Global Health & Medicine. 2025; 7(1):1-12. REVIEW
DOI: 10.35772/ghm.2024.01072

A review of epidemiology, diagnosis, and management of Mpox: The role of One Health

Chien-Yuan Huang[1], Shih-Bin Su[2], Kow-Tong Chen[3,4,*]

[1] Division of Occupational Medicine, Chi-Mei Medical Center, Liouying, Tainan, Taiwan;
[2] Department of Occupational Medicine, Chi-Mei Medical Center, Tainan, Taiwan;
[3] Department of Occupational Medicine, Tainan Municipal Hospital (managed by Show Chwan Medical Care Corporation), Tainan, Taiwan;
[4] Department of Public Health, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

Abstract: Human monkeypox (Mpox) is an emerging zoonotic disease. Its clinical features are similar to but less severe than those of smallpox. The etiology of this disease is the monkeypox virus. This virus is a double-stranded DNA virus that is classified into the genus *Orthopoxvirus* and the family *Poxviridae*. Human monkeypox was first identified in 1970 and mainly occurred in Central and Western Africa. In 2022, outbreaks of Mpox virus infection occurred in several non-endemic countries and caused a potential threat to humans. It is urgent to take immediate action to control and prevent the outbreak of the Mpox virus infection. This paper summarizes the current status of Mpox and generated strategies for managing the Mpox epidemic. Although progress in the diagnostic methods and treatment of Mpox produces better knowledge, we argue that the sensitive surveillance for animal and human Mpox virus infection and evidence-based response and management of Mpox outbreaks is critical. This study highlights the need for further research on preventive and control strategies for Mpox disease approached through the One Health concept.

***Keywords*:** Mpox, epidemiology, diagnosis, treatment, One Health

Introduction

Monkeypox (Mpox) is an emerging zoonosis caused by the monkeypox virus (Mpoxv), which is classified into the genus Orthopoxvirus member, and family *Poxviridae*. Four species, including smallpox or *variola virus*, *cowpox virus*, *vaccinia virus*, and Mpox, can cause human infection in the family *Poxviridae* (*1*). Poxviruses are large double-stranded DNA viruses that replicate within the host cell cytoplasm of various vertebrates and invertebrates (*2*). Mpoxv is categorized into Clade I and II, with Clade II further divided into Clade IIa and IIb (*3,4*). The two genetic subtypes of Mpoxv are associated with disease patterns in Central and West Africa. The Central African Mpox viruses are often linked to more severe health outcomes, higher mortality rates, and an increased risk of human-to-human transmission compared to their West African counterparts (*3,4*). The natural reservoirs of the virus in endemic areas are not known. Before the Mpox outbreaks in 2022, many Mpox cases occurred in Central and West Africa. However, since May 2022, the emergence of the Mpox epidemic has occurred in non-endemic countries and has become a significant threat to human health (*5-9*). Investigating the spatial distribution characteristics and risk factors associated with Mpoxv infections is essential to prevent its global spread effectively (*10,11*). In addition, the One Health approach has been proposed as an optimal strategy for preventing and controlling zoonotic infectious diseases (*12,13*). This review provides an overview of the epidemiology, transmission, and management of Mpox disease, offering strategic recommendations for managing and preventing its outbreaks.

Biology and genetics of Mpoxv

Mature poxvirus particles measure approximately 200 nm in diameter and 300 nm in length, exhibiting an ovoid or brick-like shape (*1*). They feature surface tubules and possess a distinctive dumbbell-shaped nucleoprotein core that houses the viral genome (*1,2*). Mpoxv produces three distinct infectious viral particles: the intracellular mature virus, the cell-associated enveloped virus, and the extracellular virus (*2*). As illustrated in Figure 1, the replication cycle begins with the virus attaching to host cells, leading to the fusion of viral and cellular membranes, releasing the viral core into the cytoplasm

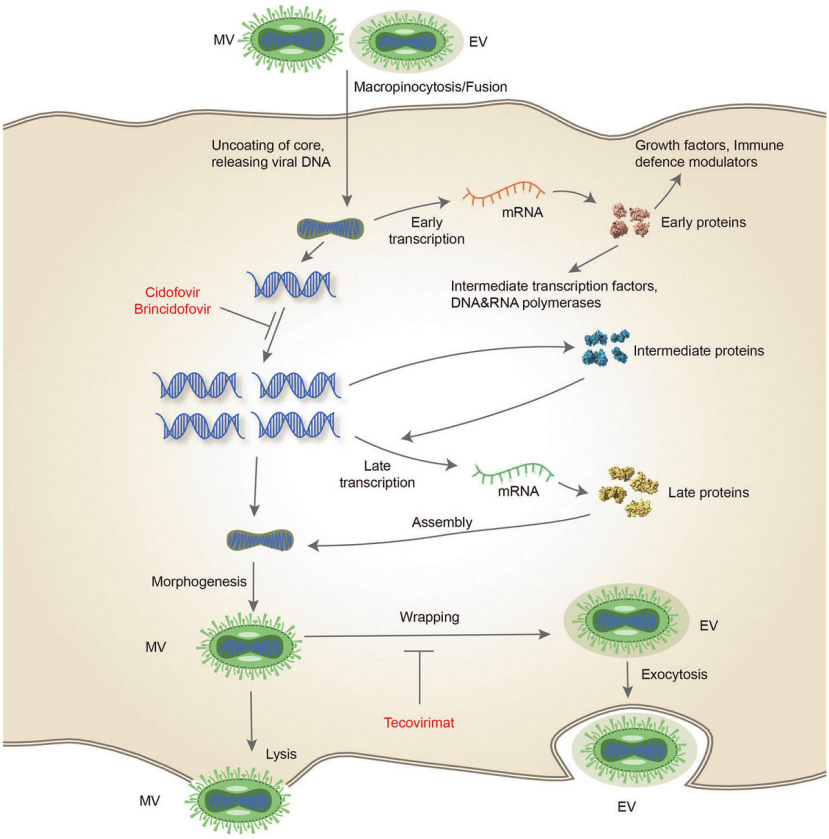

Figure 1. Mpox virus life cycle. This diagram depicts the life cycle of the Mpox virus inside a human cell. Notably, the replication cycle of the Mpox virus occurs in the host cell's cytoplasm. MV, mature virus; EV, enveloped virus. (We have obtained permission to use this figure from the journal's editor, and the photograph is courtesy of Huang Y *et al.* (*13*)).

(*13,14*). Notably, poxviruses have a unique characteristic of generating two types of infectious particles: the extracellular virus and mature virions (MVs), each possessing distinct surface epitopes (*14*). Depending on their infectious forms, poxviruses enter host cells through various mechanisms. Mature virions (MVs) possess a single outer membrane, while enveloped virions (EVs) have additional membranes and exhibit different protein compositions (*15*).

Within the viral core, transcription activation takes place, resulting in the synthesis of 118 early messenger RNAs (mRNAs) from the vaccinia virus (*16*). These mRNAs encode enzymes essential for genome replication in the cytoplasm, as well as intermediate-stage transcription factors and immune defense proteins (*13,16*). Following genome replication, 93 mRNAs are transcribed from intermediate and late genes assembled into mature virions (*15,16*). The Mpoxv evolution rate is estimated at 2 × 10^-6, significantly lower than that of SARS-CoV-2, which ranges from 0.8 to 2.38 × 10^-3 (*16*). *In vitro* studies indicate transient gene duplications may occur before further mutational events in orthopoxviruses, potentially facilitating accelerated adaptation to host antiviral defenses (*1,16*).

Epidemiological characteristics of Mpoxv infection

In 1958, the virus was first reported among monkeys transported from Africa to an animal facility in Denmark (*17*). Mpoxv has been detected in various wild animals (*17,18*). However, the first human case of Mpoxv infection was diagnosed in a patient aged 9 years old who lived in the Democratic Republic of Congo in August 1970 (*19*). The disease has become endemic in Central and Western Africa since the discovery of the Mpox case; some sporadic cases of infection by local wildlife have been reported among humans (*20,21*). The first outbreak of Mpoxv infection outside the African regions was reported in the United States in 2003 (*22,23*). The attack involved 47 people in five states in the United States and was associated with marmots imported from Ghana, Africa (*23*). Subsequently, imported cases of Mpox have been found in Israel (*24*), the United Kingdom (*25*), and Singapore (*26*).

Twenty cases of Mpoxv infection were first reported in England in May 2022, then the number of Mpox cases rapidly rose worldwide (*27*). It is noted that the first patient with Mpoxv infection in the United Kingdom in 2022 had a history of visiting Nigeria before he was diagnosed. Therefore, all the other confirmed patients would have experienced visiting Nigeria or Africa (*28,29*). This result indicated

that Mpoxv had developed a pattern of community transmission (*28*). The subsequent occurrence of the Mpox epidemic became known worldwide, and it has been proposed that the Mpox epidemic is a potential threat to whole human populations (*30-34*). The Mpox outbreak of 2022 constituted a Public Health Emergency of International Concern, which the WHO declared on 23 July 2022 (*26,27*). On 28 November 2022, the WHO suggested using the word "Mpox" as a replacement for "monkeypox". Both terms will be used for one year, and "monkeypox" is being phased out (*35*).

Figure 2 illustrates the global distribution of Mpox cases reported by the WHO in 2024 (*35*). Since 1 January 2022, Mpox cases have been reported to the WHO by 121 member states across all six WHO regions. As of 31 July 2024, 103,038 laboratory-confirmed cases and 186 probable cases, including 53 fatalities, were reported to the WHO (*35,36*). The ten most affected countries from 1 January 2022 are the United States (*n* = 33,556), Brazil (*n* = 11,841), Spain (*n* = 8,104), the Democratic Republic of the Congo (*n* = 4,385), France (*n* = 4,283), Colombia (*n* = 4,256), Mexico (*n* = 4,132), the United Kingdom (*n* = 4,018), Peru (*n* = 3,939), and Germany (*n* = 3,886). Collectively, these countries account for 80.0% of the global cases reported. In 2024, as of 1 September 2024, 15 countries have reported 3,891 confirmed cases, including 32 deaths. The three countries with the highest number of cases in 2024 are the Democratic Republic of the Congo (*n* = 3,361), Burundi (*n* = 328), and Nigeria (*n* = 48) (*35*).

According to their molecular characteristics, cases of Mpoxv infection reported from Central Africa and West Africa are classified into the Congo Basin (Clade I) and West Africa (Clades IIa and IIb) groups (*3,4*). Previous studies showed that the diseases caused by Clades IIa and IIb most closely resemble the cases in 2022, which occurred in non-endemic countries (*37,38*). It was reported that the fatality rate of the cases caused by Clade IIa and IIb was only approximately 1% (*39*). In contrast, the disease caused by the Clade I virus had a more severe condition, with a case fatality rate of 10% (*37,38*). The evolutionary changes of the viruses in the current outbreak are possibly activated by apolipoprotein B messenger RNA (*40,41*).

Mpox disease has been present in Central and Western Africa since its discovery. The emergence of the Mpox epidemic in 2022 in non-endemic countries has triggered widespread panic globally, raising concerns about a significant threat to human health (*42*). The ongoing Mpox pandemic is attributed to the same viral strain (Clade IIb) that caused outbreaks in Nigeria in 2017 and 2018. The factors contributing to the current Mpox outbreak remain unclear, suggesting that mutations in viral proteins may be affecting phenotype and pathogenesis (*43*). Several risk factors, including climate change, increased international travel, human behavior, and deforestation, are influencing the recent epidemiological trends of Mpox in Africa, where cases are now being reported in non-endemic countries (*44-46*). Given the limited understanding of the epidemiological characteristics of the current outbreak, it is crucial to conduct further detailed epidemiological studies, serosurveys, and continuous surveillance using

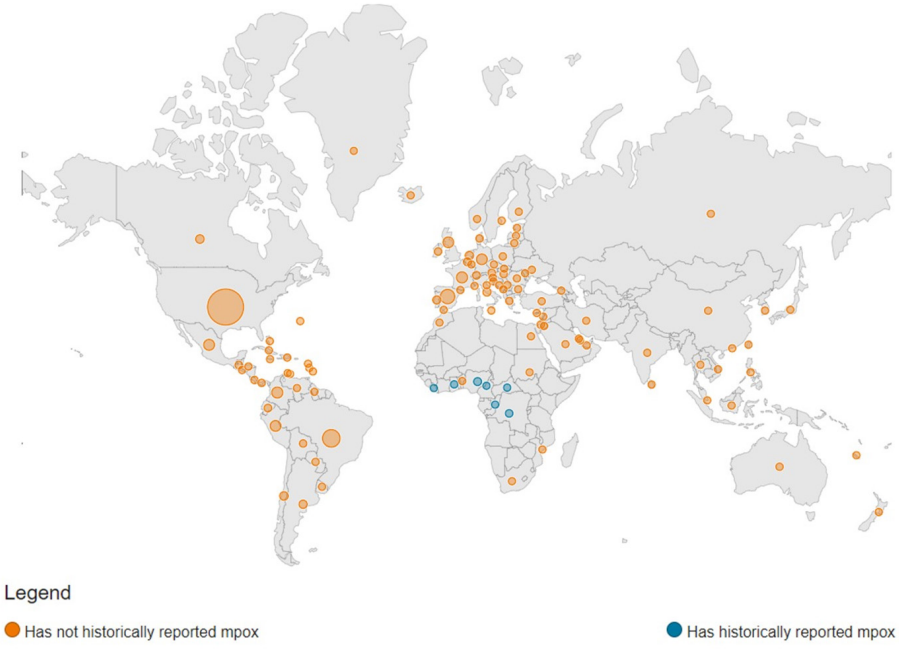

Figure 2. Distribution Of Mpox Cases by Country between January 2022 and December 2023. The circle size reflects the number of cases in each country. (The figure is free to use, and the photograph is courtesy of the World Health Organization (*35*)).

the One Health approach to monitor new cases.

Transmission

While the definitive host reservoir for Mpoxv is not yet fully established, it is believed that the transmission of Mpoxv to humans is facilitated by wild animals such as squirrels, sooty mangabeys (Cerocebus atys), and Gambian rats, which play significant roles in this process (*47-49*). Figure 3 depicts the potential modes of Mpoxv transmission. Humans can become infected with Mpoxv through animal interactions and person-to-person contact (*47,48*). In endemic countries, Mpox transmission primarily occurs from animals to humans through direct contact with infected animals, often during activities such as hunting, capturing, and processing these animals or their bodily fluids (*5*). This contact can involve scratches, bites, injuries sustained while preparing bushmeat, and direct or indirect exposure to bodily fluids or lesion material (*50*). The virus has been isolated from various species, including the rope squirrel, sooty mangabey, prairie dog, pouched rat, African dormouse, African giant pouched rats, and the elephant shrew (*51*). However, the precise mechanisms by which humans are exposed to infectious sources from these animals remain unclear (*52,53*).

Human-to-human transmission of Mpoxv has been observed in Nigeria and West Africa (*53*). This transmission can occur through several routes, including respiratory droplets, direct contact, vertical transmission, percutaneous transmission, and fomites (*11,50*). Factors recognized as risk factors for infection — including living in the same household, sharing dishes with an infected individual, close contact with skin lesions, and exposure to large respiratory droplets — can elevate the risk of infection to as high as 9% (*11,37,53*). However, during the 2022 outbreak, household transmission was relatively rare, accounting for less than 3% of cases (*9*). This finding suggests that Mpoxv infection is not transmitted through casual contact; instead, it likely requires extended or repeated contact with lesions from individuals infected with Mpoxv.

Additionally, it has been established that contact with contaminated materials, such as sex toys, can facilitate the transmission of Mpoxv infection (*54*). The 2022 Mpox outbreak demonstrated that 73% of individuals in the cohort presented with lesions in the anogenital region, indicating that close contact with infectious sores or lesions on mucous membranes may serve as a primary route of transmission (*9,39,55*). Table 1 shows the demographic characteristics of persons with Mpox infection; the highest risk age group is 31-40 years (39.7%), followed by 21-30 years (29.3%), 41-50 (18.9%); homosexuals, bisexuals, and men who have sex with men (MSM) are the main targets of Mpoxv infection (Table 1) (*9,36*). In endemic countries, children, pregnant women, and immunocompromised subjects are high-risk groups for Mpoxv infection; however, during an outbreak of Mpox in 2022, few children, adolescents, and pregnant women were infected (*9,11,36*).

While some studies have detected Mpoxv in semen (*55,56*), it remains unclear whether Mpox

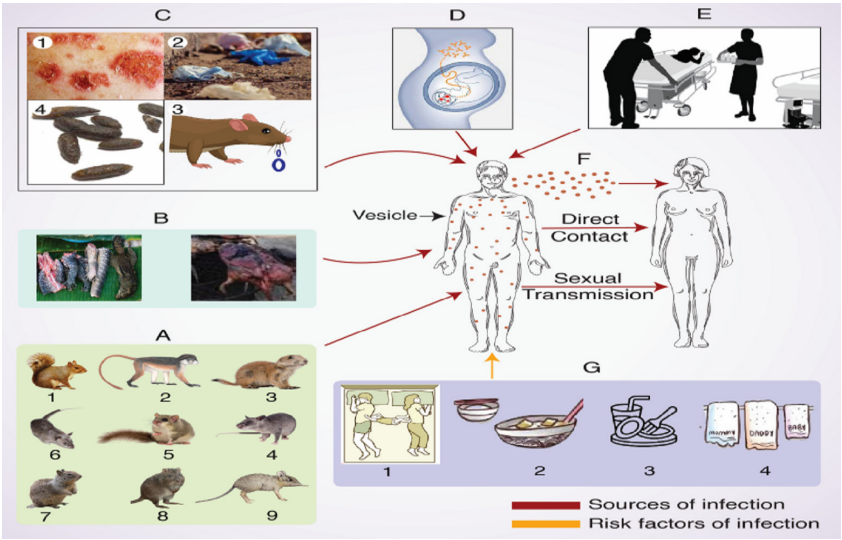

Figure 3. Transmission of Mpox virus. This schematic illustration shows the different transmission routes. (A) The number corresponds to the following animals: 1. rope squirrel; 2. sooty mangabey; 3. prairie dog; 4. Gambian pouched rat; 5. African dormice rodent; 6. African giant pouched rat; 7. sun squirrel; 8. rufous-nosed rat; and 9. elephant shrew. **(B)** Represents bush meat consumption as a potential route of transmission. **(C)** The number corresponds to the following: 1. Skin crust; 2. Patients' used materials; 3. Contaminated saliva; 4. Fecal material. **(D)** Illustrates trans-placental transmission, indicating the possibility of the virus passing from mother to fetus. **(E)** Highlights nosocomial infections, which are acquired in healthcare settings. **(F)** Depicts transmission through respiratory droplets and direct contact between individuals. **(G)** Represents scenarios involving sharing personal items such as beds, food, glasses, utensils, and hand towels. (We have obtained permission to use this figure from the authors and the photograph courtesy of Zinnah MA *et al*. (*51*)).

can be transmitted through genital, vaginal, or other bodily secretions (*56,57*). Additionally, it is uncertain if Mpoxv can infect individuals who do not have skin lesions or the extent of the infection risk associated with sexual contact, regardless of sexual orientation or gender identity. Nonetheless, those in close contact with individuals infected with Mpoxv, as well as workers in animal breeding facilities, laborers involved in the slaughter of wild animals, and pet owners, are considered high-risk groups for contracting Mpoxv infection (*36*).

Controlling Mpox will not be feasible without understanding the relationship between the biological characteristics of Mpoxv and human immunity. The rise in reported cases across various countries suggests that specific genomic changes in Mpoxv may have resulted in more efficient transmission and dispersal mechanisms, potentially facilitating sexual transmission (*58*). However, further research is necessary to corroborate this hypothesis.

Table 1. Demographic characteristics of persons with monkeypox in the United States, 17 May 2022 – 15 March 2023

Variables	Number (%)
Total	29,894 (100)
Age group (years)	
≤ 10	46 (0.2)
11-20	692 (2.3)
21-30	8,771 (29.3)
31-40	11,861 (39.7)
41-50	5,641 (18.9)
≥ 51	2,883 (9.6)
Gender identity	
Man	28,441 (95.1)
Transgender man	67 (0.2)
Woman	879 (2.9)
Transgender woman	272 (0.9)
Undetermined	235 (0.8)

Data collected from Centers for Disease Control and Prevention and workout this table. (Source: Centers for Disease Control and Prevention (*36*).

Diagnosis

Clinical characteristics of Mpoxv infection

Mpox is generally considered a mild and self-limiting disease, with a mean incubation period of approximately 7.6 days (95% CI: 6.2-9.7) (*36,48*). The primary classic symptoms of Mpox include fever, malaise, headache, and fatigue, followed by the appearance of bumps, skin lesions, and eventual scarring after scabs have formed (Figure 4) (*5,48,59,60*). Skin lesions are primarily localized on the face, palms, soles, oral mucosa, genitals, and conjunctiva. These lesions evolve and typically resolve in 2 to 4 weeks, transitioning from plaques to pimples to blisters, pimples, and scabs before shedding (*5,61,62*). Skin lesions may appear on the body in quantities ranging from a few to several thousand (*17*). These lesions tend to be uniform in stage and size. While pain associated with the lesions can be significant, it is not universally experienced (*63*). Patients may also exhibit lymphadenopathy or face complications such as secondary bacterial infections (*17,64*). The case fatality rate associated with Mpox ranges from 1% to 10% in the general population. Children and individuals with specific underlying immunodeficiency conditions are at a higher risk for severe complications, including pneumonia, encephalitis, and eye infections, as well as increased mortality (*39*). In contrast to the classic symptoms of Mpoxv infections, common symptoms in the outbreak in 2022 are present with skin rashes or

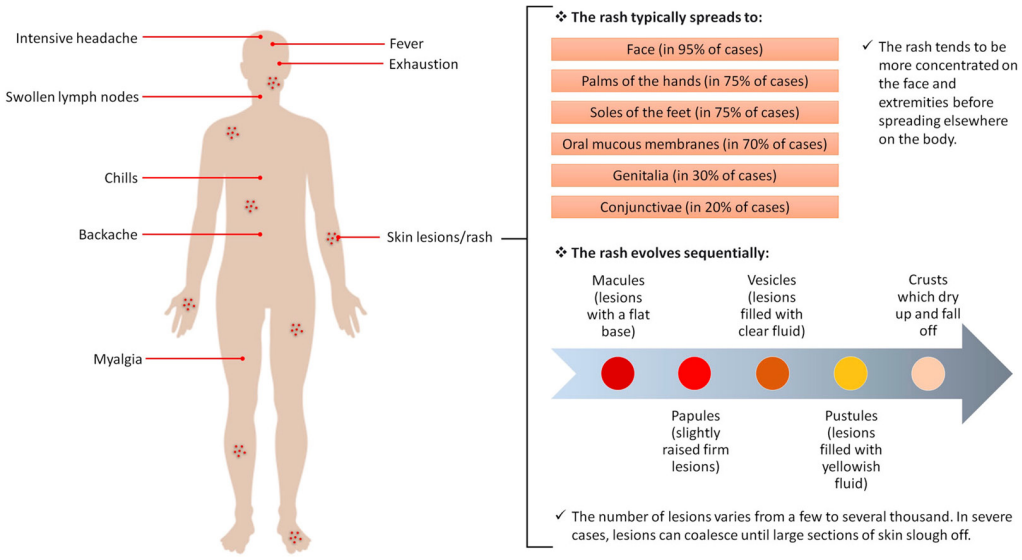

Figure 4. The main symptoms occur following exposure to the Mpox virus. (We have obtained permission to use this figure from the authors, and the photograph is courtesy of Hatmal MM *et al.* (*60*)).

lesions (95%), mainly located on the anogenital and perioral mucosal area (*6,9,36,65*). Other symptoms, including fever (58%), lymphadenopathy (53%), lethargy (39%), myalgia (31%), and headache (30%), have also been described in previous studies but do not always precede skin lesions (*8,9,61*). The earlier research, including 528 patients across 16 countries, showed that the most common anatomical sites of skin ulcerations occurred on the anogenital region (73%), body, upper or lower extremities (55%), face (25%), and palms and soles (10%); a majority of persons (90%) presented with multiple skin ulcerations, and approximately 10% of persons had only one single lesion in the genital area (*9*). These findings suggest the relationship between lesions' location and vaccination sites.

Laboratory tests for Mpoxv

Mpoxv infection presents as a smallpox-like disease, making it challenging to distinguish Mpox from other conditions that exhibit similar skin lesions at various stages of development. These conditions include herpes simplex virus, varicella-zoster virus, molluscum contagiosum, enterovirus infections, measles, scabies, syphilis, bacterial skin infections, rickettsialpox, drug allergies, papillomaviruses, and other related disorders (*66*). Therefore, laboratory tests are essential for accurately confirming Mpoxv infection (*67,68*). Various laboratory tests are available to diagnose Mpoxv infection. Nucleic acid amplification testing (NAAT), which includes both real-time and conventional polymerase chain reaction (PCR), is used to confirm Mpoxv infection (*69-71*). PCR plays a critical role in distinguishing between viral clades — effectively differentiating the Congo Basin strain (Clade I) from the West African strain (Clade II) — whether used alone or in combination with sequencing methods (*70,71*). PCR tests are the standard method for confirming a diagnosis of Mpox. Patients exhibiting skin lesions associated with Mpoxv infection should undergo further laboratory investigation. However, PCR tests are often expensive and difficult to obtain, particularly in underdeveloped countries. There is a pressing need for more affordable and easily accessible commercial tests to facilitate the detection of Mpox cases.

Other tests for diagnosis

Serological testing for Mpoxv can aid in diagnosing Mpox, mainly when NAAT testing is not feasible (*72*). The detection of IgM antibodies in acutely ill patients (within 4 to 56 days after rash onset) or the identification of IgG antibodies in paired serum samples — collected at least 21 days apart, with the first sample obtained during the first week of illness — can contribute to the diagnosis (*11*). However, the effectiveness of Mpoxv-specific serological tests may be compromised by the potential for cross-reactivity with antibodies against other orthopoxviruses and with those generated by recent or historical vaccination (*72,73*). Consequently, it is recommended that serological testing be conducted only in reference laboratories until further evidence supports the use of serological or antibody-detecting point-of-care (POC) tests in other settings (*73*). This approach highlights the complex role of serology within the diagnostic framework, emphasizing its potential usefulness in certain conditions and noting the necessity for rigorous validation and adherence to application standards.

Electron microscopy offers a technique for visually identifying potential poxviruses within specimens (*74*). However, due to the need for specific technical expertise, requisite facilities, and the proliferation of more accessible molecular assays, its application in Mpoxv diagnosis is not widespread (*74*). Consequently, electron microscopy is infrequently utilized in the routine diagnostic assessment of poxviruses.

Virus isolation and culture are long-established techniques for diagnosing viral diseases, including Mpoxv (*17*). This process is essential for comprehensive characterization through sequencing, which facilitates antiviral testing, vaccine development, and the formulation of clinical applications and research methodologies (*22*). Isolating viruses from critical cases is vital for outbreak investigation and containment efforts, as it allows for identifying the virus's origin, detecting mutations, and reconstructing transmission chains through genomic and phenotypic comparisons among isolates. Mpoxv exhibits strong growth in various mammalian cell lines, including HeLa, Vero, BSC-1, and RK-13, as well as in chicken embryos, which are particularly susceptible to poxviruses (*24*). The virus induces cytopathic effects in chicken embryos' chorioallantoic membranes (CAMs), observable 1 to 4 days post-inoculation. These effects include cell rounding, granulation, cytoplasmic bridging, and syncytium formation (*75*). Conversely, when cultured in Vero cells, typical rounded and detached cells become noticeable within approximately 24 hours, enabling the identification of virus particles using immunofluorescence and specific antibodies (*24,75*). Although this method is precise, its lengthy detection timeframe, the necessity for high-level biosafety laboratories (Biosafety Level 3 or higher), the requirement for experienced personnel, and the inherent risk of infection — even with complete personal protective equipment — significantly limit its widespread application.

Whole-genome sequencing (WGS), a leading technology in next-generation sequencing, enables the complete sequencing of an organism's genome. It is the most accurate method for distinguishing the Mpoxv from orthopoxviruses (OPVs), providing broader pathogen coverage than other molecular

diagnostics (*76*). Genome sequencing of the Mpoxv responsible for the 2022 outbreak has been conducted, and whole-genome sequencing is regarded as the gold standard for differentiating Mpoxv infections from other orthopoxvirus diseases (*77,78*). WGS supports comprehensive bioinformatic analyses, advancing virological research and facilitating the development of related immunoassays. This technique is particularly effective in identifying specific strains and genetic variants, which can help trace the origins of outbreaks, especially in instances where transmission chains are unknown (*79*).

Skin tissue biopsies are additional clinical samples that may be considered for diagnostic testing when clinically warranted (*11*). The histological characteristics of Mpox are similar to those of smallpox, vaccinia, and cowpox, which can assist in distinguishing it from other infections, such as herpes simplex (*11*).

In summary, Mpox represents a significant public health concern. Early diagnosis and prompt management are essential for preventing the spread of Mpoxv infection. Physicians must maintain high vigilance in suspecting Mpoxv infection and be aware of the atypical presentations observed in 2022. There should be a heightened clinical suspicion of Mpox in patients displaying isolated lesions, particularly among high-risk groups (*65*). Diagnosing Mpox requires a comprehensive assessment that includes clinical symptoms, epidemiological information, and laboratory tests (*6*). Additionally, a detailed travel and sexual history, along with any close contact with known Mpox cases, should be thoroughly investigated.

Treatment

No specific antiviral drug exists to treat patients with Mpoxv infection; the most common therapies are symptomatic and supportive care (*80*). Treatment is only recommended for high-risk groups, including young children, persons with immunocompromised conditions, and those with complications. Several antivirals (tecovirimat, cidofovir, and brincidofovir) are supposed to be effective in treating Mpoxv infections, but the efficacy of these drugs has yet to be thoroughly determined (*6*). Tecovirimat (TPOXX or ST-246) is the first antiviral drug to treat smallpox based on data from animal studies (*81-85*). Mpox and smallpox belong to the *Orthopoxvirus* genus in the family *Poxiviridae*. Therefore, while no drug is approved for Mpox, tecovirimat is used to treat Mpox through the procedures of an expanded-access Investigation New Drug (IND) protocol (*84,85*). Tecovirimat is a virus inhibitor that inhibits the envelope protein VP37 of *Orthopoxvirus*, thus blocking the virus's growth within an infected host (*86*). However, the efficacy of tecovirimat against Mpox in humans has not been identified.

Although tecovirimat is available for treating Mpox and might rapidly improve Mpox clinical symptoms/signs and outcomes, the safety and efficacy of tecovirimat in humans have yet to be proven. The efficacy data of tecovirimat studied in animals only sometimes translates directly into effectiveness in the human population (*81,87*). Additionally, the current worldwide outbreak involves a different strain of Mpoxv than that which generally causes Mpoxv infection in Africa, and some of the clinical presentations of the epidemic in 2022 and affected populations differ from those in countries where Mpox is endemic (*9*). Therefore, further study of the safety and effectiveness of antiviral drugs against Mpoxv infection is needed.

Alternative plant-based therapies

Despite Mpox occurring endemic in Africa for years, efficacy studies of drugs or vaccines for treating Mpox have yet to be completed. Microtubules provide scaffolding for cells, facilitate cellular long-distance traffic, and serve as essential components of multiple biological processes (*88*). The virus often interacts with the cytoskeleton and requires an intact microtubule network. Pharmacological modulation of microtubules has been proposed to interfere with virus replications and spread, indicating their potential as broad-spectrum antivirals. Therefore, studying the molecular mechanism underlying these plant-based therapies and identifying their pharmacological effects on treating Mpoxv infection is crucial.

Preventive measures

Vaccine development

Currently, there is no specific commercial vaccine available for Mpoxv infection. However, previous studies suggest that individuals vaccinated with the smallpox vaccine may experience a protective effect against Mpoxv infection and a reduction in the severity of clinical symptoms associated with the infection (*89,90*). One study indicated that the effectiveness of smallpox vaccination with the vaccinia virus in preventing Mpox was approximately 85% (*91*). Two vaccines are currently available for preventing smallpox and Mpox among those at risk of exposure: ACAM2000 and JYNNEOS (also known as IMVAMUNE, IMVANEX, or MVA-BN) (*32,87,92*).

JYNNEOS is a replication-deficient Vaccinia virus vaccine and is an attenuated live virus vaccine produced from the third-generation modified vaccinia Ankara-Bavarian Nordic (MVA-BN) (*36,83*). Replication-deficient Vaccinia virus vaccines do not cause clinical infection because they do not develop infectious viruses in humans (*93,94*). The U.S. Food and Drug Administration (FDA) approved this vaccine as an alternative to ACAM2000 to prevent infection with the

smallpox virus and Mpox disease in people aged 18 years or older, a high-risk infection group with Orthopoxvirus infection (*36,93,94*). The European Medicine Agency (EMA) has approved this vaccine to prevent smallpox (*94*). JYNNEOS is vaccinated subcutaneously using a 2-dose series (0.5 mL per dose), 28 days apart; on 9 August 2022, an emergency use authorization was issued by US FDA for dose-sparing intradermal administration of JYNNEOS as a 2-dose series (0.1 mL per dose, 4-weeks apart); no significant cutaneous or systemic reactions are expected because JYNNEOS is a replication-deficient virus vaccine; JYNNEOS boosters are recommended every two years; JYNNEOS does not produce a lesion at the vaccine site, which is often recognized as a sign of successful vaccination with replication-competent vaccines (*93-96*). A case-control study using data from the Epic Cosmos platform indicated the estimated vaccine effectiveness was 66.0% (95% CI: 47.4-78.1) for patients with 2-dose vaccination, and 35.8% (95% CI: 22.1-47.1) for patients with one-dose immunization (*95*). In contrast to the ACAM2000 vaccine, the JYNNEOS vaccine can be administered to patients with atopic dermatitis and immunocompromised people (*97*).

ACAM2000 is a replication-competent live vaccinia vaccine used against orthopoxvirus infection to eradicate smallpox (*94*). Because the replication-competent poxvirus strain can produce an infectious virus in humans, there is a risk of causing severe adverse reactions (*81,94*). The FDA approves ACAM2000 for vaccination in persons at high risk for smallpox infection; the CDC can authorize the emergency use of ACAM2000 for MPOXV infection (*36*). In 2003, during the outbreak of Mpoxv infection in the United States, ACAM2000 was found to reduce the severity of Mpoxv infection (*92*). Still, side effects occurred in patients with atopic dermatitis and individuals with immunodeficiency. ACAM2000 is vaccinated percutaneously *via* a multiple punctures (scarification) technique using a stainless-steel bifurcated needle (*94*). ACAM2000 is applied in one dose of the vaccine, and boosters are recommended every three years; the peak vaccine protection occurs within 28 days; after successfully administering the vaccine, a skin lesion is produced, which contains the infectious vaccinia virus, which causes close contact infection (*94,97*).

Aventis Pasteur Smallpox Vaccine (APSV) is a replication-competent vaccina vaccine that may be used under an IND or Emergency Use Authorization (EUA) to prevent smallpox if licensed vaccines are available or contraindicated (*83,98*). However, it is unknown if this vaccine could be used for Mpox.

Vaccinating ACAM2000 or JYNNEOS in the general population is not recommended. Data must still be collected to convince us that smallpox vaccines could effectively prevent Mpoxv infection in endemic areas (*64,99*). More research is needed to study the efficacy and safety of the Mpox vaccine in humans.

Recently, a study indicated that mRNA-A-LNP and mRNA-B-LNP appear to be safe and effective vaccine candidates against Mpox epidemics and outbreaks caused by other orthopoxviruses, including the smallpox virus (*100,101*).

Surveillance strategies through One Health approach

Mpox is a viral zoonosis characterized by symptoms similar to those in smallpox patients. The global outbreaks of Mpox have significantly impacted public health, highlighting the urgent need for comprehensive preventive measures to strengthen the resilience of healthcare systems (*102*). For timely alerts for potential Mpox outbreaks, it is essential to develop more advanced surveillance systems that facilitate early detection and investigation of the causes behind Mpox epidemics (*103*).

As an infectious disease that affects both animals and humans, Mpox warrants a One Health approach to surveillance, which enhances collaboration between human and veterinary health services. This approach is cost-effective for monitoring human and animal health (*104-106*). Implementing preventive strategies aligned with the One Health framework can yield multiple benefits in controlling and preventing wildlife-associated Mpox zoonoses. It enables monitoring wild animals for signs of Mpox within their confined environments or the regions from which they originate (*104*). Overall, this approach effectively addresses shared health threats at the intersection of human, animal, and environmental health.

Education program

Raising awareness and educating the public about the risk factors associated with Mpoxv infection are crucial preventive strategies to reduce exposure to the virus (*36,60*). The risk of contracting Mpoxv in healthcare settings is low, primarily due to healthcare workers' stringent use of personal protective equipment (PPE) (*59*). The CDC recommends that healthcare workers wear gowns, gloves, eye protection, and masks while on duty. Patients diagnosed with Mpoxv infection should wear masks and be isolated in individual rooms. Those with suspected Mpox skin rashes should refrain from close contact with others until their skin rashes have entirely healed (*36*). It remains unclear whether individuals who recover from Mpoxv infection are protected against future infections; however, those who have received smallpox vaccinations appear to have some protection.

Findings from laboratory studies, field surveys, and natural experiments indicate that various animals can be infected with Mpoxv and may be capable of transmitting the virus to humans. In many regions of Africa where Mpox is prevalent, protein supplementation from wild animal sources is crucial. For instance, in rural areas of

the Democratic Republic of the Congo (DRC), residents living near forests frequently encounter the carcasses of rodents, primates, and other animals (*107*). This situation underscores the need for Mpox education campaigns to prioritize reducing human contact with potentially infected animals, particularly those commonly utilized as protein sources, such as primates and larger rodents (*108*).

Observations from the current Mpox outbreak have revealed distinct characteristics of at-risk groups and highlighted the inadequacies of existing sexual health infrastructure. This new Mpox pandemic has indicated that men who have sex with men (MSM) and transgender individuals are among the highest-risk populations (*13,20*). Consequently, there is an urgent need to develop a robust sexual health infrastructure and enhance genomic surveillance (*109,110*). Sexual health clinics play a critical role in controlling Mpox, and it is essential to establish an effective sexually transmitted infection (STI) surveillance framework within public health systems. Active measures for monitoring Mpox cases are also necessary (*111*).

Conclusions

Since May 2022, the outbreak of Mpoxv infection has affected more than 116 countries (*35*), drawing global attention. Although Mpox has been endemic in Africa for years, comprehensive efficacy studies on drugs or vaccines for its treatment have yet to be completed. The 2022 outbreaks outside Africa's endemic regions underscore the urgent need for global investigation into Mpox disease. This current epidemic highlights the critical importance of not neglecting Global Health. Furthermore, it is essential to bolster foundational research on both animal and human poxvirus diseases, including the epidemiology of Mpox, the development of diagnostic tools (*e.g.*, laboratory tests), formulation of preventive strategies (*e.g.*, effective surveillance systems), and the creation of preventive measures (*e.g.,* vaccines and treatments). Education programs will also be vital. Additionally, enhancing international cooperation through the One Health concept is crucial for reducing the risk of Mpoxv infection.

Funding: We greatly appreciate the financial support from the grant (No. RD-11302) of the Tainan Municipal Hospital (managed by Show Chwan Medical Care Corporation) and Chi-Mei Medical Center, Tainan, Taiwan.

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Frey SE, Belshe RB. Poxvirus zoonoses--putting pocks into context. N Engl J Med. 2004; 350:324-327.
2. Kugelman JR, Johnston SC, Mulembakani PM, *et al*. Genomic variability of monkeypox virus among humans, Democratic Republic of the Congo. Emerg Infect Dis. 2014; 20:232-239.
3. Nakazawa Y, Mauldin MR, Emerson GL, Reynolds MG, Lash RR, Gao J, Zhao H, Li Y, Muyembe JJ, Kingebeni PM, Wemakoy O, Malekani J, Karem KL, Damon IK, Carroll DS. A phylogeographic investigation of African monkeypox. Viruses. 2015; 7:2168-2184.
4. Chen N, Li G, Liszewski MK, *et al.* Virulence differences between monkeypox virus isolates from West Africa and the Congo basin. Virology. 2005; 340:46-63.
5. Bryer J, Freeman EE, Rosenbach M. Monkeypox emerges on a global scale: A historical review and dermatologic primer. J Am Acad Dermatol. 2023; 88:e259.
6. Elsayed S, Bondy L, Hanage WP. Monkeypox virus infections in humans. Clin Microbiol Rev. 2022; 35:e0009222.
7. Tarín-Vicente EJ, Alemany A, Agud-Dios M, *et al.* Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: A prospective observational cohort study. Lancet. 2022; 400:661-669.
8. Philpott D, Hughes CM, Alroy KA, *et al.* Epidemiologic and clinical characteristics of monkeypox cases - United States, May 17-July 22, 2022. MMWR Morb Mortal Wkly Rep. 2022; 71:1018-1022.
9. Thornhill JP, Barkati S, Walmsley S, *et al*. Monkeypox virus infection in humans across 16 countries - April-June 2022. N Engl J Med. 2022; 387:679-691.
10. Martín-Delgado MC, Martín Sánchez FJ, Martínez-Sellés M, *et al*. Monkeypox in humans: A new outbreak. Rev Esp Quimioter. 2022; 35:509-518.
11. Mitjà O, Ogoina D, Titanji BK, Galvan C, Muyembe JJ, Marks M, Orkin CM. Monkeypox. Lancet. 2023; 401:60-74.
12. Gao S, Zeng Z, Zhai Y, Chen F, Feng X, Xu H, Kan W, Lu J, Zhou J, Chen Z. Driving effect of multiplex factors on Mpox in global high-risk region, implication for Mpox based on one health concept. One Health. 2023; 17:100597.
13. Huang Y, Mu L, Wang W. Monkeypox: epidemiology, pathogenesis, treatment and prevention. Signal Transduct Target Ther. 2022; 7:373.
14. Smith GL, Vanderplasschen A, Law M. The formation and function of extracellular enveloped vaccinia virus. J Gen Virol. 2002; 83:2915-2931.
15. Schmidt FI, Bleck CK, Mercer J. Poxvirus host cell entry. Curr Opin Virol. 2012; 2:20-27.
16. Moss B. Understanding the biology of monkeypox virus to prevent future outbreaks. Nat Microbiol. 2024; 9:1408-1416.
17. Petersen E, Kantele A, Koopmans M, Asogun D, Yinka-Ogunleye A, Ihekweazu C, Zumla A. Human monkeypox: Epidemiologic and clinical characteristics, diagnosis, and prevention. Infect Dis Clin North Am. 2019; 33:1027-1043.
18. Islam MM, Dutta P, Rashid R, Jaffery SS, Islam A, Farag E, Zughaier SM, Bansal D, Hassan MM. Pathogenicity and virulence of monkeypox at the human-animal-ecology interface. Virulence. 2023; 14:2186357.
19. Marennikova SS, Seluhina EM, Mal'ceva NN, Cimiskjan KL, Macevic GR. Isolation and properties of the causal agent of a new variola-like disease (monkeypox) in man. Bull World Health Organ. 1972; 46:599-611.
20. Hayes R, Dakin F, Smuk M, Paparini S, Apea V, Dewsnap

C, Waters L, Anderson J, Orkin CM. Cross-sectional survey of sexual health professionals' experiences and perceptions of the 2022 mpox outbreak in the UK. BMJ Open. 2024; 14:e080250.
21. Wang X, Gu Z, Sheng S, Song R, Jin R. The current state and progress of Mpox vaccine Research. China CDC Wkly. 2024; 6:118-125.
22. Reed KD, Melski JW, Graham MB, *et al.* The detection of monkeypox in humans in the Western Hemisphere. N Engl J Med. 2004; 350:342-350.
23. Sale TA, Melski JW, Stratman EJ. Monkeypox: An epidemiologic and clinical comparison of African and US disease. J Am Acad Dermatol. 2006; 55:478-481.
24. Erez N, Achdout H, Milrot E, *et al.* Diagnosis of imported monkeypox, Israel, 2018. Emerg Infect Dis. 2019; 25:980-983.
25. Vaughan A, Aarons E, Astbury J, *et al.* Two cases of monkeypox imported to the United Kingdom, September 2018. Euro Surveill. 2018; 23:1800509.
26. Ng OT, Lee V, Marimuthu K, Vasoo S, Chan G, Lin RTP, Leo YS. A case of imported monkeypox in Singapore. Lancet Infect Dis. 2019; 19:1166.
27. The Lancet. Monkeypox: A global wake-up call. Lancet. 2022; 400:337.
28. Mahase E. Monkeypox: what do we know about the outbreaks in Europe and North America? BMJ. 2022; 377:o1274.
29. Mauldin MR, McCollum AM, Nakazawa YJ, *et al.* Exportation of monkeypox virus from the African continent. J Infect Dis. 2022; 225:1367-1376.
30. Perez Duque M, Ribeiro S, Martins JV, *et al*. Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022. Euro Surveill. 2022; 27:2200424.
31. Minhaj FS, Ogale YP, Whitehill F, *et al.* Monkeypox Outbreak - Nine States, May 2022. MMWR Morb Mortal Wkly Rep. 2022; 71:764-769.
32. Iñigo Martínez J, Gil Montalbán E, Jiménez Bueno S, *et al.* Monkeypox outbreak predominantly affecting men who have sex with men, Madrid, Spain, 26 April to 16 June 2022. Euro Surveill. 2022; 27:2200471.
33. Suárez Rodríguez B, Guzmán Herrador BR, Díaz Franco A, *et al.* Epidemiologic features and control measures during monkeypox outbreak, Spain, June 2022. Emerg Infect Dis. 2022; 28:1847-1851.
34. Ilic I, Zivanovic Macuzic I, Ilic M. Global outbreak of human monkeypox in 2022: Update of epidemiology. Trop Med Infect Dis. 2022; 7:264.
35. The World Health Organization (WHO). 2022-24 Mpox (monkeypox) outbreak: Global trends. *https://worldhealthorg.shinyapps.io/mpx_global/* (accessed September 5, 2024).
36. Centers for Disease Control and Prevention. 2022 monkeypox outbreak global map. *http://cdc.gov/poxvirus/monkeypox/response/2022/world-map.html* (accessed December 19, 2023).
37. Lane HC, Fauci AS. Monkeypox - Past as prologue. N Engl J Med. 2022; 387:749-750.
38. Likos AM, Sammons SA, Olson VA, *et al*. A tale of two clades: Monkeypox viruses. J Gen Virol. 2005; 86:2661-2672.
39. Ogoina D, Izibewule JH, Ogunleye A, Ederiane E, Anebonam U, Neni A, Oyeyemi A, Etebu EN, Ihekweazu C. The 2017 human monkeypox outbreak in Nigeria-Report of outbreak experience and response in the Niger Delta University Teaching Hospital, Bayelsa State, Nigeria. PLoS One. 2019; 14:e0214229.
40. Yinka-Ogunleye A, Aruna O, Dalhat M, *et al.* Outbreak of human monkeypox in Nigeria in 2017-18: A clinical and epidemiological report. Lancet Infect Dis. 2019; 19:872-879.
41. Isidro J, Borges V, Pinto M, *et al*. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. Nat Med. 2022; 28:1569-1572.
42. Meo SA, Klonoff DC. Human monkeypox outbreak: Global prevalence and biological, epidemiological and clinical characteristics - observational analysis between 1970-2022. Eur Rev Med Pharmacol Sci. 2022; 26:5624-5632.
43. Kannan SR, Sachdev S, Reddy AS, Kandasamy SL, Byrareddy SN, Lorson CL, Singh K. Mutations in the monkeypox virus replication complex: Potential contributing factors to the 2022 outbreak. J Autoimmun. 2022; 133:102928.
44. Durski KN, McCollum AM, Nakazawa Y, Petersen BW, Reynolds MG, Briand S, Djingarey MH, Olson V, Damon IK, Khalakdina A. Emergence of monkeypox - West and Central Africa, 1970-2017. MMWR Morb Mortal Wkly Rep. 2018; 67:306-310.
45. Thomassen HA, Fuller T, Asefi-Najafabady S, *et al.* Pathogen-host associations and predicted range shifts of human monkeypox in response to climate change in Central Africa. PLoS One. 2013; 8:e66071.
46. Haddad N. The presumed receptivity and susceptibility to monkeypox of European animal species. Infect Dis Now. 2022; 52:294-298.
47. Hraib M, Jouni S, Albitar MM, Alaidi S, Alshehabi Z. The outbreak of monkeypox 2022: An overview. Ann Med Surg (Lond). 2022; 79:104069.
48. Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox virus in Nigeria: Infection biology, epidemiology, and evolution. Viruses. 2020; 12:1257.
49. Webb E, Rigby I, Michelen M, *et al.* Availability, scope and quality of monkeypox clinical management guidelines globally: A systematic review. BMJ Glob Health. 2022; 7:e009838.
50. Ihekweazu C, Yinka-Ogunleye A, Lule S, Ibrahim A. Importance of epidemiological research of monkeypox: Is incidence increasing? Expert Rev Anti Infect Ther. 2020; 18:389-392.
51. Zinnah MA, Uddin MB, Hasan T, Das S, Khatun F, Hasan MH, Udonsom R, Rahman MM, Ashour HM. The re-emergence of Mpox: Old illness, modern challenges. Biomedicines. 2024; 12:1457.
52. McCollum AM, Damon IK. Human monkeypox. Clin Infect Dis. 2014; 58:260-267.
53. Karagoz A, Tombuloglu H, Alsaeed M, Tombuloglu G, AlRubaish AA, Mahmoud A, Smajlović S, Ćordić S, Rabaan AA, Alsuhaimi E. Monkeypox (mpox) virus: Classification, origin, transmission, genome organization, antiviral drugs, and molecular diagnosis. J Infect Public Health. 2023; 16:531-541.
54. Guarner J, Del Rio C, Malani PN. Monkeypox in 2022 – what clinicians need to know. JAMA. 2022; 328:139-140.
55. Reda A, Abdelaal A, Brakat AM, Lashin BI, Abouelkheir M, Abdelazeem B, Rodriguez-Morales AJ, Sah R. Monkeypox viral detection in semen specimens of confirmed cases: A systematic review and meta-analysis. J Med Virol. 2023; 95:e28250.
56. Islam MR, Nowshin DT, Khan MR, Shahriar M, Bhuiyan

MA. Monkeypox and sex: Sexual orientations and encounters are key factors to consider. Health Sci Rep. 2023; 6:e1069.
57. Lapa D, Carletti F, Mazzotta V, *et al.* 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. 2022; 22:1267-1269.
58. Sharma R, Chen KT, Sharma R. Emerging evidence on monkeypox: Resurgence, global burden, molecular insights, genomics and possible management. Front Cell Infect Microbiol. 2023; 13:1134712.
59. Titanji BK, Tegomoh B, Nematollahi S, Konomos M, Kulkarni PA. Monkeypox: A contemporary review for healthcare professionals. Open Forum Infect Dis. 2022; 9:ofac310.
60. Hatmal MM, Al-Hatamleh MAI, Olaimat AN, Ahmad S, Hasan H, Ahmad Suhaimi NA, Albakri KA, Abedalbaset Alzyoud A, Kadir R, Mohamud R. Comprehensive literature review of monkeypox. Emerg Microbes Infect. 2022; 11:2600-2631.
61. Pourriyahi H, Aryanian Z, Afshar ZM, Goodarzi A. A systematic review and clinical atlas on mucocutaneous presentations of the current monkeypox outbreak: With a comprehensive approach to all dermatologic and nondermatologic aspects of the new and previous monkeypox outbreaks. J Med Virol. 2023; 95:e28230.
62. Mileto D, Riva A, Cutrera M, Moschese D, Mancon A, Meroni L, Giacomelli A, Bestetti G, Rizzardini G, Gismondo MR, Antinori S. New challenges in human monkeypox outside Africa: A review and case report from Italy. Travel Med Infect Dis. 2022; 49:102386.
63. Anwar F, Haider F, Khan S, Ahmad I, Ahmed N, Imran M, Rashid S, Ren ZG, Khattak S, Ji XY. Clinical manifestation, transmission, pathogenesis, and diagnosis of monkeypox virus: A Comprehensive Review. Life (Basel). 2023; 13:522.
64. Brown K, Leggat PA. Human monkeypox: Current state of knowledge and implications for the future. Trop Med Infect Dis. 2016; 1:8.
65. Prasad S, Galvan Casas C, Strahan AG, *et al.* A dermatologic assessment of 101 mpox (monkeypox) cases from 13 countries during the 2022 outbreak: Skin lesion morphology, clinical course, and scarring. J Am Acad Dermatol. 2023; 88:1066-1073.
66. Altindis M, Puca E, Shapo L. Diagnosis of monkeypox virus - An overview. Travel Med Infect Dis. 2022; 50:102459.
67. Macneil A, Reynolds MG, Braden Z, Carroll DS, Bostik V, Karem K, Smith SK, Davidson W, Li Y, Moundeli A, Mombouli JV, Jumaan AO, Schmid DS, Regnery RL, Damon IK. Transmission of atypical varicella-zoster virus infections involving palm and sole manifestations in an area with monkeypox endemicity. Clin Infect Dis. 2009; 48:e6-e8.
68. Huggett JF, French D, O'Sullivan DM, Moran-Gilad J, Zumla A. Monkeypox: Another test for PCR. Euro Surveill. 2022; 27:2200497.
69. Tan DHS, Pico Espinosa O, Matelski J, *et al.* Longitudinal analysis of mpox virus DNA detectability from multiple specimen types during acute illness: A cohort study. Open Forum Infect Dis. 2024; 11:ofae073.
70. Davi SD, Kissenkötter J, Faye M, Böhlken-Fascher S, Stahl-Hennig C, Faye O, Faye O, Sall AA, Weidmann M, Ademowo OG, Hufert FT, Czerny CP, Abd El Wahed A. Recombinase polymerase amplification assay for rapid detection of monkeypox virus. Diagn Microbiol Infect Dis. 2019; 95:41-45.
71. Nörz D, Brehm TT, Tang HT, *et al.* Clinical characteristics and comparison of longitudinal qPCR results from different specimen types in a cohort of ambulatory and hospitalized patients infected with monkeypox virus. J Clin Virol. 2022; 155:105254.
72. Beer EM, Rao VB. A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy. PLoS Negl Trop Dis. 2019; 13:e0007791.
73. Weaver JR, Isaacs SN. Monkeypox virus and insights into its immunomodulatory proteins. Immunol Rev. 2008; 225:96-113.
74. Müller M, Ingold-Heppner B, Stocker H, Heppner FL, Dittmayer C, Laue M. Electron microscopy images of monkeypox virus infection in 24-year-old man. Lancet. 2022; 400:1618.
75. Hutson CL, Kondas AV, Mauldin MR, Doty JB, Grossi IM, Morgan CN, Ostergaard SD, Hughes CM, Nakazawa Y, Kling C, Martin BE, Ellison JA, Carroll DS, Gallardo-Romero NF, Olson VA. Pharmacokinetics and efficacy of a potential smallpox therapeutic, brincidofovir, in a lethal monkeypox virus animal model. mSphere. 2021; 6:e00927-20.
76. Farlow J, Ichou MA, Huggins J, Ibrahim S. Comparative whole genome sequence analysis of wild-type and cidofovir-resistant monkeypoxvirus. Virol J. 2010; 7:110.
77. Cohen-Gihon I, Israeli O, Shifman O, Erez N, Melamed S, Paran N, Beth-Din A, Zvi A. Identification and whole-genome sequencing of a monkeypox virus strain isolated in Israel. Microbiol Resour Announc. 2020; 9:E01524-19.
78. Wassenaar TM, Wanchai V, Ussery DW. Comparison of monkeypox virus genomes from the 2017 Nigeria outbreak and the 2022 outbreak. J Appl Microbiol. 2022; 133:3690-3698.
79. Vazquez C, Fonseca V, de la Fuente AG, *et al.* Exploring the genomic dynamics of the monkeypox epidemic in Paraguay. Viruses 2024; 16:83.
80. Centers for Disease Control and Prevention, US. Monkeypox—treatment. Updated 10 December 2024. *http://www.cdc.gov/mpox/hcp/clinical-care/index.html* (accessed December 25, 2023).
81. O'Laughlin K, Tobolowsky FA, Elmor R, Overton R, O'Connor SM, Damon IK, Petersen BW, Rao AK, Chatham-Stephens K, Yu P, Yu Y; CDC Monkeypox Tecovirimat Data Abstraction Team. Clinical use of tecovirimat (Tpoxx) for treatment of monkeypox under an investigational new drug protocol - United States, May-August 2022. MMWR Morb Mortal Wkly Rep. 2022; 71:1190-1195.
82. Grosenbach DW, Honeychurch K, Rose EA, Chinsangaram J, Frimm A, Maiti B, Lovejoy C, Meara I, Long P, Hruby DE. Oral tecovirimat for the treatment of smallpox. N Engl J Med. 2018; 379:44-53.
83. Rizk JG, Lippi G, Henry BM, Forthal DN, Rizk Y. Prevention and treatment of monkeypox. drugs. 2022; 82:957-963.
84. Yang G, Pevear DC, Davies MH, *et al.* An orally bioavailable antipoxvirus compound (ST-246) inhibits extracellular virus formation and protects mice from lethal orthopoxvirus challenge. J Virol. 2005; 79:13139-13149.
85. Gong Q, Wang C, Chuai X, Chiu S. Monkeypox virus: A re-emergent threat to humans. Virol Sin. 2022; 37:477-482.

86. Russo AT, Grosenbach DW, Chinsangaram J, Honeychurch KM, Long PG, Lovejoy C, Maiti B, Meara I, Hruby DE. An overview of tecovirimat for smallpox treatment and expanded anti-orthopoxvirus applications. Expert Rev Anti Infect Ther. 2021; 19:331-344.
87. Sherwat A, Brooks JT, Birnkrant D, Kim P. Tecovirimat and the treatment of monkeypox - past, present, and future considerations. N Engl J Med. 2022; 387:579-581.
88. Kaul R, Risinger AL, Mooberry SL. Microtubule-targeting drugs: More than antimitotics. J Nat Prod. 2019; 82:680-685.
89. Heymann DL, Szczeniowski M, Esteves K. Re-emergence of monkeypox in Africa: A review of the past six years. Br Med Bull. 1998; 54:693-702.
90. Hammarlund E, Lewis MW, Carter SV, Amanna I, Hansen SG, Strelow LI, Wong SW, Yoshihara P, Hanifin JM, Slifka MK. Multiple diagnostic techniques identify previously vaccinated individuals with protective immunity against monkeypox. Nat Med. 2005; 11:1005-1011.
91. El Eid R, Allaw F, Haddad SF, Kanj SS. Human monkeypox: A review of the literature. PLoS Pathog. 2022; 18:e1010768.
92. Doellinger J, Schaade L, Nitsche A. Comparison of the cowpox virus and vaccinia virus mature virion proteome: analysis of the species- and strain-specific proteome. PLoS One. 2015; 10:e0141527.
93. Rao AK, Petersen BW, Whitehill F, Razeq JH, Isaacs SN, Merchlinsky MJ, Campos-Outcalt D, Morgan RL, Damon I, Sánchez PJ, Bell BP. Use of JYNNEOS (Smallpox and Monkeypox Vaccine, Live, Nonreplicating) for preexposure vaccination of persons at risk for occupational exposure to orthopoxviruses: Recommendations of the advisory committee on immunization practices - United States, 2022. MMWR Morb Mortal Wkly Rep. 2022; 71:734-742.
94. Petersen BW, Harms TJ, Reynolds MG, Harrison LH. Use of vaccinia virus smallpox vaccine in laboratory and health care personnel at risk for occupational exposure to orthopoxviruses – recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015. MMWR Morb Mortal Wkly Rep. 2016; 65:257-262.
95. Deputy NP, Deckert J, Chard AN, Sandberg N, Moulia DL, Barkley E, Dalton AF, Sweet C, Cohn AC, Little DR, Cohen AL, Sandmann D, Payne DC, Gerhart JL, Feldstein LR. Vaccine Effectiveness of JYNNEOS against mpox disease in the United States. N Engl J Med. 2023; 388:2434-2443.
96. Dalton AF, Diallo AO, Chard AN, *et al.* Estimated effectiveness of JYNNEOS vaccine in preventing mpox: A multijurisdictional case-control study - United States, August 19, 2022-March 31, 2023. MMWR Morb Mortal Wkly Rep. 2023; 72:553-558.
97. Petersen BW, Kabamba J, McCollum AM, Lushima RS, Wemakoy EO, Muyembe Tamfum JJ, Nguete B, Hughes CM, Monroe BP, Reynolds MG. Vaccinating against monkeypox in the Democratic Republic of the Congo. Antiviral Res. 2019; 162:171-177.
98. US Centers for Disease Control and Prevention (CDC). Smallpox vaccines. Updated on 23 October 2024. *http://www.cdc.gov/smallpox/vaccines/index.html* (accessed December 25, 2023).
99. Petersen E, Abubakar I, Ihekweazu C, *et al.* Monkeypox - enhancing public health preparedness for an emerging lethal human zoonotic epidemic threat in the wake of the smallpox post-eradication era. Int J Infect Dis. 2019; 78:78-84.
100. Sang Y, Zhang Z, Liu F, *et al.* Monkeypox virus quadrivalent mRNA vaccine induces immune response and protects against vaccinia virus. Signal Transduct Target Ther. 2023; 8:172.
101. Letafati A, Sakhavarz T. Monkeypox virus: A review. Microb Pathog. 2023; 176:106027.
102. Zhang XX, Jin YZ, Lu YH, Huang LL, Wu CX, Lv S, Chen Z, Xiang H, Zhou XN. Infectious disease control: from health security strengthening to health systems improvement at global level. Glob Health Res Policy. 2023; 8:38.
103. Acharya KP, Subramanya SH, Lopes BS. Combatting antimicrobial resistance in Nepal: The need for precision surveillance programmes and multi-sectoral partnership. JAC Antimicrob Resist. 2019; 1:dlz066.
104. Reynolds MG, Doty JB, McCollum AM, Olson VA, Nakazawa Y. Monkeypox re-emergence in Africa: A call to expand the concept and practice of One Health. Expert Rev Anti Infect Ther. 2019; 17:129-139.
105. World Bank. People, Pathogens and our planet: The economics of one health; World Bank: Washington, DC, USA. 2012; 2:1-65. *https://openknowledge.worldbank.org/handle/10986/11892* (accessed November 24, 2023).
106. Caceres P, Awada L, Barboza P, Lopez-Gatell H, Tizzani P. The World Organisation for Animal Health and the World Health Organization: Intergovernmental disease information and reporting systems and their role in early warning. Rev Sci Tech. 2017; 36:539-548.
107. Monroe BP, Doty JB, Moses C, Ibata S, Reynolds M, Carroll D. Collection and utilization of animal carcasses associated with zoonotic disease in Tshuapa district, the Democratic Republic of the Congo, 2015. J Wildl Dis. 2012; 51:734-738.
108. Doty JB, Malekani JM, Kalemba LN, *et al*. Assessing monkeypox virus prevalence in small mammals at the human-animal interface in the Democratic Republic of the Congo. Viruses. 2017; 9:283.
109. Golden MR, Wasserheit JN. Monkeypox - A sobering sentinel for pandemic preparedness and sexual health system capacity. N Engl J Med. 2022; 387:1826-1829.
110. Chen NFG, Chaguza C, Gagne L, *et al.* Development of an amplicon-based sequencing approach in response to the global emergence of human monkeypox virus. PLoS Biol. 2023; 21:e3002151.
111. Patel M, Adnan M, Aldarhami A, Bazaid AS, Saeedi NH, Alkayyal AA, Saleh FM, Awadh IB, Saeed A, Alshaghdali K. Current insights into diagnosis, prevention strategies, treatment, therapeutic targets, and challenges of monkeypox (mpox) infections in human populations. Life (Basel). 2023; 13:249.

Received September 19, 2024; Revised December 11, 2024; Accepted December 30, 2024.

Released online in J-STAGE as advance publication January 9, 2025.

**Address correspondence to*:
Kow-Tong Chen, Department of Occupational Medicine, Tainan Municipal Hospital (managed by Show Chwan Medical Care Corporation), No. 670, Chongde Road, East District, Tainan, Taiwan.
E-mail: ktchen@mail.ncku.edu.tw