

Review / Derleme

Monkeypox and other zoonotic poxviruses

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Received date: 21.07.2022 - Accepted date: 20.09.2022

Abstract: Poxviruses have caused the most important diseases for humanity for a long time. An important triumph was achieved with the eradication of smallpox, defined by the World Health Organization in 1979. Poxviruses include significant agents that cause important animal diseases that are non-zoonotic and zoonotic. While humanity has been battling COVID-19, a new battle against monkeypox has recently emerged due to an increase in case numbers and the outbreak's global spread. The other points of the 2022 monkeypox outbreak that make it more serious than previous outbreaks are severe clinical outcomes such as encephalitis and death, and also the higher transmission rate, which occurs at approximately 99% in men, especially those who have sex with men. The 2022 monkeypox virus outbreak has focused public and scientific attention on poxviruses and potential bioterrorism risks posed by poxviruses. Therefore, it is aimed at writing a review that compiles information about monkeypox, cowpox, vaccinia, bovine papular stomatitis, orf, pseudocowpox, gray seal pox, and red deerpox viruses.

Keywords: Monkeypox, poxvirus, zoonotic infection.

Maymun çiçeği ve diğer zoonotik poksvirüsler

Özet: Poksvirüsler uzun zamanlardan beri insanlık açısından çok önemli hastalıklara yol açmıştır. Dünya Sağlık Örgütü'nün önderliğinde Poksvirüslerle özdeşleşen çiçek hastalığının (smallpox) 1979 yılında eradikasyonu ile önemli bir zafer kazanılmıştır. Poksvirüs ailesinde sadece hayvanlarda hastalık oluşturan zoonotik olmayan etkenler ile bazı zoonotik etkenler yer almaktadır. Günümüzde insanlık COVID-19 ile mücadele ederken, son zamanlarda artan vaka sayıları ve salgının dünya çapındaki dağılımı nedeniyle maymun çiçeği ile de savaşmak zorunda kalmaktadır. 2022 maymun çiçeği salgını önceki salgınlardan daha ciddi hale getiren diğer noktalar, ensefalit ve ölüm gibi ciddi klinik sonuçlar ve erkeklerle seks yapan erkeklerde yaklaşık %99 oranında görülmesidir. 2022 yılı maymun çiçeği salgını hem halkın hem de bilim camiasının ilgisinin tekrar poksvirüslere ve bunlarla ilgili potansiyel biyoterörizm risklerine yönelmesine sebep olmuştur. Bu nedenle bu virüs ailesi içerisindeki zoonotik etkenler arasında yer alan maymun çiçeği, sığır çiçeği, vaccina, sığır papüller stomatit, orf, yalancı sığır çiçeği, gri fok çiçeği ve kızıl geyik çiçeği virüsleri hakkında bilgi veren bir derleme yazılması amaçlanmıştır.

Anahtar sözcükler: Maymun çiçeği, poksvirüsler, zoonotik infeksiyon.

Introduction

Poxviruses belong to the family *Poxviridae*, which is classified into the *Varidnaviria* realm, *Bamfordvirae* kingdom, *Nucleocyotiviricota* phylum, *Pokkesviricetes* class, and *Chitovirales* order. The *Poxviridae* family consists of two subfamilies: *Chordopoxvirinae* (includes poxviruses of vertebrates) and *Entomopoxvirinae* (includes poxviruses of insects). There are 18 genera in the *Chordopoxvirinae* subfamily and they are summarized in Table 1. Virions of poxviruses are large (220-450 nm ×

140-260 nm), pleomorphic, and brick-shaped with an irregular arrangement of surface tubules (most genera) or ovoid with a regular crisscross arrangement of surface tubules (*Parapoxvirus* genus). The genome of poxviruses consists of 130 to 360 kilobase pairs (kbp) linear double-stranded DNA and encodes 130 to 320 proteins. Unlike other DNA viruses, poxviruses replicate in the cytoplasm of the host cell due to encoding all the enzymes required for transcription and replication (83, 97).

Table 1. Classification of *Poxviridae* family.

Family: <i>Poxviridae</i>	
Subfamily: <i>Chordopoxvirinae</i>	
Genus: <i>Avipoxvirus</i>	Species: <i>Canarypox virus, Flamingopox virus, Fowlpox virus, Juncopox virus, Mynahpox virus, Penguinpox virus, Pigeonpox virus, Psittacinepox virus, Quailpox virus, Sparrowpox virus, Starlingpox virus, Turkeypox virus</i>
Genus: <i>Capripoxvirus</i>	Species: <i>Goatpox virus, Lumpy skin disease virus, Sheeppox virus</i>
Genus: <i>Centapoxvirus</i>	Species: <i>Murmansk microtuspox virus, Yokapox virus</i>
Genus: <i>Cervidpoxvirus</i>	Species: <i>Mule deerpox virus</i>
Genus: <i>Crocodylidpoxvirus</i>	Species: <i>Nile crocodilepox virus</i>
Genus: <i>Leporipoxvirus</i>	Species: <i>Hare fibroma virus, Myxoma virus, Rabbit fibroma virus, Squirrel fibroma virus</i>
Genus: <i>Macropopoxvirus</i>	Species: <i>Eastern kangaroopox virus, Western kangaroopox virus</i>
Genus: <i>Molluscipoxvirus</i>	Species: <i>Molluscum contagiosum virus</i>
Genus: <i>Mustelpoxvirus</i>	Species: <i>Sea otterpox virus</i>
Genus: <i>Orthopoxvirus</i>	Species: <i>Abatino macacapox virus, Akhmeta virus, Camel痘 virus, Cowpox virus*, Ectromelia virus, Monkeypox virus*, Raccoonpox virus, Skunkpox virus, Taterapox virus, Vaccinia virus*, Variola virus, Volepox virus</i>
Genus: <i>Oryzopoxvirus</i>	Species: <i>Cotia virus</i>
Genus: <i>Parapoxvirus</i>	Species: <i>Bovine papular stomatitis virus*, Grey sealpox virus*, Orf virus*, Pseudocowpox virus*, Red deerpox virus*</i>
Genus: <i>Pteropoxvirus</i>	Species: <i>Pteropox virus</i>
Genus: <i>Salmonpoxvirus</i>	Species: <i>Salmon gillpox virus</i>
Genus: <i>Sciuripoxvirus</i>	Species: <i>Squirrelpox virus</i>
Genus: <i>Suipoxvirus</i>	Species: <i>Swinepox virus</i>
Genus: <i>Vespertilionpoxvirus</i>	Species: <i>Eptesipox virus</i>
Genus: <i>Yatapoxvirus</i>	Species: <i>Tanapox virus*, Yaba monkey tumor virus*</i>

* Indicates zoonotic poxviruses.

Poxviruses are ancient viruses for humanity. Poxviral DNA is found in ancient human remains dated as far back as AD 600 (175). The method of cutaneous inoculation, called variolation, was practiced frequently in the Ottoman Empire. Mary Wortley Montague had written letters about variolation in Istanbul, the Ottoman Empire's capital city, which led to the introduction of variolation in England. The variolation had also introduced to Europe in the 18th century by the travellers returning from Istanbul (16, 159). Edward Jenner used the cowpox virus for vaccination against smallpox. Jenner termed this inoculation procedure "vaccination" due to the Latin word "vaccinia" that means cowpox (159).

Orthopoxvirus and *Parapoxvirus* genera contain significant zoonotic agents: monkeypox, cowpox, vaccinia, bovine papular stomatitis, orf, pseudocowpox, grey sealpox, and red deerpox viruses (Table 1). This review aims to substantially focus on monkeypox and the beforementioned zoonotic orthopoxviruses and parapoxviruses, considering the recent scientific data and global health emergency.

Monkeypox virus

Etiology: Monkeypox virus (MPXV), with another called the human monkeypox virus (hMPXV), has a 197

kb linear DNA genome and contains close to 190 non-overlapping ORFs, each longer than 60 amino acid residues (169). The virus is phylogenetically classified into 3 clades: Clade I (formerly 'Central African' or 'Congo Basin' clade), clade IIa ('West African' clade), and clade IIb ('West African' clade, and also including clade IIa). The clade IIb includes A.1, A.2, A.1.1, and B.1 lineages. Lineage A.1 consists of the MPXVs that are from 2018 and 2019 cases, mainly from the United Kingdom, Israel, and Singapore. The viruses of the 2022 monkeypox outbreak belong mainly to the lineage B.1, which is a descendant of lineage A.1 and some of the current isolates are determined to be classified in lineage A.2 (77, 85, 89).

The lineage B.1 viruses contain approximately 50 single-nucleotide polymorphisms (SNPs) in comparison to the MPXVs from the 2018–2019 outbreaks, indicating that lineage B1 has an increased mutation rate (85). A recent study reported that 9 MPXV isolates from the 2021–2022 cases in the USA, India, and Thailand are classified as lineage A.2 and have 16 distinct genetic variations when compared to other lineages, including 9 nonsynonymous, 3 synonymous, 1 stop gained variation, and 3 amino acid deletion in the OPG174 gene (89). The lineage A.2 has a lower nucleotide substitution rate than the B.1 lineage. The mean nucleotide substitution rates of

the A.2 and B.1 lineages are determined as 5.53×10^{-5} and 1.13×10^{-4} substitutions per base/year, respectively. The higher mutation rate of lineage B.1 viruses may be the reason for the increasing number of monkeypox cases and the accelerated transmission speed of the virus in the 2022 monkeypox outbreak (85, 89).

Recent studies reported that the majority of the current MPXV isolates have GA > AA and TC > TT nucleotide replacement motifs that are typical for a host enzyme called apolipoprotein B mRNA editing catalytic polypeptide-like3 (APOBEC3). The genome of MPXV isolates between 2017 and 2022 in the clade IIa has more GA > AA mutations in comparison to the clade I and the isolates prior to 2017 in the clade IIa. Most of the SNPs detected in the genomes of 2022 MPXV isolates are also GA > AA and TC > TT nucleotide replacements (69, 85). In another study, it was reported that a genomic comparison of viral isolates from 2015 to 2022 showed that 2022 monkeypox isolates have 30 T bases in length in the middle of the viral genome, which of the role is unknown (149). A study showed that D2L-like, OPG023, OPG047, OPG071, OPG105, OPG109, A27L-like, OPG153, OPG188, and OPG210 proteins of 2022 MPXV isolates have the highest number of mutations throughout the whole viral genome (197). Alignment against the first public sequence of the 2022 monkeypox outbreak (ON563414.3) indicated that novel mutations had occurred, but the viral genes involved in immune evasion, host range, cell proliferation such as A45L, C1L, D7L, D10L genes, drug resistance such as L3R, L6R, and A25R genes, and vaccine development such as the A25R gene have lower mutation rates (114). All these cumulative changes in the viral genome might be responsible for the recent rapid evolution of hMPXV1 and a possible explanation of the faster human-to-human transmission (11, 122). The virus is characterized as a Biosafety Level 3 (high threat) pathogen in the European Union and is on the list of selected agents in the United States following the recent situation (103).

Epidemiology: In 1958 in Denmark, "pox-like" non-fatal outbreaks occurred in cynomolgus monkeys, and the causative agent was named monkeypox virus (195). The first confirmed monkeypox virus human case was a 9-month-old indigenous boy hospitalized because of fever and rashes in the Democratic Republic of the Congo in 1970 (100). Monkeypox viruses were isolated from the kidneys of healthy chimpanzee and cynomolgus monkeys in the Democratic Republic of the Congo and the Netherlands, respectively, and from monkeys with clinical monkeypox disease in the USA (120). In 1970 and 1971, human cases of monkey pox were reported in Liberia, Nigeria, and Sierra Leone. When the humans (most of whom are aged 4–9 years) with monkeypox virus infection were epidemiologically investigated, most of them

revealed that they occasionally consumed monkeys for food and played with the internal organs of the killed monkeys (62, 110). In total, 48 confirmed and suspected monkeypox virus cases were reported in the Democratic Republic of the Congo, Cameroon, Côte d'Ivoire, Liberia, Nigeria, and Sierra Leone between 1970 and 1979 (25) (Table 2).

In the 1980s and 1990s, monkeypox cases have only been reported from African countries, and human monkeypox virus infection has been accepted as endemic to some African countries since 2003 (Table 2). The Centers for Disease Control and Prevention (CDC) declared that some human cases with fever, papular rash, respiratory symptoms, lymphadenopathy, and sore throat were confirmed as monkeypox virus infection in 2003 in some states (Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin) of the United States of America (USA). All of the patients have had contact with animals such as prairie dogs, Gambian giant rats, and rabbits (animal-to-human transmission), and some have been infected through direct contact with other infected humans (human-to-human transmission). Following traceback investigations, the CDC has reported that the source of the monkeypox virus that was introduced to the USA is Gambian giant rats that were exported from Ghana and co-housed with prairie dogs (28, 29).

In the 2010s, besides endemic countries, monkeypox cases were reported from non-endemic countries such as Israel and the United Kingdom (UK), which were related to the export of travellers (55, 191) (Table 2). On May 6, 2022, a patient with rashes who travelled from the UK to Nigeria and returned to the UK had been confirmed as monkeypox virus, and on May 7, 2022, the World Health Organization (WHO) was informed of this confirmed case of monkeypox in the UK (200). Despite the fact that the number of monkeypox cases has been increasing globally, WHO announced that monkeypox was not a global health treat on June 25, 2022, after more than 4100 cases were recorded in 46 countries (162). Alas, contrary to this announcement, on July 23, 2022, WHO declared monkeypox a public health emergency of international concern (116). On August 4, 2022, the USA declared the monkeypox outbreak a national public health emergency as the virus has infected more than 6,600 people and cases have been recorded in 48 states (95). According to the report of WHO on September 5, 2022, there have been a total of 52,015 laboratory confirmed cases and 395 probable cases (including 18 deaths) of monkeypox virus (204) (Figure 1, Table 2). Türkiye has reported the first case of human monkeypox virus infection on June 30, 2022, and five monkeypox cases in total since August 2, 2022 (157, 186). The USA, where the majority of global monkeypox cases have been reported, confirmed the first death of a monkeypox-infected patient recently (12).

Table 2. Human monkeypox virus infection cases in between 1970 and 2022 by year and country.

Years	Number of cases*	Countries reported cases	References
1970-79	48	Democratic Republic of the Congo, Cameroon, Côte d'Ivoire, Liberia, Nigeria, Sierra Leone	
1980-89	357	Democratic Republic of the Congo, Cameroon, Côte d'Ivoire, Gabon, Central African Republic	
1990-99	520	Democratic Republic of the Congo, Gabon	
2000-09	10,166	Democratic Republic of the Congo, Congo, South Sudan, United States of America	
2010-19	19,071	Democratic Republic of the Congo, Congo, Cameroon, Central African Republic, Nigeria, Liberia, Sierra Leone, Singapore, Israel, United Kingdom	
2020	6,257	Democratic Republic of the Congo	
2021	3,190	Democratic Republic of the Congo, Nigeria, The United Kingdom, United States of America	4, 25, 41, 156, 201, 203
2022**	52,015 laboratory confirmed cases and 395 probable cases	Andorra, Argentina, Aruba, Australia, Austria, Bahamas, Barbados, Belgium, Benin, Bermuda, Bolivia, Bosnia and Herzegovina, Brazil, Bulgaria, Cameroon, Canada, Central African Republic, Chile, China, Colombia, Congo, Costa Rica, Croatia, Cuba, Curaçao, Cyprus, Czechia, Democratic Republic of the Congo, Denmark, Dominican Republic, Ecuador, El Salvador, Estonia, Finland, France, Georgia, Germany, Ghana, Gibraltar, Greece, Greenland, Guadeloupe, Guatemala, Guyana, Honduras, Hungary, Iceland, India, Indonesia, Iran, Ireland, Israel, Italy, Jamaica, Japan, Latvia, Lebanon, Liberia, Lithuania, Luxembourg, Malta, Martinique, Mexico, Monaco, Montenegro, Morocco, Netherlands, New Caledonia, New Zealand, Nigeria, Norway, Panama, Paraguay, Peru, Philippines, Poland, Portugal, Puerto Rico, Qatar, Republic of Korea, Republic of Moldova, Romania, Russian Federation, Saint Martin, Saudi Arabia, Serbia, Singapore, Slovakia, Slovenia, South Africa, Spain, Sudan, Sweden, Switzerland, Thailand, The United Kingdom, Türkiye, United Arab Emirates, United States of America, Uruguay, Venezuela	

*Monkeypox virus cases which are laboratory confirmed or suspected are given in the numbers.

**Case numbers are given according to 5 September 2022 report of the WHO (200).

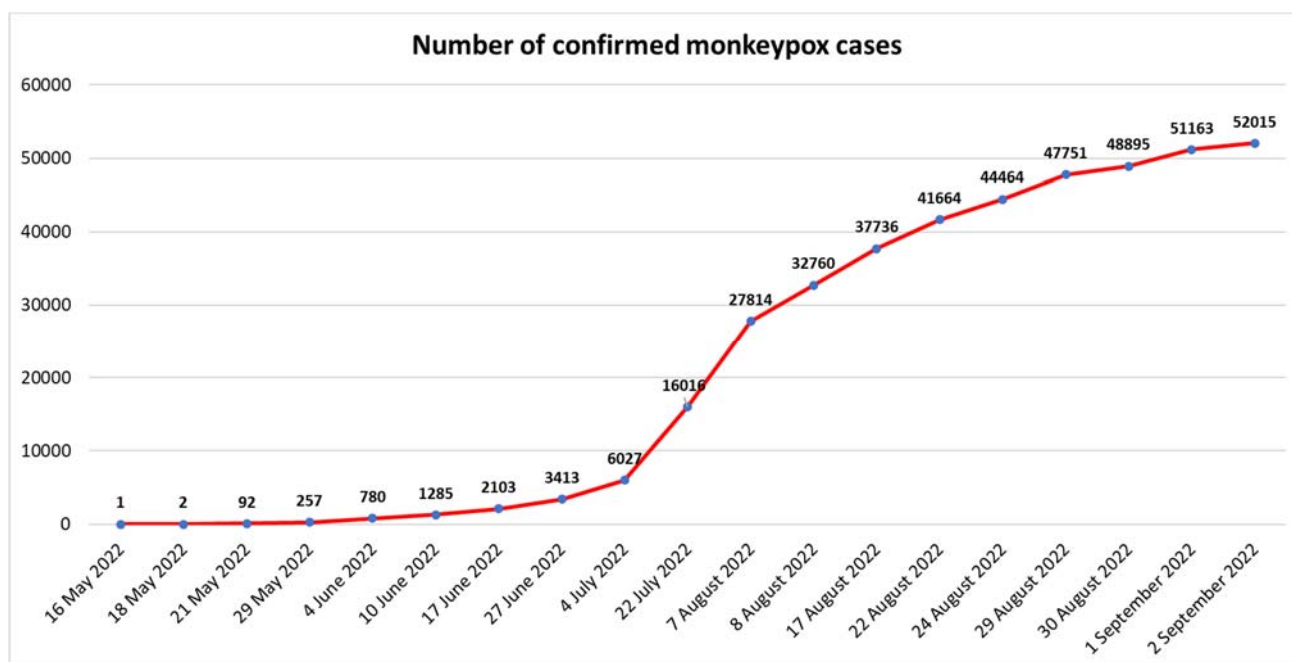


Figure 1. Number of confirmed monkeypox cases reported by WHO between 16 May 2022 and 2 September 2022.

Many mammals and non-human primates (i.e., sooty mangabey monkey, Gambian-pouched rat, rhesus macaques, cynomolgus macaques, Asian monkeys, Southern opossum, sun squirrel, African hedgehogs, jerboas, woodchucks, shot-tailed opossum, porcupines, giant anteaters, prairie dogs, elephant shrew, domestic pigs, rope squirrel, and African dormice) may have a role in transmission of monkeypox virus infection and can be a reservoir of the virus (8). Several outbreaks and cases were recorded in different monkey species both in laboratories and in the wild (132, 144, 147, 153).

The monkeypox virus can be transmitted by animal-to-human and human-to-human. Animal-to-human transmission can occur via direct contact with an infected animal's blood, body fluids, and pox-associated skin or mucosal lesions. Another possible route of transmission of monkeypox virus is through the bites of infected non-human primates or mammals (108, 131).

Human-to-human transmission of monkeypox virus can be achieved through close and direct contact with an infected person's respiratory secretions or droplets, skin or mucosal lesions, body fluids, or indirectly via virus-contaminated fomites (8, 192). Blood, skin and mucosal lesions, saliva, nasal/nasopharyngeal/throat swabs, rectal swabs, faeces, urine, and semen of the infected person are found to be positive for monkeypox and this may play a role in viral transmission (4, 134, 145, 184). Infectious virus is isolated from the semen of monkeypox-infected men, indicating the potential transmission via semen (104). The monkeypox virus is found in the household environment of an infected person and is infectious mainly on porous surfaces such as bedding, underwear, and towels. Although low viral titres were determined, which indicate a limited potential for indirect transmission, the household environment may play a role in transmission of the virus via contaminated fomites (129).

Recently, evidence for human-to-animal transmission of monkeypox has been reported in an Italian greyhound dog whose owner had monkeypox infection (165). The CDC is suggesting that monkeypox infected people should avoid contact with animals, including pets, domestic animals, and wildlife, in order to prevent the spread of the virus. If pets had close contact with monkeypox-infected people, they should be quarantined at home for 21 days, away from other animals and people (33).

Sexual transmission is reported as an important route for monkeypox infection, especially in people who have had close contact with an infected individual and in men who have sex with other men (75, 143). According to recent research, monkeypox is most common in men, particularly men who have sex with men, bisexual men, and men who have multiple sexual partners (107, 196). Interview-based epidemiological data from a recent study

indicated that monkeypox transmission in the UK has been related to the sexual networks of gay and bisexual men who are all cisgender (196). An epidemiological study showed that 99% of the monkeypox cases were men in the USA and 94% of them had sexual or close intimate contact with men (152). The risk factors for monkeypox are determined as having sex with men, engaging in condomless sex, human immunodeficiency virus (HIV) positivity, and a story of previous sexually transmitted infections (23).

Clinical Signs: The incubation period of monkeypox is an average of 13 days but can be up to 34 days. The studies about the 2022 monkeypox outbreak reported that the incubation period is approximately 9–10 days and can be prolonged to 17–20 days. So, one can speculate that the lineage B.1 viruses have a shorter incubation period than other clades and lineages (128, 135, 184, 206). Even though 13% of the people who were sick were hospitalized, most of those who were admitted did not have serious problems (168).

Clinical manifestations of monkeypox virus infection vary, including gastrointestinal (diarrhoea, nausea, vomiting), upper and lower respiratory (runny nose, sore throat, wheeze, cough, respiratory distress), and systemic (lymphadenopathy, fever, sweats, chills, pruritus, myalgia, back pain, headache, asthenia, and abdominal pain) symptoms. However, the first clinical signs and common are usually fever, lymphadenopathy, exanthema, asthenia, fatigue, and headache. Skin and mucosal lesions can appear anywhere on the body, but they are most common on the face, limbs, palms of the hands, soles of the feet, oral and genital mucosa, and, in rare cases, conjunctivae and cornea. Lesions consist of rashes, macules, papules, vesicles, pustules, crusts, ulceration (23, 137, 158).

Interestingly, it is reported that monkeypox can be asymptomatic in some men who have sex with men, and these cases remain undiagnosed (45). Monkeypox lesions can also be without exanthem and a robust cellular immune response can be determinative for the occurrence of skin lesions (108). Following healing of skin lesions, sequelae can be observed, such as hyperpigmented or hypopigmented atrophic scars, patchy alopecia, hypertrophic skin scarring, and deformities of facial muscles following healing of ulceration (137). According to an observational study in the Democratic Republic of Congo, monkeypox virus infection of pregnant women can lead to miscarriage and foetal death with diffuse cutaneous maculopapillary skin lesions or healthy birth (123).

Monkeypox virus infection can cause genital lesions such as painless genital rash, macular rash, painful inguinal lymphadenopathy, ulcerated lesions, umbilicated pustules, painless white pustules on the penis, and pruritis

(75, 143). HIV positive men who have sex with men are reported to be at more risk for monkeypox virus infection and develop monkeypox-associated genital lesions (75, 127, 143).

Monkeypox lesions can be clinically misdiagnosed because of their resemblance to the lesions that are caused by other viral infections or may remain undiagnosed. Differential diagnosis for monkeypox and coxsackie virus infection should be performed for suspected lesions by virological diagnosis (107). Another recently published retrospective study from Belgium showed that men who had been misdiagnosed with gonorrhoea and/or chlamydia could be monkeypox positive with or without any lesions (45).

Some monkeypox cases can be fatal (86, 154). The mortality rate of monkeypox infection is in the range of 1-10%, but recently has been around 3-6% (21, 26, 202). The clade I viruses are associated with more severe disease and higher case fatality than the clade IIa viruses (177). The clade IIb viruses that drive the current monkeypox outbreak have case fatality ratios below 1% (85).

Control and Treatment: There is no specific therapy for monkeypox virus infection in humans. Some governments carry out 21 day mandatory quarantines for monkeypox infected people in order to control transmission of the disease. Several cases are recovered without any specific antiviral therapy (9, 23, 56). Non-specific therapies such as antibiotics and analgesics can be administered to monkeypox virus-infected patients. Antibiotics are frequently used for prevention or treatment of secondary bacterial infections (75, 143). Antiviral agents such as tecovirimat, a p37 protein inhibitor that is used for orthopoxvirus infections, and brincidofovir, a replication inhibitor of a variety of DNA viruses, can be used for monkeypox virus infection (4, 52, 156). Treatment of brincidofovir can lead to an increase in liver enzymes, whereas no adverse effects occurred with Tecovirimat treatment (4).

Due to cross-protection between orthopoxviruses, people vaccinated against smallpox are 85% protected against monkeypox virus infection. Vaccines containing live, replication-competent, different vaccinia virus strains, called first-generation smallpox vaccines, were used for smallpox eradication between 1967 and 1979, which was coordinated by the WHO. The U.S. Food and Drug Administration (FDA) has approved three smallpox vaccines: JYNNEOS (Imvamune or Imvanex/replication-deficient live virus vaccine), ACAM2000 (Live cowpox Vaccinia virus vaccine), and Aventis Pasteur Smallpox Vaccine (APSV/replication-competent vaccinia virus vaccine) (6, 60). Because of some concerns about first-generation vaccines, such as inadvertent transmission to other people, re-emergence of live viruses, and vaccine-associated adverse effects, third-generation smallpox

vaccines that contain replication-deficient vaccinia viruses (e.g., modified vaccinia Ankara (MVA) and LC16m8) are preferred to prevent and control orthopoxvirus infections. In some countries, healthcare workers and laboratory personnel are vaccinated with third-generation smallpox vaccines (i.e., modified vaccinia Ankara (MVA) and LC16m8) for protection against orthopoxviruses including monkeypox virus (32, 150, 202). In a multi-center cohort enrolling in France, JYNNEOS (Imvanex or Imvamune) has begun to be used for vaccination for post-exposure prophylaxis to unvaccinated adults over 18 years who have been exposed to monkeypox less than 14 days ago or adults who have been vaccinated with a first dose less than 28 days earlier and have been exposed to monkeypox (112).

Other Zoonoses in *Orthopoxvirus* and *Parapoxvirus* genus

Cowpox virus

Epidemiology: Cowpox virus, an Orthopoxvirus, infection has been reported in many animal species including primates (e.g., Barbary macaque, marmoset, cotton-top tamarins), felids (e.g., cats, cheetah, lynx, lion, black panther, jaguar, puma), dog, fox, wild boar, cow, llama, horse, elephant, anteaters, beaver, bank voles, gray-sided vole, red-backed voles, field vole, root vole, wood mice, yellow-necked mice, house mice, common rat, giant gerbil, gerbil, ground squirrel, Patagonian cavy, common shrew, etc. (57, 92). Unlike many other animal species that can be infected by cowpox virus, direct transmission to humans has only been reported by infected cats, rats, cows, cheetahs, and Asian elephants (27, 74, 78, 133, 182). Infected rats can also infect other animal species (121). Possible human-to-human transmission was reported (183). However, this transmission route is not proven. Human cowpox virus infection is rare and there have been less than 150 reported cases.

Clinical Signs: Symptoms of cowpox virus infection in cats include oedema, hyperaemia, ulceration, exudation, and plaque-like alterations in the hindlimbs (91). Captive banded mongooses in a zoological park in Germany have exhibited papular, vesicular, or pustular skin lesions, crusts, anorexia, lethargy, imbalance, severe dyspnoea, wheezing, and death due to generalized cowpox virus infection (164). Virus infections in captive cheetahs in zoos and parks lead to skin (including ulcerations) and mucosal lesions, exudative pleuritis, and acute hemorrhagic pneumonia, with high morbidity and mortality (18, 119, 178). Cowpox virus infection of a pregnant mare can culminate in abortion of a foal with cutaneous papules throughout the entire skin and the oral mucosa (65).

Lesions in human cases of cowpox are macules, papules, vesicles, pustules, and black crusts and are usually restricted to the hands and face. Cowpox virus infection typically causes one lesion, but multiple inoculations, autoinoculation, and immunosuppression can lead to multiple lesions and generalized infections (44). Fever, lymphadenitis (sometimes necrotizing), cellulitis, ulcerated and necrotizing skin lesions are reported in patients who have had direct contact with infected domestic cats (142, 207). Cowpox cases generally recover in 6–8 weeks, but it can take 12 weeks to heal in some cases (44). A generalized infection caused by cowpox virus was reported in a patient with haemorrhagic and ulcerated nodules, oedema, fever, and lymphadenopathy (73). Some human cases of generalized cowpox virus infection in kidney transplant patients who were scratched by their cats with ulcerating nodules culminated in death (68, 198). Ocular cowpox virus infection can lead to necrosis of the eyelid, necrotic granulomatous conjunctivitis, keratitis, leucomatous opacity, conjunctival oedema, necrotic eschar, and vision loss (51, 98). An atypical cowpox virus infection was recorded in a smallpox vaccinated patient with clinical manifestations such as painful cellulitis, multiple subcutaneous abscesses, and axillary adenopathy (10). Foetus can be infected by cowpox virus during pregnancy and can result in miscarriage (61).

Control and Treatment: Attenuated modified vaccinia virus Ankara (MVA) strains are used for vaccination against cowpox virus and are shown to be protective in elephants, rhinos, and captive cheetahs (53, 178). There is no specific vaccine against the cowpox virus for humans.

Vaccinia virus

Epidemiology: Vaccinia virus was used in the WHO eradication campaign for smallpox, which is an acute contagious disease caused by the variola virus of the orthopoxviruses. The Vaccinia virus strain Ankara, which was developed at the vaccine institute in Ankara, Turkey by propagating the virus on the skin of calves and donkeys (through donkey-calf-donkey inoculation), was passaged in chicken embryo fibroblast culture in Germany and, after the 516th passage, the virus was named Modified Vaccinia virus Ankara (MVA). Preferably safer smallpox vaccines were used during the last years of the smallpox eradication campaign (180, 194). Moreover, MVA serves as a safe and effective vector platform, such as in vaccines for rabies, Chikungunya, malaria, etc. (67, 115, 166).

In countries such as Uruguay, Brazil, and Colombia, reported cases of vaccinia virus infection (63, 190). Bovine vaccinia virus outbreaks that occurred in Brazil caused zoonotic infection of humans (13, 125, 173). Human-to-human transmission of vaccinia virus can be

directly or indirectly (37, 146). Vaccinia virus can be isolated from the household environment of infected people, and this may be a route of human-to-human transmission (13). Another potential route of infection is consuming contaminated raw milk or raw milk products, and these can play a role in occupational infection of cheesemakers (37, 47).

Clinical Signs: According to the results of experimental infection of milking cows with vaccinia virus, lesions started at 2–4 days post-inoculation, healed averagely in 18 days, all infected cows exhibited DNAemia, some of them had viremia, and animals shed vaccinia virus in their faeces (160). Infectious vaccinia virus is detected in milk samples of naturally infected cows, and in milk samples, milk products, and even in pasteurized milk of experimentally infected cows (1, 47). Furthermore, vaccinia virus DNA was detected in dogs, cats, horses, wild coatis, and opossums, but transmission of the virus from these animals has not been reported yet (38, 39, 147, 148).

Vaccinia virus typically infects farmers, milkers, and their close contacts. Vaccinia virus-infected people showed skin lesions mainly on the hands, forearms, legs, and face, and generalized outcomes such as fever, headache, malaise, myalgia, and lymphadenopathy (173). Skin lesions usually start with itching, local oedema, pustules, vesicles, and ulcers (49, 173). Ocular lesions can occur (109). HIV positive patients who are vaccinia virus infected can develop progressive and more severe clinical outcomes (102). A patient who was in contact with cows that had lesions on their teats and udders, developed an ulcerated-pustule skin lesion, fever, headache, malaise, myalgia, and lymphadenopathy and was diagnosed as co-infected with vaccinia and pseudocowpox viruses (2). Occupational vaccinia virus infections can occur. Employees of a biopharmaceutical laboratory where vaccinia virus was inoculated to rabbits developed clinical infection in China (111).

Control and Treatment: Vaccinia virus has been used as a vaccine in both humans and animals against orthopoxviruses (32, 150, 178, 202). There is no specific treatment for vaccinia virus infection.

Bovine papular stomatitis virus

Epidemiology: The host spectrum of bovine papular stomatitis virus (BPSV), a member of the Parapoxvirus family, is restricted to cattle and humans. Humans can be infected through direct contact with infected animal lesions (22, 80). Occupational infections of BPSV were reported in milkers, veterinarians, and veterinary students. BPSV infection is frequently transmitted to milkers, especially if the teats of dairy cows are affected. (22, 48). Some tick species are reported as BPSV PCR positive and houseflies can be a mechanical vector for BPSV,

indicating that vectors may play a role in transmission and epidemiology of the disease (141, 171).

Clinical signs: BPSV infection in cattle leads to lesions such as papules, nodules, pustules, vesicles, ulcers, erosions, scabby proliferative lesions, crusts, and scabs that are usually on the muzzle, lips, gingiva, palate, tongue, and teats (88, 93, 126, 136, 170). Affected calves with oral lesions may refuse to be fed, and affected dairy cows with teat lesions may not allow milking because of local pain (48, 126). The erosive lesions on the oral mucosa can be observed as a ring or a horseshoe (43). In some cases, there could be papules and ulcers in the oesophagus, rumen, and omasum in cattle (88, 126, 170). Extensive proliferative scabby lesions and dermatitis of the teats were also reported in cows, sometimes leading to occlusion of the teat canal (84, 106). Infected cattle generally recover in 13–18 days with no treatment (136).

Symptoms of BPSV infection in humans include painful papules, nodules, pustules, vesicles, ulcers, and scars that are mainly restricted to the hands and rarely on the face and arms (48, 80, 124, 136).

Diagnosis and treatment: There is no specific treatment or vaccine for BPSV in animals or humans. Hygiene, disinfection, and isolation of infected animals can be the main procedures for preventing the spread of the virus to other animals and workers (93).

Orf virus

Epidemiology: Orf virus is a parapoxvirus and the causative agent of contagious pustular dermatitis (syn. contagious ecthyma, orf, sore mouth, scabby mouth) that results in infection of primarily sheep and goats, and also cattle, camels, other wild ruminants, and cervids (7, 167, 176, 187). Orf has a worldwide distribution with high morbidity and low mortality. Animals younger than 1 year of age are more susceptible to the disease and their inability to feed due to severe lesions leads to loss of weight gain and even death, and as a consequence, economic loss (15).

Between animals, orf is transmitted via direct contact and contaminated fomites. A recent report showed that the infectious orf virus is present in saliva and milk samples of goats without clinical symptoms, and the isolated virus is infectious to other orf-free goats under experimental conditions (113).

Sheep and goats, and rarely camels and cats can infect humans (7, 31, 64, 99). Orf virus is transmitted by direct contact with infected animals, contaminated fomites and, especially for children, infected animal bites can be the cause of infection (105, 185). Orf infection mostly occurred in farmers, animal workers, shepherds, wool shearers, veterinarians, butchers, and hunters, or was sometimes observed in people after Eid al-Adha (19, 82, 96, 193). Household injuries that happen during meat

preparation and animal slaughter are reported to cause the development of orf infection in humans (31). Orf can be transmitted human-to-human via commonly used contaminated fomites (189). In a case of human orf, mother-to-child transmission has occurred and exophytic nodules and papules have developed on the scrotum and buttocks of the child (155). Autoinoculation is a possible way to spread the orf virus from lesions to other parts of the body (50, 179).

Clinical signs: Symptoms of orf in animals are characterized by erythematous macules, papules, vesicles, pustules, ulcers, scabbing and proliferative skin lesions which are mostly formed on the mouth, gums, lips, muzzle, nostrils, face, eyelids, ears, udder, and teats, and sometimes on the inner thigh, abdomen, axilla, tail, perineum, and extremities (46, 99, 174). In some cases, necrotizing cheilitis and dermatitis, crusting, hyperpigmentation, and oedema can develop and may result in partial obstruction of the nostrils (42). Wild ruminants can exhibit orf lesions on nostrils, lips, eyelids, face, chin, ear, nares, neck, leg, hooves/corony band, interdigital space (187).

In humans, orf virus causes vesicles, pustules, painful erythematous, violaceous plaques, erythematous maculopapular lesions, targetoid bulla, weeping nodule, crusted papule, papilloma, ulceration, desquamation, or sometimes non-pruritic purulent yellow-whitish nodules, which usually occur on hands, fingers, and arms and can be single or multiple (70, 99, 117, 163, 185, 193). Orf may lead to the formation of hyperkeratotic nodules underneath fingernails, and erythematous, centrally ulcerated, hemorrhagic fragile nodules, and papillomatous projections on the face (71, 72). A nodular mass with erythema on the nose caused by orf virus infection is also reported (14). In a human case (140), Orf lesions that are formed as fungating and painful masses and cause obliteration of the toenail can be observed on the toe in a human case (140). Erythema multiforme development is reported in several human cases following orf infection (66, 90). Orf infection does not result in any pathology in the foetus during pregnancy and culminates with healthy labour and babies (24, 181).

Control and treatment: There are vaccines against orf in animals, but despite vaccination, there can be outbreaks of orf in small ruminant herds (42). Local antiseptics can be applied to the lesions of an affected animal, antibiotics can be used for secondary bacterial infection, and supportive treatment should be administered to young animals that cannot be fed due to oral lesions (176).

For humans, there is no specific orf vaccine. The orf lesions in humans generally spontaneously heal within 2–8 weeks without any specific treatment (30, 189) and local antiseptic therapy is usually sufficient in order to prevent

secondary infections (99). For exophytic lesions of the orf in humans, curettage and cautery can be an alternative treatment (94).

Pseudocowpox virus

Epidemiology: Pseudocowpox virus is a parapoxvirus and its infection, usually referred to as milker's nodule, affects cattle, other wild ruminants, and humans. Veterinarian, milkers, farmers, and animal workers are occupationally predisposed to pseudocowpox virus infection (5, 87, 199). Infection develops by direct contact with the lesions of an affected animal, usually during milking or following a bite of infected cattle (5, 34, 87, 118, 199).

Pseudocowpox virus is detected in cattle, American bison, water buffalo, camels, and cats (3, 58, 101, 172). Some tick species that are collected from cattle are found to be positive for pseudocowpox virus by PCR, indicating that ticks can play a role in pseudocowpox virus epidemiology (35, 141). Houseflies on barns can be a mechanical vector for the pseudocowpox virus (171).

Clinical signs: Pseudocowpox virus infection leads to lesions described as "ring" or "horseshoe", which are pathognomonic for the disease, and nodules, pustules, and ulceration, usually on the teats and udders (97, 138). Rare cases show vesicles, erosions, papules, and scabs on the vulva and vaginal mucosa, and also, development of hyperemia and white vesicles on the sublingual mucosa is reported in pseudocowpox virus infection in cattle (139). In experimental infection, hyperemic foci, ulceration, fibrinotic and scabby lesions were observed on the muzzle and lips of calves (54). Pseudocowpox virus infection is exhibited as multiple cutaneous nodules on the skin which are wart-like, proliferative, and keratinized in an American bison (172). In water buffalos, pseudocowpox symptoms are peeling of the tongue epithelium and oral ulcers (101). Pseudocowpox virus infection in camels causes papules, pustules, ulcers, and scabs on the lips, muzzles, and eyelids (3).

Milker's nodule has 5-15 days of incubation period, and lesions progress through six stages: maculopapular (erythematous nodule), targetoid (central papule with an erythematous outer ring and a pale inner ring), acute (ulceration and draining of nodule), regenerative (firm nodules, black papules, and crusts develop), papillomatous, and regression (76). Milker's nodule is clinically presented as erythema, small red macule, papule, nodule (can be with blue-violet bulla or crusted), blue-black nodulopustule, yellowish plaque, papulovesicule, erosion, crusting, and usually heals without eschar, but sometimes discoloration may develop (5, 34, 87, 118, 199). Complications such as lymphadenopathy, lymphadenomegaly, lymphangitis, erythematous papular rash, erythema multiforme, bacterial infection, etc. may occur (34, 151, 205).

Control and treatment: There is no specific vaccine for humans or animals against the pseudocowpox virus. Because most cases heal spontaneously, there is no need for treatment. However, if needed, infected humans and animals can be treated with antiseptics and antibiotics in order to prevent secondary bacterial infections (3, 76).

Grey sealpox virus

Sealpox virus is in the Parapoxvirus genus. Its infection is zoonotic and it primarily infects pinnipeds (seals and sea lions). The high-risk groups of humans are the marine mammal workers and handlers in rehabilitation facilities and parks, veterinary technicians, and veterinarians. The virus is transmitted from animal-to-human via direct contact or biting of an infected animal. The lesions of sealpox in pinnipeds are firm skin nodules that develop throughout the body, such as on the head, neck, thorax, abdomen, flippers, and white-gray verrucose nodules on the oral mucosa and tongue. The lesions usually heal spontaneously with a slightly raised, grey, furless scar formation. Infection of young animals that causes oral lesions may be fatal due to aversion to food intake. The sealpox virus causes lesions like orf and milker's nodule in humans. Tender nodule, grey bullous lesion, lesion with a red center and a pale margin, and scab are the most common lesions on the hands. There is no vaccine or specific treatment against sealpox infection for both humans and animals (20, 36, 40, 79, 130, 161, 188).

Red deerpox virus

Deerpox virus, which is a parapoxvirus, is a very rare zoonotic agent that causes lesions on the muzzle of deer. A possible transmission route is direct skin-to-skin contact with an affected animal. In deer, papillomatous lesions, alopecic, flat, proliferative dermal lesions, ulcers, and scabby lesions may develop in a variety of parts of the body, i.e., lips, oral cavity, tongue, muzzle, velvet, nose, ears, ventral thorax, limbs, abdomen. In human cases of deerpox virus infection, tumour-like painless greyish necrotic lesions, haemorrhagic crust, and granulomatous lesions with greyish spots are developed on the hands and face. Some human cases may have fever, lymphadenopathy, and nausea. There is no vaccine or specific treatment against deerpox virus infection (17, 59, 81).

Conclusion

The monkeypox outbreak in 2022 showed that challenges between humanity and viruses continue and will go on. The monkeypox outbreak that makes it more serious than previous outbreaks are severe clinical outcomes such as encephalitis and death, and also the higher transmission rate, which occurs at approximately 99% in men, especially men who have sex with men. The

presence of the aforementioned zoonotic infections in many different animal species is a problem and a big challenge to fighting the diseases. It is a matter of debate why the monkeypox virus 2022 outbreak spread so quickly but not in other poxviruses. Variables such as increased mutation rate due to natural evolution, suspicion of bioterrorism, overpopulation, the possibility and ease of travel between continents and countries, and changes in lifestyle may have influenced the epidemiology and treatment of the monkeypox virus 2022 outbreak. The availability of an effective vaccine against monkeypox virus provides a good protection and control strategy. However, mandatory or optional use of the vaccine or difficulties in accessing the vaccine in all countries should be a topic for discussion by health organizations, scientists, and policy makers.

Financial Support

This research received no grant from any funding agency/sector.

Ethical Statement

This study does not present any ethical concerns.

Conflict of Interest

The authors declared that there is no conflict of interest.

References

1. **Abrahão JS, Oliveira TM, Campos RK, et al** (2009): *Bovine vaccinia outbreaks: detection and isolation of vaccinia virus in milk samples*. Foodborne Pathog Dis, **6**, 1141-1146.
2. **Abrahão JS, Silva-Fernandes AT, Assis FL, et al** (2010): *Human Vaccinia virus and Pseudocowpox virus co-infection: clinical description and phylogenetic characterization*. J Clin Virol, **48**, 69-72.
3. **Abubakr MI, Abu-Elzein EM, Housawi FM, et al** (2007): *Pseudocowpox virus: the etiological agent of contagious ecthyma (Auzdyk) in camels (Camelus dromedarius) in the Arabian Peninsula*. Vector Borne Zoonotic Dis, **7**, 257-260.
4. **Adler H, Gould S, Hine P, et al** (2022): *Clinical features and management of human monkeypox: a retrospective observational study in the UK*. Lancet Infect Dis, **22**, 1153-1162.
5. **Adriano AR, Quiroz CD, Acosta ML, et al** (2015): *Milker's nodule--Case report*. An Bras Dermatol, **90**, 407-410.
6. **Ajmera KM, Goyal L, Pandit T, et al** (2022): *Monkeypox - An emerging pandemic*. IDCases, **29**, e01587.
7. **Alajlan AM, Alsubeeh NA** (2020): *Orf (ecthyma contagiosum) transmitted from a camel to a human: a case report*. Am J Case Rep, **21**, e927579.
8. **Alakunle E, Moens U, Nchinda G, et al** (2020): *Monkeypox Virus in Nigeria: Infection Biology, Epidemiology, and Evolution*. Viruses, **12**, 1257.
9. **Anderson MG, Frenkel LD, Homann S, et al** (2003): *A case of severe monkeypox virus disease in an American child: emerging infections and changing professional values*. Pediatr Infect Dis J, **22**, 1093-1098.
10. **Andreani J, Arnault JP, Bou Khalil JY, et al** (2019): *Atypical Cowpox Virus Infection in Smallpox-Vaccinated Patient, France*. Emerg Infect Dis, **25**, 212-219.
11. **Anonymous** (2022): *An APOBEC3 molecular clock to estimate the date of emergence of hMPXV*. Available at <https://virological.org/t/an-apobec3-molecular-clock-to-estimate-the-date-of-emergence-of-hmpvx/885> (Accessed August 10, 2022).
12. **Anonymous** (2022): *Texas Confirms First Death of a Person with Monkeypox*. Available at <https://dshs.texas.gov/news-alerts/texas-confirms-first-death-of-a-person-with-monkeypox/> (Accessed September 4, 2022).
13. **Assis FL, Borges IA, Mesquita VS, et al** (2013): *Vaccinia virus in household environment during bovine vaccinia outbreak, Brazil*. Emerg Infect Dis, **19**, 2045-2047.
14. **Ata N, Gögüş HE, Kiliç S** (2017): *Giant orf on the nose*. J Craniofac Surg, **28**, e234-e235.
15. **Bala JA, Balakrishnan KN, Abdullah AA, et al** (2018): *The re-emerging of orf virus infection: A call for surveillance, vaccination and effective control measures*. Microb Pathog, **120**, 55-63.
16. **Barquet N, Domingo P** (1997): *Smallpox: the triumph over the most terrible of the ministers of death*. Ann Intern Med, **127**, 635-642.
17. **Baughman B, Zhang S, Jin L, et al** (2011): *Diagnosis of deerpox virus infection in a white-tailed deer (Odocoileus virginianus) fawn*. J Vet Diagn Invest, **23**, 965-970.
18. **Baxby D, Ashton DG, Jones DM, et al** (1982): *An outbreak of cowpox in captive cheetahs: virological and epidemiological studies*. J Hyg (Lond), **89**, 365-372.
19. **Bayindir Y, Bayraktar M, Karadag N, et al** (2011): *Investigation and analysis of a human orf outbreak among people living on the same farm*. New Microbiol, **34**, 37-43.
20. **Becher P, König M, Müller G, et al** (2002): *Characterization of sealpox virus, a separate member of the parapoxviruses*. Arch Virol, **147**, 1133-1140.
21. **Beer EM, Rao VB** (2019): *A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy*. PLoS Negl Trop Dis, **13**, e0007791.
22. **Bowman KF, Barbery RT, Swango LJ, et al** (1981): *Cutaneous form of bovine papular stomatitis in man*. JAMA, **246**, 2813-2818.
23. **Bragazzi NL, Kong JD, Mahroum N, et al** (2022): *Epidemiological trends and clinical features of the ongoing monkeypox epidemic: A preliminary pooled data analysis and literature review*. J Med Virol, 2022, 1-8.
24. **Bülbül Başkan E, Yılmaz E, Doğruk S, et al** (2005): *Orf virus infection in pregnancy: a case report*. Türkiye Klinikleri J Med Sci, **25**, 137-139.
25. **Bunge EM, Hoet B, Chen L, et al** (2022): *The changing epidemiology of human monkeypox-A potential threat? A systematic review*. PLoS Negl Trop Dis, **16**, e0010141.
26. **Cabanillas B, Valdelvira R, Akdis CA** (2022): *Monkeypox outbreak in Europe, UK, North America, and*

- Australia: A changing trend of a zoonotic disease.* Allergy, **77**, 2284-2286.
27. **Campe H, Zimmermann P, Glos K, et al** (2009): *Cowpox virus transmission from pet rats to humans, Germany.* Emerg Infect Dis, **15**, 777-780.
 28. **CDC** (2003): *Multistate outbreak of monkeypox--Illinois, Indiana, and Wisconsin, 2003.* MMWR Morb Mortal Wkly Rep, **52**, 537-540.
 29. **CDC** (2003): *Update: multistate outbreak of monkeypox--Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003.* MMWR Morb Mortal Wkly Rep, **52**, 642-646.
 30. **CDC** (2006): *Orf virus infection in humans--New York, Illinois, California, and Tennessee, 2004-2005.* MMWR Morb Mortal Wkly Rep, **55**, 65-68.
 31. **CDC** (2012): *Human Orf virus infection from household exposures - United States, 2009-2011.* MMWR Morb Mortal Wkly Rep, **61**, 245-248.
 32. **CDC** (2019): *Vaccines.* Available at <https://www.cdc.gov/smallpox/clinicians/vaccines.html> (Accessed June 24, 2022).
 33. **CDC** (2022): *Pets in the Home.* Available at <https://www.cdc.gov/poxvirus/monkeypox/specific-settings/pets-in-homes.html> (Accessed August 16, 2022).
 34. **Ceović R, Pasić A, Lipozencić J, et al** (2007): *Milker's nodule--case report.* Acta Dermatovenerol Croat, **15**, 88-91.
 35. **Cicculli V, Ayhan N, Luciani L, et al** (2022): *Molecular detection of parapoxvirus in Ixodidae ticks collected from cattle in Corsica, France.* Vet Med Sci, **8**, 907-916.
 36. **Clark C, McIntyre PG, Evans A, et al** (2005): *Human sealpox resulting from a seal bite: confirmation that sealpox virus is zoonotic.* Br J Dermatol, **152**, 791-793.
 37. **Costa GB, Borges IA, Alves PA, et al** (2015): *Alternative routes of zoonotic vaccinia virus transmission, Brazil.* Emerg Infect Dis, **21**, 2244-2246.
 38. **Costa GB, Miranda JB, Almeida GG, et al** (2017): *Detection of vaccinia virus in urban domestic cats, Brazil.* Emerg Infect Dis, **23**, 360-362.
 39. **Costa GB, Ribeiro de Almeida L, et al** (2018): *Vaccinia virus among domestic dogs and wild coatis, Brazil, 2013-2015.* Emerg Infect Dis, **24**, 2338-2342.
 40. **Costa H, Klein J, Breines EM, et al** (2021): *A comparison of parapoxviruses in North American pinnipeds.* Front Vet Sci, **8**, 653094.
 41. **Costello V, Sowash M, Gaur A, et al** (2022): *Imported Monkeypox from International Traveler, Maryland, USA, 2021.* Emerg Infect Dis, **28**, 1002-1005.
 42. **da Costa RA, Cargnelutti JF, Schild CO, et al** (2019): *Outbreak of contagious ecthyma caused by Orf virus (Parapoxvirus ovis) in a vaccinated sheep flock in Uruguay.* Braz J Microbiol, **50**, 565-569.
 43. **Dal Pozzo F, Martinelle L, Gallina L, et al** (2011): *Original findings associated with two cases of bovine papular stomatitis.* J Clin Microbiol, **49**, 4397-4400.
 44. **Damon IK** (2007): *Poxviruses. 2947-2975.* In: DM Knipe, PM Howley (Eds), Fields Virology. Lippincott Williams & Wilkins, Philadelphia.
 45. **De Baetselier I, Van Dijck C, Kenyon C, et al** (2022): *Retrospective detection of asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium.* Nat Med.
 46. **de Oliveira CH, Assis FL, Neto JD, et al** (2012): *Multifocal cutaneous ORF virus infection in goats in the Amazon region, Brazil.* Vector Borne Zoonotic Dis, **12**, 336-340.
 47. **de Oliveira TML, Guedes MIMC, Rehfeld IS, et al** (2018): *Vaccinia virus detection in dairy products made with milk from experimentally infected cows.* Transbound Emerg Dis, **65**, e40-e47.
 48. **de Sant'Ana FJ, Rabelo RE, Vulcani VA, et al** (2012): *Bovine papular stomatitis affecting dairy cows and milkers in midwestern Brazil.* J Vet Diagn Invest, **24**, 442-445.
 49. **de Souza Trindade G, Drumond BP, Guedes MI, et al** (2007): *Zoonotic vaccinia virus infection in Brazil: clinical description and implications for health professionals.* J Clin Microbiol, **45**, 1370-1372.
 50. **Duchateau NC, Aerts O, Lambert J** (2014): *Autoinoculation with Orf virus (ecthyma contagiosum).* Int J Dermatol, **53**, e60-2.
 51. **Dugmore WN, Dabir ZM** (1992): *Cowpox virus.* Br J Ophthalmol, **76**, 510.
 52. **Duraffour S, Andrei G, Snoeck R** (2010): *Tecovirimat, a p37 envelope protein inhibitor for the treatment of smallpox infection.* IDrugs, **13**, 181-191.
 53. **EAZWV** (2019): *Transmissible Diseases Handbook, fifth edition.* Available at https://www.eazwv.org/page/inf_handbook (Accessed June 24, 2022).
 54. **Ebling R, Martins B, Jardim JC, et al** (2020): *Late development of pustular, erosive lesions in the muzzle of calves inoculated with Pseudocowpox virus.* Microb Pathog, **143**, 104122.
 55. **Erez N, Achdout H, Milrot E, et al** (2019): *Diagnosis of Imported Monkeypox, Israel, 2018.* Emerg Infect Dis, **25**, 980-983.
 56. **Eseigbe EE, Akude C, Osagie IA, et al** (2021): *Human Monkey Pox Virus Infection in Plateau State, North Central Nigeria: A Report of Two Cases.* West Afr J Med, **38**, 1242-1246.
 57. **Essbauer S, Pfeffer M, Meyer H** (2010): *Zoonotic poxviruses.* Vet Microbiol, **140**, 229-236.
 58. **Fairley RA, Mercer AA, Copland CI, et al** (2013): *Persistent pseudocowpox virus infection of the skin of a foot in a cat.* N Z Vet J, **61**, 242-243.
 59. **Falk ES** (1978): *Parapoxvirus infections of reindeer and musk ox associated with unusual human infections.* Br J Dermatol, **99**, 647-654.
 60. **FDA** (2022): *Smallpox Preparedness and Response Updates from FDA.* Available at [https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/smallpox-preparedness-and-response-updates-fda#:~:text=Aventis%20Pasteur%20Smallpox%20Vaccine%20\(APS,depleted%20or%20not%20readily%20available](https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/smallpox-preparedness-and-response-updates-fda#:~:text=Aventis%20Pasteur%20Smallpox%20Vaccine%20(APS,depleted%20or%20not%20readily%20available). (Accessed August 16, 2022).
 61. **Ferrier A, Frenois-Veyrat G, Schvoerer E, et al** (2021): *Fatal Cowpox Virus Infection in Human Fetus, France, 2017.* Emerg Infect Dis, **27**, 2570-2577.
 62. **Foster SO, Brink EW, Hutchins DL, et al** (1972): *Human monkeypox.* Bull World Health Organ, **46**, 569-576.
 63. **Franco-Luiz AP, Oliveira DB, Pereira AF, et al** (2016): *Detection of vaccinia virus in dairy cattle serum samples from 2009, Uruguay.* Emerg Infect Dis, **22**, 2174-2177.

64. Frandsen J, Enslow M, Bowen AR (2011): *Orf parapoxvirus infection from a cat scratch*. Dermatol Online J, **17**, 9.
65. Franke A, Kershaw O, Jenckel M, et al (2016): *Fatal cowpox virus infection in an aborted foal*. Vector Borne Zoonotic Dis, **16**, 431-433.
66. Gallina L, Veronese F, Farinelli P, et al (2016): *Erythema multiforme after orf virus infection*. Epidemiol Infect, **144**, 88-89.
67. Garcia-Arriaza J, Esteban M, López D (2021): *Modified vaccinia virus Ankara as a viral vector for vaccine candidates against chikungunya virus*. Biomedicines, **9**, 1122.
68. Gazzani P, Gach JE, Colmenero I, et al (2017): *Fatal disseminated cowpox virus infection in an adolescent renal transplant recipient*. Pediatr Nephrol, **32**, 533-536.
69. Gigante CM, Korber B, Seabolt MH, et al (2022): *Multiple lineages of Monkeypox virus detected in the United States, 2021- 2022*. bioRxiv preprint.
70. Ginzburg VE, Liauchonak I (2017): *Human orf: Atypical rash in an urban medical practice*. Can Fam Physician, **63**, 769-771.
71. Gore Karaali M, Gurel MS, Sarı Y, et al (2022): *Solitary Subungual Orf*. J Hand Surg Am, **47**, 194.e1-194.e3.
72. Gore Karaali M, Koku Aksu AE, Kara Polat A, et al (2021): *Solitary facial lesion of orf: An unusual presentation*. North Clin Istanbul, **8**, 626-628.
73. Grönemeyer LL, Baltzer A, Broekaert S, et al (2017): *Generalised cowpox virus infection*. Lancet, **390**, 1769.
74. Haddadeen C, Van Ouwerkerk M, Viecek T, et al (2020): *A case of cowpox virus infection in the UK occurring in a domestic cat and transmitted to the adult male owner*. Br J Dermatol, **183**, e190.
75. Hammerschlag Y, MacLeod G, Papadakis G, et al (2022): *Monkeypox infection presenting as genital rash, Australia, May 2022*. Euro Surveill, **27**, 2200411.
76. Handler NS, Handler MZ, Rubins A, et al (2018): *Milker's nodule: an occupational infection and threat to the immunocompromised*. J Eur Acad Dermatol Venereol, **32**, 537-541.
77. Happi C, Adetifa I, Mbala P, et al (2022): *Urgent need for a non-discriminatory and non-stigmatizing nomenclature for monkeypox virus*. PLoS Biol, **20**, e3001769.
78. Hemmer CJ, Littmann M, Löbermann M, et al (2010): *Human cowpox virus infection acquired from a circus elephant in Germany*. Int J Infect Dis, **14**, e338-340.
79. Hicks BD, Worthy GA (1987): *Sealpox in captive grey seals (Halichoerus grypus) and their handlers*. J Wildl Dis, **23**, 1-6.
80. Holmes P, Richey M, McInnes C, et al (2011): *Zoonotic transmission of bovine papular stomatitis virus*. Vet Rec, **169**, 235-236.
81. Horner GW, Robinson AJ, Hunter R, et al (1987): *Parapoxvirus infections in New Zealand farmed red deer (Cervus elaphus)*. N Z Vet J, **35**, 41-45.
82. Hosamani M, Scagliarini A, Bhanuprakash V, et al (2009): *Orf: an update on current research and future perspectives*. Expert Rev Anti Infect Ther, **7**, 879-893.
83. ICTV (2021): *Virus Taxonomy: 2021 Release*. Available at <https://talk.ictvonline.org/taxonomy/> (Accessed June 24, 2022).
84. Inoshima Y, Nakane T, Sentsui H (2009): *Severe dermatitis on cattle teats caused by bovine papular stomatitis virus*. Vet Rec, **164**, 311-312.
85. Isidro J, Borges V, Pinto M, et al (2022): *Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus*. Nat Med.
86. Janseghers L, Matamba M, Colaert J, et al (1984): *Fatal monkeypox in a child in Kikwit, Zaire*. Ann Soc Belg Med Trop, **64**, 295-298.
87. Jayasree P, Kaliyadan F, Abraham R (2020): *Milker's Nodule*. JAMA Dermatol, **156**, 93.
88. Jeckel S, Bidewell C, Everest D, et al (2011): *Severe oesophagitis in an adult bull caused by bovine papular stomatitis virus*. Vet Rec, **169**, 317.
89. Jolly B, Scaria V (2022): *A distinct phylogenetic cluster of Monkeypox genomes suggests an early and cryptic spread of the virus*. J Infect, S0163-4453(22)00476-5.
90. Joseph RH, Haddad FA, Matthews AL, et al (2015): *Erythema multiforme after orf virus infection: a report of two cases and literature review*. Epidemiol Infect, **143**, 385-390.
91. Jungwirth N, Puff C, Köster K, et al (2018): *Atypical cowpox virus infection in a series of cats*. J Comp Pathol, **158**, 71-76.
92. Kalthoff D, Bock WI, Hühn F, et al (2014): *Fatal cowpox virus infection in cotton-top tamarins (Saguinus oedipus) in Germany*. Vector Borne Zoonotic Dis, **14**, 303-305.
93. Kato M, Kawashima D, Ito Y, et al (2021): *Successful measures to prevent the spread of bovine papular stomatitis in a dairy farm*. J Vet Med Sci, **83**, 304-308.
94. Key SJ, Catania J, Mustafa SF, et al (2007): *Unusual presentation of human giant orf (ecthyma contagiosum)*. J Craniofac Surg, **18**, 1076-1078.
95. Kimball S (2022): *Biden administration declares monkeypox outbreak a public health emergency in the U.S.* Available at <https://www.cnn.com/2022/08/04/biden-administration-will-declare-monkeypox-outbreak-a-public-health-emergency-in-the-us.html> (Accessed August 8, 2022).
96. Kitchen M, Müller H, Zobl A, et al (2014): *ORF virus infection in a hunter in Western Austria, presumably transmitted by game*. Acta Derm Venereol, **94**, 212-214.
97. Knowles D (2011): *Poxviridae*. 151-165. In: NJ MacLachlan, EJ Dubovi (Eds), Fenner's Veterinary Virology. Academic Press, San Diego.
98. Krankowska DC, Woźniak PA, Cybula A, et al (2021): *Cowpox: How dangerous could it be for humans? Case report*. Int J Infect Dis, **104**, 239-241.
99. Kromer C, Bierschenk C, Czerny CP, et al (2018): *Orf (ecthyma contagiosum) in a sheep and a shepherd*. Lancet Infect Dis, **18**, 122.
100. Ladnyj ID, Ziegler P, Kima E (1972): *A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo*. Bull World Health Organ, **46**, 593-597.
101. Laguardia-Nascimento M, de Oliveira AP, Fernandes FR, et al (2017): *Detection of pseudocowpox virus in water buffalo (Bubalus bubalis) with vesicular disease in the state of São Paulo, Brazil, in 2016*. Vet Q, **37**, 16-22.
102. Laiton-Donato K, Ávila-Robayo P, Pérez-Martínez A, et al (2020): *Progressive vaccinia acquired through zoonotic*

- transmission in a patient with HIV/AIDS, Colombia. Emerg Infect Dis*, **26**, 601-605.
103. **Lansiaux E, Jain N, Laivacuma S, et al** (2022): The virology of human monkeypox virus (hMPXV): a brief overview. Available at https://www.researchgate.net/publication/361245313_The_Virology_of_Human_Monkeypox_Virus_hMPXV_A_Brief_Overview (Accessed August 10, 2022).
 104. **Lapa D, Carletti F, Mazzotta V, et al** (2022): Monkeypox virus isolation from a semen sample collected in the early phase of infection in a patient with prolonged seminal viral shedding. *Lancet Infect Dis*, **22**, 1267-1269.
 105. **Lederman ER, Austin C, Trevino I, et al** (2007): ORF virus infection in children: clinical characteristics, transmission, diagnostic methods, and future therapeutics. *Pediatr Infect Dis J*, **26**, 740-744.
 106. **Leonard D, Otter A, Everest D, et al** (2009): Unusual bovine papular stomatitis virus infection in a British dairy cow. *Vet Rec*, **164**, 65.
 107. **Lewis A, Josiowicz A, Hirmas Riade SM, et al** (2022): Introduction and differential diagnosis of monkeypox in Argentina, 2022. *Emerg Infect Dis*, **28**.
 108. **Lewis MW, Graham MB, Hammarlund E, et al** (2007): Monkeypox without exanthem. *N Engl J Med*, **356**, 2112-2114.
 109. **Lima MT, Oliveira GP, Assis FL, et al** (2018): Ocular vaccinia infection in dairy worker, Brazil. *Emerg Infect Dis*, **24**, 161-162.
 110. **Lourie B, Bingham PG, Evans HH, et al** (1972): Human infection with monkeypox virus: laboratory investigation of six cases in West Africa. *Bull World Health Organ*, **46**, 633-639.
 111. **Lu B, Cui LB, Gu MH, et al** (2019): Outbreak of vaccinia virus infection from occupational exposure, China, 2017. *Emerg Infect Dis*, **25**, 1192-1195.
 112. **Luong Nguyen LB, Ghosn J, Durier C, et al** (2022): A prospective national cohort evaluating ring MVA vaccination as post-exposure prophylaxis for monkeypox. *Nat Med*.
 113. **Ma W, Pang M, Lei X, et al** (2022): Orf Virus Detection in the Saliva and Milk of Dairy Goats. *Front Microbiol*, **13**, 837808.
 114. **Ma Y, Chen M, Bao Y, et al** (2022): MPoxVR: A comprehensive genomic resource for monkeypox virus variant surveillance. *Innovation (Camb)*, **3**, 100296.
 115. **Maki J, Guiot AL, Aubert M, et al** (2017): Oral vaccination of wildlife using a vaccinia-rabies-glycoprotein recombinant virus vaccine (RABORAL V-RG®): a global review. *Vet Res*, **48**, 57.
 116. **Mandavilli A** (2022): W.H.O. Declares Monkeypox Spread a Global Health Emergency. Available at <https://www.nytimes.com/2022/07/23/health/monkeypox-pandemic-who.html> (Accessed August 8, 2022).
 117. **Maor D, Yu LL, Brand R** (2017): A case of orf disease in a patient with scleroderma. *JAAD Case Rep*, **3**, 155-157.
 118. **Marckmann D, Frasnelli A** (2020): Milker's nodule (Pseudocowpox) in a female patient following a calf bite. *Dtsch Arztebl Int*, **117**, 870.
 119. **Marennikova SS, Maltseva NN, Korneeva VI, et al** (1977): Outbreak of pox disease among carnivora (felidae) and edentata. *J Infect Dis*, **135**, 358-366.
 120. **Marennikova SS, Seluhina EM, Mal'ceva NN, et al** (1972): Poxviruses isolated from clinically ill and asymptotically infected monkeys and a chimpanzee. *Bull World Health Organ*, **46**, 613-620.
 121. **Martina BE, van Doornum G, Dorrestein GM, et al** (2006): Cowpox virus transmission from rats to monkeys, the Netherlands. *Emerg Infect Dis*, **12**, 1005-1007.
 122. **Marty AM** (2022): Why is there expanding community transmission of monkeypox in 2022? *Lancet Microbe*, **S2666-5247(22)00200-2**.
 123. **Mbala PK, Huggins JW, Riu-Rovira T, et al** (2017): Maternal and fetal outcomes among pregnant women with human monkeypox infection in the Democratic Republic of Congo. *J Infect Dis*, **216**, 824-828.
 124. **McEvoy JD, Allan BC** (1972): Isolation of bovine papular stomatitis virus from humans. *Med J Aust*, **1**, 1254-1256.
 125. **Megid J, Borges IA, Abrahão JS, et al** (2012): Vaccinia virus zoonotic infection, São Paulo State, Brazil. *Emerg Infect Dis*, **18**, 189-191.
 126. **Micheloud JF, Aguirre LS, Sandoval GV, et al** (2020): Detection and first molecular characterization of bovine papular stomatitis virus in dairy calves in Argentina. *Trop Anim Health Prod*, **52**, 453-459.
 127. **Mileto D, Riva A, Cutrera M, et al** (2022): New challenges in human monkeypox outside Africa: A review and case report from Italy. *Travel Med Infect Dis*, **49**, 102386.
 128. **Miura F, van Ewijk CE, Backer JA, et al** (2022): Estimated incubation period for monkeypox cases confirmed in the Netherlands, May 2022. *Euro Surveill*, **27**, 2200448.
 129. **Morgan CN, Whitehill F, Doty JB, et al** (2022): Environmental Persistence of Monkeypox Virus on Surfaces in Household of Person with Travel-Associated Infection, Dallas, Texas, USA, 2021. *Emerg Infect Dis*, **28**.
 130. **Müller G, Gröters S, Siebert U, et al** (2003): Parapoxvirus infection in harbor seals (*Phoca vitulina*) from the German North Sea. *Vet Pathol*, **40**, 445-454.
 131. **Mutombo M, Arita I, Jezek Z** (1983): Human monkeypox transmitted by a chimpanzee in a tropical rain-forest area of Zaire. *Lancet*, **1**, 735-737.
 132. **Nicholas AH** (1970): A poxvirus of primates. I. Growth of the virus in vitro and comparison with other poxviruses. *J Natl Cancer Inst*, **45**, 897-905.
 133. **Ninove L, Domart Y, Vervel C, et al** (2009): Cowpox virus transmission from pet rats to humans, France. *Emerg Infect Dis*, **15**, 781-784.
 134. **Noe S, Zange S, Seilmaier M, et al** (2022): Clinical and virological features of first human monkeypox cases in Germany. *Infection*, **1-6**.
 135. **Nolen LD, Osadebe L, Katomba J, et al** (2016): Extended Human-to-Human Transmission during a Monkeypox Outbreak in the Democratic Republic of the Congo. *Emerg Infect Dis*, **22**, 1014-1021.
 136. **Oem JK, Lee EY, Lee KK, et al** (2013): Bovine papular stomatitis virus (BPSV) infections in Korean native cattle. *J Vet Med Sci*, **75**, 675-678.
 137. **Ogoina D, Iroezindu M, James HI, et al** (2020): Clinical Course and Outcome of Human Monkeypox in Nigeria. *Clin Infect Dis*, **71**, e210-e214.

138. Oğuzoğlu TÇ, Koç BT, Kirdeci A, et al (2014): *Evidence of zoonotic pseudocowpox virus infection from a cattle in Turkey*. *Virusdisease*, **25**, 381-384.
139. Ohtani A, Yokoyama A, Narushige H, et al (2017): *First isolation and genetic characterization of pseudocowpox virus from cattle in Japan*. *Virol J*, **14**, 172.
140. Opene C, Fung MA, Silverstein M (2021): *Orf progressiva: giant progressive and destructive infections in the immunocompromised*. *Dermatol Online J*, **27**, 13030/qt97d3k1pr.
141. Ouedraogo A, Luciani L, Zannou O, et al (2020): *Detection of two species of the genus Parapoxvirus (bovine papular stomatitis virus and pseudocowpox virus) in ticks infesting cattle in Burkina Faso*. *Microorganisms*, **8**, 644.
142. Pahlitzsch R, Hammarin AL, Widell A (2006): *A case of facial cellulitis and necrotizing lymphadenitis due to cowpox virus infection*. *Clin Infect Dis*, **43**, 737-742.
143. Patrocinio-Jesus R, Peruzzi F (2022): *Monkeypox Genital Lesions*. *N Engl J Med*, **387**, 66.
144. Patrono LV, Pléh K, Samuni L, et al (2020): *Monkeypox virus emergence in wild chimpanzees reveals distinct clinical outcomes and viral diversity*. *Nat Microbiol*, **5**, 955-965.
145. Peiró-Mestres A, Fuertes I, Camprubí-Ferrer D, et al (2022): *Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022*. *Euro Surveill*, **27**, 2200503.
146. Pereira Oliveira G, Tavares Silva Fernandes A, Lopes de Assis F, et al (2014): *Intrafamilial transmission of Vaccinia virus during a bovine Vaccinia outbreak in Brazil: a new insight in viral transmission chain*. *Am J Trop Med Hyg*, **90**, 1021-1023.
147. Peres MG, Bacchiega TS, Appolinário CM, et al (2018): *Vaccinia virus in blood samples of humans, domestic and wild mammals in Brazil*. *Viruses*, **10**, 42.
148. Peres MG, Barros CB, Appolinário CM, et al (2016): *Dogs and opossums positive for vaccinia virus during outbreak affecting cattle and humans, São Paulo State, Brazil*. *Emerg Infect Dis*, **22**, 271-273.
149. Perez JC, Lounnas V (2022): *May 2022: Peculiar Evolution of the Monkeypox Virus Genomes*. Available at https://www.researchgate.net/publication/361024980_May_2022_Peculiar_Evolution_of_the_Monkeypox_Virus_Genomes (Accessed August 10, 2022).
150. Petersen BW, Kabamba J, McCollum AM, et al (2019): *Vaccinating against monkeypox in the Democratic Republic of the Congo*. *Antiviral Res*, **162**, 171-177.
151. Phillips ZC, Holfeld KI, Lang AL, et al (2020): *A case of milker's nodules in Saskatchewan, Canada*. *SAGE Open Med Case Rep*, **8**, 2050313X20984118.
152. Philpott D, Hughes CM, Alroy KA, et al (2022): *Epidemiologic and Clinical Characteristics of Monkeypox Cases - United States, May 17-July 22, 2022*. *MMWR Morb Mortal Wkly Rep*, **71**, 1018-1022.
153. Prier JE, Sauer RM (1960): *A pox disease of monkeys*. *Ann N Y Acad Sci*, **85**, 951-959.
154. Radonić A, Metzger S, Dabrowski PW, et al (2014): *Fatal monkeypox in wild-living sooty mangabey, Côte d'Ivoire, 2012*. *Emerg Infect Dis*, **20**, 1009-1011.
155. Rajkomar V, Hannah M, Coulson IH, et al (2016): *A case of human to human transmission of orf between mother and child*. *Clin Exp Dermatol*, **41**, 60-63.
156. Rao AK, Schulte J, Chen TH, et al (2022): *Monkeypox in a Traveler Returning from Nigeria - Dallas, Texas, July 2021*. *MMWR Morb Mortal Wkly Rep*, **71**, 509-516.
157. Reuters (2022): *Turkey records first case of monkeypox - health minister*. Available at <https://www.reuters.com/world/middle-east/turkey-records-first-case-monkeypox-health-minister-2022-06-30/> (Accessed July 25, 2022).
158. Reynolds MG, Yorita KL, Kuehnert MJ, et al (2006): *Clinical manifestations of human monkeypox influenced by route of infection*. *J Infect Dis*, **194**, 773-80.
159. Riedel S (2005): *Edward Jenner and the history of smallpox and vaccination*. *Proc (Bayl Univ Med Cent)*, **18**, 21-25.
160. Rivetti AV Jr, Guedes MI, Rehfeld IS, et al (2013): *Bovine vaccinia, a systemic infection: evidence of fecal shedding, viremia and detection in lymphoid organs*. *Vet Microbiol*, **162**, 103-111.
161. Roess AA, Levine RS, Barth L, et al (2011): *Sealpox virus in marine mammal rehabilitation facilities, North America, 2007-2009*. *Emerg Infect Dis*, **17**, 2203-2208.
162. Saey TH, Garcia de Jesús EI (2022): *Monkeypox is not a global health emergency for now, WHO says*. Available at <https://www.sciencenews.org/article/monkeypox-who-not-global-public-health-emergency> (Accessed August 8, 2022).
163. Sasmaz S, Uzel M, Sener S, et al (2011): *Rare presentation of human orf as multiple lesions*. *J Dermatol*, **38**, 825-826.
164. Schmiedeknecht G, Eickmann M, Köhler K, et al (2010): *Fatal cowpox virus infection in captive banded mongooses (Mungos mungo)*. *Vet Pathol*, **47**, 547-552.
165. Seang S, Burrell S, Todesco E, et al (2022): *Evidence of human-to-dog transmission of monkeypox virus*. *Lancet*, **S0140-6736(22)01487-8**.
166. Sebastian S, Gilbert SC (2016): *Recombinant modified vaccinia virus Ankara-based malaria vaccines*. *Expert Rev Vaccines*, **15**, 91-103.
167. Şevik M (2019): *Orf virus circulation in cattle in Turkey*. *Comp Immunol Microbiol Infect Dis*, **65**, 1-6.
168. Sharma A, Priyanka, Fahrni ML, et al (2022): *Monkeypox outbreak: New zoonotic alert after the COVID-19 pandemic*. *Int J Surg*, **6**, 106812.
169. Shchelkunov SN, Totmenin AV, Babkin IV, et al (2001): *Human monkeypox and smallpox viruses: genomic comparison*. *FEBS Lett*, **509**, 66-70.
170. Shimizu K, Badr Y, Okada A, et al (2020): *Bovine papular stomatitis virus and pseudocowpox virus coinfection in dairy calves in Japan*. *Arch Virol*, **165**, 2659-2664.
171. Shimizu K, Takase H, Okada A, et al (2022): *Possibility of mechanical transmission of parapoxvirus by houseflies (Musca domestica) on cattle and sheep farms*. *J Vet Med Sci*, 2022 Jul 27.
172. Shivanna V, Cino-Ozuna AG, Heskett C, et al (2020): *Pseudocowpox virus infection in an American bison (Bison bison)*. *BMC Vet Res*, **16**, 241.
173. Silva-Fernandes AT, Travassos CE, Ferreira JM, et al (2009): *Natural human infections with Vaccinia virus during bovine vaccinia outbreaks*. *J Clin Virol*, **44**, 308-313.

174. Simulundu E, Mtine N, Kapalamula TF, et al (2017): Genetic characterization of orf virus associated with an outbreak of severe orf in goats at a farm in Lusaka, Zambia (2015). *Arch Virol*, **162**, 2363-2367.
175. Spinney L (2020): Smallpox and other viruses plagued humans much earlier than suspected. *Nature*, **584**, 30-32.
176. Spyrou V, Valiakos G (2015): Orf virus infection in sheep or goats. *Vet Microbiol*, **181**, 178-182.
177. Srivastava G, Srivastava G (2022): Human Monkeypox Disease. *Clin Dermatol*, S0738-081X(22)00113-4.
178. Stagegaard J, Kurth A, Stern D, et al (2017): Seasonal recurrence of cowpox virus outbreaks in captive cheetahs (*Acinonyx jubatus*). *PLoS One*, **12**, e0187089.
179. Stead JW, Henry CM, Simpson RH (1992): Rare case of autoinoculation of orf. *Br J Gen Pract*, **42**, 395-396.
180. Sutter G, Staib C (2003): Vaccinia vectors as candidate vaccines: the development of modified vaccinia virus Ankara for antigen delivery. *Curr Drug Targets Infect Disord*, **3**, 263-271.
181. Taieb A, Guillot M, Carlotti D, et al (1988): Orf and pregnancy. *Int J Dermatol*, **27**, 31-33.
182. Talarek E, Marczyńska M (2018): Cowpox Virus Infection. *N Engl J Med*, **378**, 181.
183. Tamulyte G, Lauraitis J, Ganceviciene R, et al (2019): Cowpox virus infection in two brothers with possible human-to-human transmission. *J Eur Acad Dermatol Venereol*, **33**, e8-e10.
184. Thornhill JP, Barkati S, Walmsley S, et al (2022): Monkeypox Virus Infection in Humans across 16 Countries - April-June 2022. *N Engl J Med*.
185. Tobler C, Ritter-Schenk C, Zimmermann P (2022): Orf Virus Infection: *Ecthyma Contagiosum*. *J Pediatr*, **243**, 236-237.
186. TRT Haber (2022): Türkiye'de kaç maymun çiçeği vakası var? Bakan Koca açıkladı. Available at <https://www.trthaber.com/haber/gundem/turkiyede-kac-maymun-cicegi-vakasi-var-bakan-koca-acikladi-698760.html> (Accessed August 8, 2022).
187. Tryland M, Beckmen KB, Burek-Huntington KA, et al (2018): Orf virus infection in Alaskan mountain goats, Dall's sheep, muskoxen, caribou and Sitka black-tailed deer. *Acta Vet Scand*, **60**, 12.
188. Tryland M, Klein J, Nordøy ES, et al (2005): Isolation and partial characterization of a parapoxvirus isolated from a skin lesion of a Weddell seal. *Virus Res*, **108**, 83-87.
189. Turk BG, Senturk B, Dereli T, et al (2014): A rare human-to-human transmission of orf. *Int J Dermatol*, **53**, e63-65.
190. Usme-Ciro JA, Paredes A, Walteros DM, et al (2017): Detection and molecular characterization of zoonotic poxviruses circulating in the Amazon region of Colombia, 2014. *Emerg Infect Dis*, **23**, 649-653.
191. Vaughan A, Aarons E, Astbury J, et al (2018): Two cases of monkeypox imported to the United Kingdom, September 2018. *Euro Surveill*, **23**, 1800509.
192. Vaughan A, Aarons E, Astbury J, et al (2020): Human-to-Human Transmission of Monkeypox Virus, United Kingdom, October 2018. *Emerg Infect Dis*, **26**, 782-785.
193. Vellucci A, Manolas M, Jin S, et al (2020): Orf virus infection after Eid al-Adha. *IDCases*, **21**, e00854.
194. Volz A, Sutter G (2017): Modified vaccinia virus Ankara: History, value in basic research, and current perspectives for vaccine development. *Adv Virus Res*, **97**, 187-243.
195. von Magnus P, Andersen EK, Petersen KB, et al (1959): A pox-like disease in cynomolgus monkeys. *Acta Pathol Microbiol Scand*, **46**, 156-76.
196. Vusirikala A, Charles H, Balasegaram S, et al (2022): Epidemiology of Early Monkeypox Virus Transmission in Sexual Networks of Gay and Bisexual Men, England, 2022. *Emerg Infect Dis*, **28**.
197. Wang L, Shang J, Weng S, et al (2022): Genomic annotation and molecular evolution of monkeypox virus outbreak in 2022. *J Med Virol*, 2022 Jul 29.
198. Wendt R, Tittelbach J, Schrick L, et al (2021): Generalized cowpox virus infection in an immunosuppressed patient. *Int J Infect Dis*, **106**, 276-278.
199. Werchniak AE, Herfort OP, Farrell TJ, et al (2003): Milker's nodule in a healthy young woman. *J Am Acad Dermatol*, **49**, 910-911.
200. WHO (2022): 2022 Monkeypox Outbreak: Global Trends. Available at https://worldhealthorg.shinyapps.io/mpx_global/ (Accessed August 18, 2022).
201. WHO (2022): Disease Outbreak News; Monkeypox–United Kingdom of Great Britain and Northern Ireland. Available at <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON381> (Accessed June 24, 2022).
202. WHO (2022): Disease Outbreak News; Multi-country monkeypox outbreak in non-endemic countries: Update. Available at <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON396> (Accessed June 24, 2022).
203. WHO (2022): Monkeypox. Available at <https://www.who.int/news-room/fact-sheets/detail/monkeypox> (Accessed June 24, 2022).
204. WHO (2022): Weekly bulletin on outbreaks and other emergencies. Week 4: 17 – 23 January 2022. Available at <https://apps.who.int/iris/bitstream/handle/10665/351164/OEW04-1723012022.pdf> (Accessed June 24, 2022).
205. Wu K, de Menezes S, Robinson A (2021): Erythema multiforme induced by a "milker's nodule" pseudocowpox infection: a case report and review of literature. *Case Rep Dermatol Med*, **2021**, 5584773.
206. Yinka-Ogunleye A, Aruna O, Dalhat M, et al (2019): Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. *Lancet Infect Dis*, **19**, 872-879.
207. Žaba R, Jalowska M, Kowalczyk MJ, et al (2017): Cowpox virus infection in a child after contact with a domestic cat: a case report. *New Microbiol*, **40**, 148-150.