), disease outbreaks have not been documented in other animals (Housawi, 2007). Therefore, it is impossible to completely rule out the potential that sheep and goats are CMLV carriers who do not exhibit any symptoms. The degree of the illness is also determined by the virulence of the virus strain that is causing it and can vary from minor cutaneous lesions to severe systemic infections (Wernery and Kaaden, 2002). Humans can potentially contract CMLV after close contact with sick animals, and affected herders can spread the infection to other animals (Khalafalla *et al.*, 2015).

Public Health Importance

Sheep, goats, cattle, and other animal species are not infected by CMLV since it is host specific. CMLV was once thought to be a zoonotic agent, yet there is currently insufficient data from Somalia on unvaccinated individuals to substantiate this claim (Kriz, 1982). However, just one probable incidence of camelpox in humans has been reported due to modest skin lesions linked to the disease, highlighting the low public health significance of camelpox (Pfeffer *et al.*, 1998b). It is quite likely that camelpox cannot spread to people, even according to surveys conducted in camelpox-endemic areas. Human camelpox is extremely rare,

despite earlier indications in the literature that humans can contract the disease by handling diseased camels. This was demonstrated during the 1978–1979 smallpox eradication effort in Somalia (Kriz, 1982). It has the potential to be a biowarfare agent as well. Kemungkinan terjadinya infeksi CMLV pada manusia yang mengalami gangguan kekebalan tubuh bisa lebih tinggi tetapi masih belum diketahui (Balamurugan *et al*., 2013). There is currently no epidemiological proof that a human camelpox infection can cause clinical or subclinical symptoms, mostly because there aren't many well-documented human cases. Consequently, immunological tests for camelpox-specific antibodies in vulnerable unvaccinated herders may aid in assessing the likelihood of human camelpox transmission (Joseph *et al*., 2021). Therefore, it is necessary to evaluate the potential of a zoonotic infection.

Treatment

The literature makes no reference of post-exposure treatment methods for camelpox infection. Nonetheless, the use of antibiotics and supplements may help lessen the severity of the illness (Duraffour *et al*., 2007). Antiviral medications could be an alternative therapy option, particularly for young camels. Like other smallpox virus infections, camelpox has been found to respond well to a number of kinds of antiviral medications. Strong antiviral compounds that are effective against the smallpox virus, including OPV, both in vitro and in vivo may be used to treat camelpox (Smee, 2008). Among these are compounds from the acyclic nucleoside phosphonate (ANP) family, such as ST-246 (SIGA Inc., OR, USA), cidofovir (Gilead, CA, USA), and its lipid derivative CMX001 (Chimerix Inc., NC, USA) (De Clercq *et al*., 1987; Kern *et al*., 2002; Yang *et al*., 2005). Poxviruses are among the many DNA viruses that cidofovir and CMX001 are effective against. Both substances target and block the activity of the OPV viral DNA polymerase (Andrei *et al*., 2006). Oral antiviral medications that target cellular enzymes (IMP dehydrogenase inhibitors, like ribavirin, and tyrosine kinase inhibitors, like STI-571, also known as imatinib mesylate, or Gleevec) and viral enzymes, such as inhibitors of viral morphogenesis (TTP-6171), viral release (ST-246), and viral DNA synthesis (ANP analogs, like HPMPC), are effective against poxviruses, including CMLV (Snoeck *et al*., 2007). ST-246 is just a strong OPV inhibitor. This medication targets VACV's F13L protein, which is necessary for both extracellular enveloped viral generation and intracellular enveloped mature virus (Duraffour *et al*., 2008; Duraffour *et al*., 2009; Yang *et al*., 2005). Numerous investigations have also demonstrated that ST-246, administered once daily for 10–14 days at a dose of 100 mg/kg, prevents illness development in animals infected with OPV. Regarding CMLV, the compounds (Cidofovir, CMX001, and ST-246) are strong inhibitors of CMLV replication whose effectiveness has only been assessed in vitro (Duraffour *et al*., 2010; Duraffour *et al*., 2011a). On the other hand, CMX001 and ST-246 have the benefit of being oral, which would make them more appealing for usage in animals (Duraffour *et al*., 2007).

To date, there is no specific post-exposure treatment protocol formally established in the literature for managing camelpox infection. However, supportive care using antibiotics and nutritional supplements can help alleviate clinical symptoms and reduce disease severity (Duraffour *et al*., 2007). Antiviral drugs have been proposed as an alternative, particularly for treating young camels. As with other orthopoxvirus-related illnesses, camelpox has shown sensitivity to several classes of antiviral agents. Compounds proven effective against smallpox viruses—including *Orthopoxviruses* (OPVs)—in both laboratory and animal studies may offer therapeutic value for camelpox as well (Smee, 2008).

Promising antiviral candidates include agents from the acyclic nucleoside phosphonate (ANP) group, such as ST-246 (produced by SIGA Technologies, Oregon, USA), cidofovir (Gilead Sciences, California, USA), and its lipid-modified derivative CMX001 (marketed by Chimerix, North Carolina, USA) (De Clercq *et al*., 1987; Kern *et al*., 2002; Yang *et al*., 2005). These compounds are effective against a broad spectrum of DNA viruses, including poxviruses, by targeting and inhibiting the viral DNA polymerase enzyme required for replication (Andrei *et al*., 2006).

Several orally administered antivirals have also demonstrated efficacy against OPVs. These include cellular enzyme inhibitors such as ribavirin (an IMP dehydrogenase inhibitor), and tyrosine kinase inhibitors like STI-571 (imatinib mesylate or Gleevec), in addition to direct-acting antivirals that inhibit specific viral processes such as morphogenesis (e.g., TTP-6171), virion release (e.g., ST-246), and DNA replication (e.g., ANP analogs like HPMPC) (Snoeck *et al*., 2007). ST-246, in particular, is a potent inhibitor of *Orthopoxviruses* and functions by targeting the F13L gene product of the vaccinia virus, which is critical for the formation of both intracellular and extracellular virions (Duraffour *et al*., 2008; Duraffour *et al*., 2009; Yang *et al*., 2005).

Multiple studies have demonstrated that ST-246, when administered orally at a dose of 100 mg/kg once daily for 10–14 days, is capable of preventing disease progression in animal models infected with *Orthopoxviruses*. In the context of camelpox virus (CMLV), cidofovir, CMX001, and ST-246 have shown potent antiviral activity in vitro (Duraffour *et al*., 2010; Duraffour *et al*., 2011a). Among these, CMX001 and ST-246 are particularly attractive options for veterinary use due to their oral bioavailability, which simplifies administration in field settings (Duraffour *et al*., 2007).

Vaccination

The best defense against any viral disease is vaccination. Camel herds should receive routine vaccinations, particularly prior to the onset of the rainy season, to ensure that the animals have enough antibody levels before the vector population becomes active (Zhugunissov *et al*., 2023). The camelpox vaccine was created as a preventative approach to stop the disease's transmission in nations that are enzootic (Zhugunissov *et al*., 2021). The global smallpox eradication sparked the development of a CMLV vaccine. It is not advised to use VACV to treat OPV infection in animals during this time due to the potential for vaccinated contact animals to spread VACV to unvaccinated people (Hafez *et al*., 1992). As a result, scientists started working on creating a vaccine to prevent camelpox by employing CMLV strains that only infect camels.

There are vaccines to prevent camelpox that are both inactivated and live attenuated. In order to control camelpox, numerous countries have extensively assessed the safety and effectiveness of three live attenuated vaccines (Jouf-78, VD47/25, and Ducapox (298/89)/DucapoxR) and one inactivated vaccine (CMLV-T8/CAMELPOXR) (El-Harrak and Loutfi, 2000; Hafez *et al*., 1992; Nguyen-Ba-Vy *et al*., 1996; Wernery and Zachariah, 1999). Saudi Arabia uses the live attenuated CMLV Jouf-78 vaccine, which has been proven to be effective in the field at dose rates of 103 to 104 TCID50 when given subcutaneously or intradermally (Hafez *et al*., 1992). Mauritania is using the cell culture-based live attenuated CMLV VD47/25 vaccine, which was demonstrated to be safe for camels at a dose of 104.7 TCID50 when administered subcutaneously (Nguyen-Ba-Vy *et al*., 1996).

Since 1994, the third live attenuated vaccination, known as DucapoxR (short for Dubai CAmelPOX vaccine), has been successfully administered in the United Arab Emirates. Even though there have been claims of protection six years after immunization, the animals used in these research were extremely small (Wernery and Zachariah, 1999). Six months is the starting age for vaccinations. A booster dose is advised for camels aged 6 to 9 months to prevent vaccination harm from maternal antibodies, even if one dose is adequate to provide protection for at least a year (Khalafalla and El-Dirdiri, 2003). South Africa is the commercial producer of the DucapoxR vaccine. The camelpox inactivated vaccine is made from the CMLV T8 strain that was discovered in Morocco in 1984. Both juvenile and adult camels have shown this vaccine to be safe and effective. One month following the initial vaccine, a second shot is necessary for effective protection, and then there is an annual booster shot (El-Harrak and Loutfi, 2000). India has recently published a live cell culture attenuated camelpox vaccine. The vaccine's thermal stability has also been assessed

using a variety of stabilizers, which will aid in its application in arid and hot camel raising regions. (Prabhu *et al*., 2014).

Vaccination remains the most effective strategy for preventing viral infections. It is essential for camel herds to undergo regular immunization, especially before the onset of the rainy season when vector activity increases, to ensure sufficient antibody titers and reduce the risk of outbreaks (Zhugunissov *et al*., 2023). To prevent the spread of camelpox in enzootic regions, specific vaccines targeting camelpox virus (CMLV) have been developed (Zhugunissov *et al*., 2021). The global success of smallpox eradication programs inspired the development of vaccines against camelpox. However, the use of vaccinia virus (VACV) for animal orthopoxvirus infections is no longer encouraged due to the potential risk of virus transmission from vaccinated animals to unvaccinated humans (Hafez *et al*., 1992). Consequently, researchers have focused on developing vaccines using CMLV strains that are specific to camels and do not pose cross-species infection risks.

Both inactivated and live attenuated vaccines have been formulated to control camelpox. Several countries have conducted extensive evaluations of the efficacy and safety of three live attenuated vaccines—Jouf-78, VD47/25, and Ducapox (298/89), also referred to as DucapoxR—as well as one inactivated vaccine, CMLV-T8 (CAMELPOXR) (El-Harrak and Loutfi, 2000; Hafez *et al*., 1992; Nguyen-Ba-Vy *et al*., 1996; Wernery and Zachariah, 1999). In Saudi Arabia, the Jouf-78 live attenuated CMLV vaccine has demonstrated field efficacy when administered via subcutaneous or intradermal injection at doses between 10^3 and 10^4 $TCID_{50}$ (Hafez *et al*., 1992). In Mauritania, the VD47/25 live attenuated vaccine—developed through cell culture—has proven safe for camels when given subcutaneously at a dose of $10^{4.7}$ $TCID_{50}$ (Nguyen-Ba-Vy *et al*., 1996).

Since 1994, the DucapoxR vaccine (Dubai CamelPOX) has been successfully utilized in the United Arab Emirates. While protection has been reported to last up to six years post-vaccination, the studies supporting this claim were conducted on limited animal populations (Wernery and Zachariah, 1999). The recommended age for initial vaccination is six months. A booster is suggested for camels aged between six and nine months to counteract the neutralizing effect of maternal antibodies, even though a single dose is generally sufficient for at least one year of immunity (Khalafalla and El-Dirdiri, 2003). The DucapoxR vaccine is commercially manufactured in South Africa.

The inactivated camelpox vaccine is derived from the CMLV T8 strain, which was isolated in Morocco in 1984. It has demonstrated safety and efficacy in both juvenile and adult camels. A second dose one month after the initial vaccination is required to achieve effective protection, followed by yearly booster shots (El-Harrak and Loutfi, 2000). More recently, India has introduced a live attenuated vaccine produced via cell culture. Its thermal stability has been tested using different stabilizing agents to improve usability in arid and high-temperature regions where camel breeding is common (Prabhu *et al*., 2014).

Control

Control actions are crucial in affected nations to prevent occasional incidences of camelpox infection (Balamurugan *et al*., 2013). The transmission of infection is prevented by limiting animal movement, implementing sanitary practices, and separating afflicted animals from healthy ones (Prabhu *et al*., 2015). The most cost-effective and efficient way to prevent camelpox is by vaccination (Zhugunissov *et al*., 2021). Camel vaccination is not necessary everywhere in the world. As an alternative, during an outbreak, a ring vaccination method might be employed. This approach proved more effective in the last stage of the smallpox eradication campaign, when rigorous and comprehensive surveillance and monitoring were employed to diagnose the disease, followed by vaccination of all nearby animals and continued disease monitoring to make sure no new cases of the disease emerged (Durafour *et al*., 2011b).

Long-term protection against camelpox is offered by the live attenuated vaccination. However, for young animals immunized prior to 6–9 months of age, booster immunization is advised. Animals should receive a vaccination every year if an inactivated vaccine is being used. Cell-mediated and humoral immunity provide protection against camelpox infection (Elliot and Tuppurainen, 2008). However, the animal's protective immunological status may not necessarily be correlated with the amount of circulating antibodies (Wernery and Kaaden, 2002). Animals that have recovered will always be protected from reinfection. Inactivated virus vaccines offer protection for a year, while live attenuated vaccines offer protection for at least six years (Wernery and Zachariah, 1999).

Efforts to manage and eradicate camelpox will depend heavily on the ability to quickly confirm a clinical diagnosis using molecular testing. Camelpox satisfies the prerequisites to be considered for eradication as it solely affects camels, the causal agent has no wildlife reservoir, and there are no diagnostic procedures or vaccines to identify the illness and prevent its spread (Balamurugan *et al*., 2013). Many common disinfectants can affect the CMLV (Yousif *et al*., 2010). Additionally, boiling for at least ten minutes, autoclaving, and brief exposure to ultraviolet radiation can all eliminate this virus (Tadesse *et al*., 2018). Similar to smallpox in people, camel herders can utilize this technique to reduce the danger of environmental contamination. The disease can be eradicated by vaccination the remaining camels with either the newly designed camelpox virus vaccine or the conventional vaccinia virus vaccine (Bray and Babiuk, 2011).

Conclusion

Camelpox is a dangerous infectious illness that primarily affects camels in impoverished nations. It has a high morbidity and fatality rate. The impact on camel populations and the livelihoods that depend on them must be lessened by effective management and prevention measures, such as immunization and better diagnostic techniques.

Acknowledgments

The authors thank to Universitas Airlangga for the funding support with grant number 397/UN3.14/PT/2020.

Conflict of interest

The authors declare that there is no conflict of interest.

References

Adedeji, A.J., Gamawa, A.A., Chima, N.C., Ahmed, A.I., 2018. First report of camel contagious ecthyma in Nigeria. Open Vet. J. 8, 208–211. doi: 10.4314/ovj.v8i2.16.

Afonso, C.L., Tulman, E.R., Lu, Z., Zsak, L., Sandybaev, N.T., Kerembekova, U.Z., Zaitsev, V.L., Kutish, G.F., Rock, D.L., 2002. The genome of camelpox virus. Virology 295, 1–9. doi: 10.1006/viro.2001.1343.

Al-Bayati, H.A.M., Albadry, M.A.S., Al-Safi, Z.H., 2022. Detection and Isolation of Camelpox Virus in Wasit Province, Iraq. Arch. Razi. Inst. 77, 1133–1138. doi: 10.22092/ARI.2022.357388.2028.

AL-Eitan, L.N., Ali, H.O., Kharmah, H.S.A., Alasmar, M.K., Khair, I.Y., Mihyar, A.H., 2024. Addressing poxvirus challenges in the Middle East to enhance biosafety and biosecurity measures. J. Biosaf. Biosecurity 6, 142–156. doi: 10.1016/j.jobb.2024.06.003.

Al-Salihi, K.A., 2018. Invited review: Camelids zoonotic diseases. J. Camelid Sci. 11(1), 1–20.

Al-Zi'abi, O., Nishikawa, H., Meyer, H., 2007. The first outbreak of camelpox in Syria. J. Vet. Med. Sci. 69, 541–543. doi: 10.1292/jvms.69.541.

Albarnaz, J.D., Torres, A.A., Smith, G.L., 2018. Modulating Vaccinia Virus Immunomodulators to Improve Immunological Memory. Viruses 10, 101. doi: 10.3390/v10030101.

Alcam, A., Khanna, A., Paul, N.L., Smith, G.L., 1999. Vaccinia virus strains Lister, USSR and Evans express soluble and cell-surface tumour necrosis factor receptors. J. Gen. Virol. 80, 949–959. doi: 10.1099/0022-1317-80-4-949.

Alcami, A., Smith, G.L., 1995. Vaccinia, cowpox, and camelpox viruses encode soluble gamma interferon receptors with novel broad species specificity. J. Virol. 69, 4633–4639. doi: 10.1128/JVI.69.8.4633-4639.1995.

Alcami, A., Symons, J.A., Khanna, A., Smith, G.L., 1998. Poxviruses: capturing cytokines and chemokines. Semin. Virol. 8, 419–427. doi: 10.1006/smvy.1997.0143.

Alkharusi, A., Al Khaldi, N., Al-Sharji, N., Altoubi, K., Alsubhi, T., Al-Garadi, M.A., Al-Gabri, N., Ali, H., 2023. Clinicopathological investigations among recurrent camelpox outbreaks in Omanis' Arabian camels (Camelus dromedarius). Austral J. Vet. Sci. 55, 176–181. doi: 10.4206/ajvs.553.03.

Andrei, G., Gammon, D.B., Fiten, P., De Clercq, E., Opdenakker, G., Snoeck, R., Evans, D.H., 2006. Cidofovir resistance in vaccinia virus is linked to diminished virulence in mice. J. Virol. 80, 9391–9401. doi: 10.1128/JVI.00605-06.

Aregawi, W.G., Feyissa, P.T., 2016. Diagnostic Approaches towards Camelpox Disease. J. Vet. Sci. Anim. Husb. 4, 303. doi: 10.15744/2348-9790.4.303.

Arog, H.A., Ahad, A.A., Gebremeskel, H.F., Kebede, I.A., 2024. Seroprevalence of camelpox and its associated risk factors in selected districts of Jarar zone, Somali Region, Ethiopia. Pastor. Res. Policy Pract. 14, 13471. doi: 10.3389/past.2024.13471.

Aryaloka, S., Khairullah, A.R., Kusala, M.K.J., Fauziah, I., Hidayatik, N., Agil, M., Yuliani, M.G.A., Novianti, A.N., Moses, I.B., Purnama, M.T.E., Wibowo, S., Fauzia, K.A., Raissa, R., Furqoni, A.H., Awwanah, M., Riwu, K.H.P., 2024. Navigating monkeypox: identifying risks and implementing solutions. Open Vet. J. 14, 3144–3163. doi: 10.5455/OVJ.2024.v14.i12.1.

Ayelet, G., Jenberie, S., Belay, A., Mohammed, A., Mola, B., Gizaw, Y., Muhie, Y., Gelaye, E., Asmare, K., Skjerve, E., 2013. The first isolation and molecular characterization of camelpox virus in Ethiopia. Antiviral Res. 98, 417–422. doi: 10.1016/j.antiviral.2013.04.002.

Baky, M.H.A., Al-Sukayran, A., Mazloum, K.S., Al-Bokmy, A.M., Al-Mujalli, D.M., 2006. Immunogenicity of camelpox virus, JOUF -78 Vaccine - strain in boskat rabbits and guinea pigs. Assiut Vet. Med. J. 52, 194–202.

Balamurugan, V., Bhanuprakash, V., Hosamani, M., Jayappa, K.D., Venkatesan, G., Chauhan, B., Singh, R.K., 2009. A polymerase chain reaction strategy for the diagnosis of camelpox. J. Vet. Diagn. Invest. 21, 231–237. doi: 10.1177/104063870902100209.

Balamurugan, V., Venkatesan, G., Bhanuprakash, V., Singh, R.K., 2013. Camelpox, an emerging orthopox viral disease. Indian J. Virol. 24, 295–305. doi: 10.1007/s13337-013-0145-0.

Barry, M., Hnatiuk, S., Mossman, K., Lee, S.F., Boshkov, L., McFadden, G., 1997. The myxoma virus M-T4 gene encodes a novel RDEL-containing protein that is retained within the endoplasmic reticulum and is important for the productive infection of lymphocytes. Virology 239, 360–377. doi: 10.1006/viro.1997.8894.

Bassiouny, A.I., Soliman, S., Hussein, H.A., Rohiam, M.A., El-Sanousi, A.A., 2014. Sequence Analysis of Camelpox virus Isolated in Egypt. Int. J. Virol. 10, 121–128. doi: 10.3923/ijv.2014.121.128.

Baxby, D., 1972. Smallpox-like viruses from camels in Iran. Lancet 2, 1063–1065. doi: 10.1016/s0140-6736(72)92343-4.

Baxby, D., 1974. Differentiation of smallpox and camelpox viruses in cultures of human and monkey cells. J. Hyg. (Lond). 72, 251–254. doi: 10.1017/s0022172400023457.

Baxby, D., Hessami, M., Ghaboosi, B., Ramyar, H., 1975. Response of camels to intradermal inoculation with smallpox and camelpox viruses. Infect. Immun. 11, 617–621. doi: 10.1128/iai.11.4.617-621.1975.

Bayisa, D.A., 2019. Review on Camel Pox: Epidemiology, Public Health and Diagnosis. ARC J. Anim. Vet. Sci. 5, 22–33. doi: 10.20431/2455-2518.0504003.

Beerli, C., Yakimovich, A., Kilcher, S., Reynoso, G.V., Fläschner, G., Müller, D.J., Hickman, H.D., Mercer, J., 2019. Vaccinia virus hijacks EGFR signalling to enhance virus spread through rapid and directed infected cell motility. Nat. Microbiol. 4, 216–225. doi: 10.1038/s41564-018-0288-2.

Bera, B.C., Shanmugasundaram, K., Barua, S., Venkatesan, G., Virmani, N., Riyesh, T., Gulati, B.R., Bhanuprakash, V., Vaid, R.K., Kakker, N.K., Malik, P., Bansal, M., Gadvi, S., Singh, R.V., Yadav, V., Sardarilal, Nagarajan, G., Balamurugan, V., Hosamani, M., Pathak, K.M., Singh, R.K., 2011. Zoonotic cases of camelpox infection in India. Vet. Microbiol. 152, 29–38. doi: 10.1016/j.vetmic.2011.04.010.

Betakova, T., Wolffe, E.J., Moss, B., 2000. The vaccinia virus A14.5L gene encodes a hydrophobic 53-amino-acid virion membrane protein that enhances virulence in mice and is conserved among vertebrate poxviruses. J. Virol. 74, 4085–4092. doi: 10.1128/jvi.74.9.4085-4092.2000.

Bhanuprakash, V., Balamurugan, V., Hosamani, M., Venkatesan, G., Chauhan, B., Srinivasan, V.A., Chauhan, R.S., Pathak, K.M.L., Singh, R.K., 2010b. Isolation and characterization of Indian isolates of camel pox virus. Trop. Anim. Health Prod. 42, 1271–1275. doi: 10.1007/s11250-010-9560-z.

Bhanuprakash, V., Prabhu, M., Venkatesan, G., Balamurugan, V., Hosamani, M., Pathak, K.M., Singh, R.K., 2010a. Camelpox: epidemiology, diagnosis and control measures. Expert. Rev. Anti Infect. Ther. 8, 1187–1201. doi: 10.1586/eri.10.105.

Blomquist, M.C., Hunt, L.T., Barker, W.C., 1984. Vaccinia virus 19-kilodalton protein: relationship to several mammalian proteins, including two growth factors. Proc. Natl. Acad. Sci. U S A 81, 7363–7367. doi: 10.1073/pnas.81.23.7363.

Bowie, A., Kiss-Toth, E., Symons, J.A., Smith, G.L., Dower, S.K., O'Neill, L.A., 2000. A46R and A52R from vaccinia virus are antagonists of host IL-1 and toll-like receptor signaling. Proc. Natl. Acad. Sci. U S A 97, 10162–10167. doi: 10.1073/pnas.160027697.

Bray, M., Babiuk, S., 2011. Camelpox: target for eradication? Antiviral Res. 92, 164–166. doi: 10.1016/j.antiviral.2011.09.006.

Bulatov, Y., Turyskeldy, S., Abitayev, R., Usembai, A., Sametova, Z., Kondybayeva, Z., Kurmasheva, A., Mazbayeva, D., Kyrgyzbayeva, A., Shorayeva, K., Amanova, Z., Toktyrova, D., 2024. Camelpox Virus in Western Kazakhstan: Assessment of the Role of Local Fauna as Reservoirs of Infection. Viruses 16, 1626. doi: 10.3390/v16101626.

Burger, P.A., Ciani, E., Faye, B., 2019. Old World camels in a modern world - a balancing act between conservation and genetic improvement. Anim. Genet. 50, 598–612. doi: 10.1111/age.12858.

Caillat, C., Topalis, D., Agrofoglio, L.A., Pochet, S., Balzarini, J., Deville-Bonne, D., Meyer, P., 2008. Crystal structure of poxvirus thymidylate kinase: an unexpected dimerization has implications for antiviral therapy. Proc. Natl. Acad. Sci. U S A 105, 16900–16905. doi: 10.1073/pnas.0804525105.

Dahiya, S.S., Kumar, S., Mehta, S.C., Narnaware, S.D., Singh, R., Tuteja, F.C., 2016. Camelpox: A brief review on its epidemiology, current status and challenges. Acta Trop. 158, 32–38. doi: 10.1016/j.actatropica.2016.02.014.

Davies, F.G., Mungai, J.N., Shaw, T., 1975. Characteristics of a Kenyan camelpox virus. J. Hyg. (Lond). 75, 381–385. doi: 10.1017/s002217240002444x.

De Clercq, E., Sakuma, T., Baba, M., Pauwels, R., Balzarini, J., Rosenberg, I., Holý, A., 1987. Antiviral activity of phosphonylmethoxyalkyl derivatives of purine and pyrimidines. Antiviral Res. 8, 261–272. doi: 10.1016/s0166-3542(87)80004-9.

Diaz, J.H., 2021. The Disease Ecology, Epidemiology, Clinical Manifestations, Management, Prevention, and Control of Increasing Human Infections with Animal *Orthopoxviruses*. Wilderness Environ. Med. 32, 528–536. doi: 10.1016/j.wem.2021.08.003.

Duraffour, S., Andrei, G., Snoeck, R., 2010. Tecovirimat, a p37 envelope protein inhibitor for the treatment of smallpox infection. IDrugs 13, 181–191.

Duraffour, S., Matthys, P., van den Oord, J.J., De Schutter, T., Mitera, T., Snoeck, R., Andrei, G., 2011b. Study of camelpox virus pathogenesis in athymic nude mice. PLoS One 6, e21561. doi: 10.1371/journal.pone.0021561.

Duraffour, S., Meyer, H., Andrei, G., Snoeck, R., 2011a. Camelpox virus. Antiviral Res. 92, 167–186. doi: 10.1016/j.antiviral.2011.09.003.

Duraffour, S., Snoeck, R., Fiten, P., Opdenakker, G., Andrei, G., 2009. Selection and characterization of (S)-1-[3-hydroxy-2-(phosphonomethoxypropyl)-2,6-diaminopurine [HPMPDAP] resistant Camelpox viruses. Antivir. Res. 82, A67–A68. doi: 10.1016/j.antiviral.2009.02.165.

Duraffour, S., Snoeck, R., Krecmerová, M., van Den Oord, J., De Vos, R., Holy, A., Crance, J.M., Garin, D., De Clercq, E., Andrei, G., 2007. Activities of several classes of acyclic nucleoside phosphonates against camelpox virus replication in different cell culture models. Antimicrob. Agents Chemother. 51, 4410–4419. doi: 10.1128/AAC.00838-07.

Duraffour, S., Vigne, S., Garcel, A., Jordan, R., Hruby, D.E., Crance, J.M., Garin, D., Andrei, G., Snoeck, R., 2008. Antiviral potency of ST-246 on the production of enveloped *Orthopoxviruses* and characterization of ST-246 resistant vaccinia, cowpox and camelpox viruses. Antivir. Res. 78, A29–A30. doi: 10.1016/j.antiviral.2008.01.049.

Eckstein, S., Ehmann, R., Gritli, A., Rhaiem, M.B., Yahia, H.B., Diehl, M., Wölfel, R., Handrick, S., Moussa, M.B., Stoecker, K., 2022. Viral and Bacterial Zoonotic Agents in Dromedary Camels from Southern Tunisia: A Seroprevalence Study. Microorganisms 10, 727. doi: 10.3390/microorganisms10040727.

El-Harrak, M., Loutfi, C., 2000. Camelpox in dromedary calves in Morocco. Proceedings of the international workshop on the camel calf, Quarzazate, Morocco, 24-26 October 1999. Rev. Elev. Med. Vet. Pays Trop. 53, 165–167.

Elliot, H., Tuppurainen, E., 2008. Camelpox. Manual of diagnostic tests and vaccines for terrestrial animals. Vol. 2, Chapter. 2.9.2. p. 177–184.

Elzein, E.M.A., Gameel, A.A., Ramadan, R.O., Housawi, F.M., 1999. An eruptive moderate form of camelpox infection in dromedary camels (Camelus dromedarius) in Saudi Arabia. Rev. Sci. Tech. 18, 749–752. doi: 10.20506/rst.18.3.1194.

Eskra, L., Mathison, A., Splitter, G., 2003. Microarray analysis of mRNA levels from RAW264.7 macrophages infected with Brucella abortus. Infect. Immun. 71(3), 1125–1133. doi: 10.1128/IAI.71.3.1125-1133.2003.

Essbauer, S., Pfeffer, M., Meyer, H., 2010. Zoonotic poxviruses. Vet. Microbiol. 140, 229–236. doi: 10.1016/j.vetmic.2009.08.026.

Evans, D.H., 2022. Poxvirus Recombination. Pathogens 11, 896. doi: 10.3390/pathogens11080896.

Fashina, T., Huang, Y., Thomas, J., Conrady, C.D., Yeh, S., 2022. Ophthalmic Features and Implications of Poxviruses: Lessons from Clinical and Basic Research. Microorganisms 10, 2487. doi: 10.3390/microorganisms10122487.

Gelderblom, H.R., Madeley, D. 2018. Rapid Viral Diagnosis of *Orthopoxviruses* by Electron Microscopy: Optional or a Must? Viruses 10, 142. doi: 10.3390/v10040142.

Geserick, P., Kaiser, F., Klemm, U., Kaufmann, S.H., Zerrahn, J., 2004. Modulation of T cell development and activation by novel members of the Schlafen (slfn) gene family harbouring an RNA helicase-like motif. Int. Immunol. 16, 1535–1548. doi: 10.1093/intimm/dxh155.

Gieryńska, M., Szulc-Dąbrowska, L., Struzik, J., Gregorczyk-Zboroch, K.P., Mielcarska, M.B., Toka, F.N., Schollenberger, A., Biernacka, Z., 2023. Orthopoxvirus Zoonoses-Do We Still Remember and Are Ready to Fight? Pathogens 12, 363. doi: 10.3390/pathogens12030363.

Greger, M., 2007. The human/animal interface: emergence and resurgence of zoonotic infectious diseases. Crit. Rev. Microbiol. 33, 243–299. doi: 10.1080/10408410701647594.

Gubser, C., Smith, G.L., 2002. The sequence of camelpox virus shows it is most closely related to variola virus, the cause of smallpox. J. Gen Virol. 83, 855–872. doi: 10.1099/0022-1317-83-4-855.

Gubser, C., Bergamaschi, D., Hollinshead, M., Lu, X., van Kuppeveld, F.J., Smith, G.L., 2007b. A new inhibitor of apoptosis from vaccinia virus and eukaryotes. PLoS Pathog. 3, e17. doi: 10.1371/journal.ppat.0030017.

Gubser, C., Goodbody, R., Ecker, A., Brady, G., O'Neill, L.A.J., Jacobs, N., Smith, G.L., 2007a. Camelpox virus encodes a schlafen-like protein that affects orthopoxvirus virulence. J. Gen. Virol. 88, 1667–1676. doi: 10.1099/vir.0.82748-0.

Hafez, S.M., al-Sukayran, A., dela Cruz, D., Mazloum, K.S., al-Bokmy, A.M., al-Mukayel, A., Amjad, A.M., 1992. Development of a live cell culture camelpox vaccine. Vaccine 10, 533–539. doi: 10.1016/0264-410x(92)90353-l.

Haller, S.L., Peng, C., McFadden, G., Rothenburg, S., 2014. Poxviruses and the evolution of host range and virulence. Infect. Genet. Evol. 21, 15–40. doi: 10.1016/j.meegid.2013.10.014.

Housawi, F.M.T., 2007. Screening of domestic ruminants sera for the presence of anti-camel pox 464 virus neutralizing antibodies. Assiut Vet. Med. J. 53, 101–105.

Joseph, S., Kinne, J., Nagy, P., Juhász, J., Barua, R., Patteril, N.A.G., Hoffmann, D., Pfaff, F., Hoffmann, B., Wernery, U., 2021. Outbreak of a Systemic Form of Camelpox in a Dromedary Herd (Camelus dromedarius) in the United Arab Emirates. Viruses 13, 1940. doi: 10.3390/v13101940.

Kachhawaha, S., Srivastava, M., Kachhawa, J.P., Tanwar, M., Sharma, A., Singh, N.K., Kachwaha, K., Rathore, S.S., Tanwar, R.K., 2014. Therapeutic management of camel pox– a case report. Adv. Anim. Vet. Sci. 2, 239–241. doi: 10.14737/journal.aavs/2014/2.4.239.241.

Kandeel, M., Al-Mubarak, A.I.A., 2022. Camel viral diseases: Current diagnostic, therapeutic, and preventive strategies. Front. Vet. Sci. 9, 915475. doi: 10.3389/fvets.2022.915475.

Kao, S., Kao, C.F., Chang, W., Ku, C., 2023. Widespread Distribution and Evolution of Poxviral Entry-Fusion Complex Proteins in Giant Viruses. Microbiol. Spectr. 11, e0494422. doi: 10.1101/2023.01.19.524718.

Kawai, M., Pan, L., Reed, J.C., Uchimiya, H., 1999. Evolutionally conserved plant homologue of the Bax inhibitor-1 (BI-1) gene capable of suppressing Bax-induced cell death in yeast(1). FEBS Lett. 464, 143–147. doi: 10.1016/s0014-5793(99)01695-6.

Kern, E.R., Hartline, C., Harden, E., Keith, K., Rodriguez, N., Beadle, J.R., Hostetler, K.Y., 2002. Enhanced inhibition of orthopoxvirus replication in vitro by alkoxyalkyl esters of cidofovir and cyclic cidofovir. Antimicrob. Agents Chemother. 46, 991–995. doi: 10.1128/AAC.46.4.991-995.2002.

Khalafalla, A.I., 2023. Zoonotic diseases transmitted from the camels. Front. Vet. Sci. 10, 1244833. doi: 10.3389/fvets.2023.1244833.

Khalafalla, A.I., Abdelazim, F., 2017. Human and Dromedary Camel Infection with Camelpox Virus in Eastern Sudan. Vector Borne Zoonotic Dis. 17, 281–284. doi: 10.1089/vbz.2016.2070.

Khalafalla, A.I., Ali, Y.H., 2007. Observations on risk factors associated with some camel viral diseases of camels in Sudan. Proceedings of the 12th International Conference of the Association of Institutions of Tropical Veterinary Medicine. Montpellier, France, 20–22 August 2007. pp. 101–105.

Khalafalla, A.I., El-Dirdiri, G.A., 2003. Laboratory and field investigation of a live and an inactivated camelpox vaccine. J. Camel Pract. Res. 10, 191–200.

Khalafalla, A.I., Al-Busada, K.A., El-Sabagh, I.M., 2015. Multiplex PCR for rapid diagnosis and differentiation of pox and pox-like diseases in dromedary Camels. Virol. J. 12, 102. doi: 10.1186/s12985-015-0329-x.

Khalafalla, A.I., Dadar, M., Sazmand, A., 2024. Editorial: Current knowledge on camelids infectious and parasitic diseases. Front. Vet. Sci. 10, 1351318. doi: 10.3389/fvets.2023.1351318.

Khalafalla, A.I., Mohamed, M.H., Ali, B.H., 1998. Camel pox in the Sudan and its isolation and identification of the causative virus. J. Camel Pract. Res. 5, 229–233.

Kinne, J., Cooper, J.E., Wernery, U., 1998. Pathological studies on camelpox lesions of the respiratory system in the United Arab Emirates (UAE). J. Comp. Pathol. 118, 257–266. doi: 10.1016/s0021-9975(07)80002-8.

Kotwal, G.J., Hügin, A.W., Moss, B., 1989. Mapping and insertional mutagenesis of a vaccinia virus gene encoding a 13,800-Da secreted protein. Virology 171, 579–587. doi: 10.1016/0042-6822(89)90627-2.

Kotwal, G.J., Isaacs, S.N., McKenzie, R., Frank, M.M., Moss, B., 1990. Inhibition of the complement cascade by the major secretory protein of vaccinia virus. Science 250, 827–830. doi: 10.1126/science.2237434.

Kriz, B., 1982. A study of camelpox in Somalia. J. Comp. Pathol. 92, 1–8. doi: 10.1016/0021-9975(82)90037-8.

Kumar, K.N., Tilakaratne, N., Johnson, P.S., Allen, A.E., Michaelis, E.K., 1991. Cloning of cDNA for the glutamate-binding subunit of an NMDA receptor complex. Nature 354, 70–73. doi: 10.1038/354070a0.

Lesse, A.S., 1909. Two diseases of young camels. J. Trop. Vet. Sci. 4, 1–7.

Liu, B., Panda, D., Mendez-Rios, J.D., Ganesan, S., Wyatt, L.S., Moss, B., 2018. Identification of Poxvirus Genome Uncoating and DNA Replication Factors with Mutually Redundant Roles. J. Virol. 92, e02152-17. doi: 10.1128/JVI.02152-17.

Lorenzo, M.M., Galindo, I., Griffiths, G., Blasco, R., 2000. Intracellular localization of vaccinia virus extracellular enveloped virus envelope proteins individually expressed using a Semliki Forest virus replicon. J. Virol. 74, 10535–10550. doi: 10.1128/jvi.74.22.10535-10550.2000.

Maikhin, K., Berdikulov, M., Abishov, A., Pazylov, Y., Mussayeva, G., Zhussambayeva, S., Janabekova, G., Shaimbetova, A., Ussenbekov, Y., Syrym, N., 2023. Characterization of the camel pox virus strain used in producing camel pox virus vaccine. Open Vet. J. 13, 558–568. doi: 10.5455/OVJ.2023.v13.i5.8.

Mambetaliyev, M., Kilibayev, S., Kenzhebaeva, M., Sarsenkulova, N., Tabys, S., Valiyeva, A., Muzarap, D., Tuyskanova, M., Myrzakhmetova, B., Rametov, N., Sarbassova, A., Nurgaziev, R., Kerimbayev, A., Babiuk, S., Zhugunissov, K., 2024. Field Trials of Live and Inactivated Camelpox Vaccines in Kazakhstan. Vaccines 12, 685. doi: 10.3390/vaccines12060685.

Meyer, H., Pfeffer, M., Rziha, H.J., 1994. Sequence alterations within and downstream of the A-type inclusion protein genes allow differentiation of Orthopoxvirus species by polymerase chain reaction. J. Gen. Virol. 75, 1975–1981. doi: 10.1099/0022-1317-75-8-1975.

Mohammadpour, R., Champour, M., Tuteja, F., Mostafavi, E., 2020. Zoonotic implications of camel diseases in Iran. Vet. Med. Sci. 6, 359–381. doi: 10.1002/vms3.239.

Mosadeghhesari, M., Oryan, A., Zibaee, S., Varshovi, H.R., 2014. Molecular investigation and cultivation of camelpox virus in Iran. Arch. Virol. 159, 3005–3011. doi: 10.1007/s00705-014-2169-1.

Moss, B., 2012. Poxvirus cell entry: how many proteins does it take? Viruses 4, 688–707. doi: 10.3390/v4050688.

Moss, B., 2013. Poxvirus DNA replication. Cold Spring Harb. Perspect. Biol. 5, a010199. doi:

10.1101/cshperspect.a010199.
Moss, B., Shisler, J.L., 2001. Immunology 101 at poxvirus U: immune evasion genes. Semin. Immunol. 13, 59–66. doi: 10.1006/smim.2000.0296.
Mossman, K., Lee, S.F., Barry, M., Boshkov, L., McFadden, G., 1996. Disruption of M-T5, a novel myxoma virus gene member of poxvirus host range superfamily, results in dramatic attenuation of myxomatosis in infected European rabbits. J. Virol. 70, 4394–4410. doi: 10.1128/JVI.70.7.4394-4410.1996.
Moussatché, N., Damaso, C.R., McFadden, G., 2008. When good vaccines go wild: Feral Orthopoxvirus in developing countries and beyond. J. Infect. Developing Countries 2, 156–173. doi: 10.3855/jidc.258.
Najarro, P., Traktman, P., Lewis, J.A., 2001. Vaccinia virus blocks gamma interferon signal transduction: viral VH1 phosphatase reverses Stat1 activation. J. Virol. 75, 3185–3196. doi: 10.1128/JVI.75.7.3185-3196.2001.
Narnaware, S.D., Ranjan, R., Dahiya, S.S., Panchbuddhe, A., Bajpai, D., Tuteja, F.C., Sawal, R.K., 2021. Pathological and molecular investigations of systemic form of camelpox in naturally infected adult male dromedary camels in India. Heliyon 7, e06186. doi: 10.1016/j.heliyon.2021.e06186.
Nguyen-Ba-Vy, Guerre, L., Saint-Martin, G., 1996. Etude préliminaire de l'innocuité et du pouvoir immunogène de la souche atténuée VD47/25 de camelpoxvirus. Rev. Elev. Med. Vet. Pays Trop. 49, 189–194. doi: 10.19182/remvt.9511.
Obermeier, P.E., Buder, S.C., Hillen, U., 2024. Poxvirus infections in dermatology – the neglected, the notable, and the notorious. J. Dtsch. Dermatol. Ges. 22, 56–93. doi: 10.1111/ddg.15257.
Pei, L., Overdahl, K.E., Shannon, J.P., Hornick, K.M., Jarmusch, A.K., Hickman, H.D., 2023. Profiling whole-tissue metabolic reprogramming during cutaneous poxvirus infection and clearance. J. Virol. 97, e0127223. doi: 10.1128/jvi.01272-23.
Perdiguero, B., Blasco, R., 2006. Interaction between vaccinia virus extracellular virus envelope A33 and B5 glycoproteins. J. Virol. 80, 8763–8777. doi: 10.1128/JVI.00598-06.
Perdiguero, B., Esteban, M., 2009. The interferon system and vaccinia virus evasion mechanisms. J. Interferon Cytokine Res. 29, 581–598. doi: 10.1089/jir.2009.0073.
Perkus, M.E., Goebel, S.J., Davis, S.W., Johnson, G.P., Limbach, K., Norton, E.K., Paoletti, E., 1990. Vaccinia virus host range genes. Virology 179, 276–286. doi: 10.1016/0042-6822(90)90296-4.
Pfeffer, M., Meyer, H., Wernery, U., Kaaden, O.R., 1996. Comparison of camelpox viruses isolated in Dubai. Vet. Microbiol. 49, 135–146. doi: 10.1016/0378-1135(95)00181-6.
Pfeffer, M., Neubauer, H., Wernery, U., Kaaden, O.R., Meyer, H., 1998b. Fatal form of camelpox virus infection. Vet. J. 155, 107–109. doi: 10.1016/s1090-0233(98)80045-2.
Pfeffer, M., Wernery, U., Kaaden, O.-R., Meyer, H., 1998a. Diagnostic procedures for poxyvirus infections in camelids. J. Camel Pract. Res. 5, 189–195.
Prabhu, M., Bhanuprakash, V., Venkatesan, G., Yogisharadhya, R., Bora, D.P., Balamurugan, V., 2014. Evaluation of stability of live attenuated camelpox vaccine stabilized with different stabilizers and reconstituted with various diluents. Biologicals 42, 169–175. doi: 10.1016/j.biologicals.2014.02.001.
Prabhu, M., Yogisharadhya, R., Pavulraj, S., Suresh, C., Sathish, G., Singh, R.K., 2015. Camelpox and buffalopox: Two emerging and re-emerging orthopox viral diseases of India. Adv. Anim. Vet. Sci. 3, 527–541. doi: 10.14737/journal.aavs/2015/3.10.527.541.
Ramyar, H., Hessami, M., 1972. Isolation, Cultivation and Characterization of Camel Pox Virus. Zentralbl. Veterinaermed. B 19, 182–189. doi: 10.1111/j.1439-0450.1972.tb00393.x.
Renner-Müller, I.C., Meyer, H., Munz, E., 1995. Characterization of camelpoxvirus isolates from Africa and Asia. Vet. Microbiol. 45, 371–381. doi: 10.1016/0378-1135(94)00143-k.
Ropp, S.L., Jin, Q., Knight, J.C., Massung, R.F., Esposito, J.J., 1995. PCR strategy for identification and differentiation of small pox and other *Orthopoxviruses*. J. Clin. Microbiol. 33, 2069–2076. doi: 10.1128/jcm.33.8.2069-2076.1995.
Sadykov, R.G., 1970. Cultivation of camelpox virus in chick embryos. VirusngBolezniSkh. Zhi'ootnykh Part I, 55.
Schwarz, D.A., Katayama, C.D., Hedrick, S.M., 1998. Schlafen, a new family of growth regulatory genes that affect thymocyte development. Immunity 9, 657–668. doi: 10.1016/s1074-7613(00)80663-9.
Senkevich, T.G., Wolffe, E.J., Buller, R.M., 1995. Ectromelia virus RING finger protein is localized in virus factories and is required for virus replication in macrophages. J. Virol. 69, 4103–4111. doi: 10.1128/JVI.69.7.4103-4111.1995.
Shchelkunov, S.N., Safronov, P.F., Totmenin, A.V., Petrov, N.A., Ryazankina, O.I., Gutorov, V.V., Kotwal, G.J., 1998. The genomic sequence analysis of the left and right species-specific terminal region of a cowpox virus strain reveals unique sequences and a cluster of intact ORFs for immunomodulatory and host range proteins. Virology 243, 432–460. doi: 10.1006/viro.1998.9039.
Shchelkunov, S.N., Totmenin, A.V., Loparev, V.N., Safronov, P.F., Gutorov, V.V., Chizhikov, V.E., Knight, J.C., Parsons, J.M., Massung, R.F., Esposito, J.J., 2000. Alastrim smallpox variola minor virus genome DNA sequences. Virology 266, 361–386. doi: 10.1006/viro.1999.0086.
Shchelkunova, G.A., Shchelkunov, S.N., 2022. Smallpox, Monkeypox and Other Human Orthopoxvirus Infections. Viruses 15, 103. doi: 10.3390/v15010103.
Smee, D.F., 2008. Progress in the discovery of compounds inhibiting *Orthopoxviruses* in animal models. Antivir. Chem. Chemother. 19, 115–124. doi: 10.1177/095632020801900302.
Smith, G.L., Symons, J.A., Alcamı, A., 1998. Poxviruses; interfering with interferon. Sem. Virol. 8, 409–418. doi: 10.1006/smvy.1997.0145.
Snoeck, R., Andrei, G., De Clercq, E., 2007. Therapy of poxvirus infections. In: Mercer AA, Schmidt A, Weber O, editors. Poxviruses. Basel: Birkhauser. p. 375–395. doi: 10.1007/978-3-7643-7557-7_18.
Symons, J.A., Alcamí, A., Smith, G.L., 1995. Vaccinia virus encodes a soluble type I interferon receptor of novel structure and broad species specificity. Cell 81, 551–560. doi: 10.1016/0092-8674(95)90076-4.
Tadesse, T., Mulatu, E., Bekuma, A., 2018. Review on Camel Pox: An Economically Overwhelming Disease of pastorals. Int. J. Adv. Res. Biol. Sci. 5, 65–73. doi: 10.22192/ijarbs.2018.05.09.006.
Taylor, J.M., Barry, M., 2006. Near death experiences: poxvirus regulation of apoptotic death. Virology 344, 139–150. doi: 10.1016/j.virol.2005.09.032.
Turner, P.C., Musy, P.Y., Moyer, R.W., 1995. Poxvirus serpins. In McFadden G, Austin, Landes RG, editors. Viroceptors, Virokines and related immune modulators encoded by DNA Viruses. TX, USA: RG Landes. p. 67–88.
Villanueva, R.A., Rouillé, Y., Dubuisson, J., 2005. Interactions between virus proteins and host cell membranes during the viral life cycle. Int. Rev. Cytol. 245, 171–244. doi: 10.1016/S0074-7696(05)45006-8.
Walter, L., Marynen, P., Szpirer, J., Levan, G., Gunther, E., 1995. Identification of a novel conserved human gene, TEGT. Genomics 28, 301–304. doi: 10.1006/geno.1995.1145.
Wernery U., Kaaden O.-R., 2002. Camel pox. In: Infectious Diseases in Camelids, Second Edition, Wernery U. & Kaaden O.-R., eds. Blackwell Science Berlin, Germany. p. 176–185.
Wernery, U., Kaaden, O.-R., Ali, M., 1997. Orthopox virus infections in dromedary camels in United Arab Emirates (U.A.E.) during winter season. J. Camel Pract. Res. 4, 51–55.
Wernery, U., Zachariah, R., 1999. Experimental Camelpox Infection in Vaccinated and Unvaccinated Dromedaries. J. Vet. Med. B 46, 131–135. doi: 10.1111/j.0931-1793.1999.00250.x.
Xu, Q., Reed, J.C., 1998. Bax inhibitor-1, a mammalian apoptosis suppressor identified by functional screening in yeast. Mol. Cell 1, 337–346. doi: 10.1016/s1097-2765(00)80034-9.
Yang, G., Pevear, D.C., Davies, M.H., Collett, M.S., Bailey, T., Rippen, S., Barone, L., Burns, C., Rhodes, G., Tohan, S., Huggins, J.W., Baker, R.O., Buller, R.L., Touchette, E., Waller, K., Schriewer, J., Neyts, J., DeClercq, E., Jones, K., Hruby, D., Jordan, R., 2005. An orally bioavailable antipoxvirus compound (ST-246) inhibits extracellular virus formation and protects mice from lethal orthopoxvirus Challenge. J. Virol. 79, 13139–13149. doi: 10.1128/JVI.79.20.13139-13149.2005.
Yao, X.D., Evans, D.H., 2003. High-frequency genetic recombination and reactivation of *Orthopoxviruses* from DNA fragments transfected into leporipoxvirus-infected cells. J. Virol. 77, 7281–7290. doi: 10.1128/JVI.77.13.7281-7290.2003.
Yousif, A.A., Al-Naeem, A.A., 2012. Recovery and molecular characterization of live Camelpox virus from skin 12 months after onset of clinical signs reveals possible mechanism of virus persistence in herds. Vet. Microbiol. 159, 320–326. doi: 10.1016/j.vetmic.2012.04.022.
Yousif, A.A., Al-Naeem, A.A., Al-Ali, M.A., 2010. Rapid non-enzymatic extraction method for isolating PCR-quality camelpox virus DNA from skin. J. Virol. Methods 169, 138–142. doi: 10.1016/j.jviromet.2010.07.013.
Zhu, S., Zimmerman, D., Deem, S.L., 2019. A Review of Zoonotic Pathogens of Dromedary Camels. EcoHealth 16, 356–377. doi: 10.1007/s10393-019-01413-7.
Zhugunissov, K., Kilibayev, S., Mambetaliyev, M., Zakarya, K., Kassenov, M., Abduraimov, Y., Bulatov, Y., Azanbekova, M., Absatova, Z., Abeuov, K., Nurgaziev, R., Renukaradhya, G.J., Tabynov, K., 2021. Development and Evaluation of a Live Attenuated Egg-Based Camelpox Vaccine. Front. Vet. Sci. 8, 721023. doi: 10.3389/fvets.2021.721023.
Zhugunissov, K., Mambetaliyev, M., Sarsenkulova, N., Tabys, S., Kenzhebaeva, M., Issimov, A., Abduraimov, Y., 2023. Development of an Inactivated Camelpox Vaccine from Attenuated Camelpox Virus Strain: Safety and Protection in Camels. Animals (Basel) 13, 1513. doi: 10.3390/ani13091513.