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Monkeypox: Re-Emerging Infectious Disease and One Health Strategy

Cheryl Ann Alexander[1] and Lidong Wang[2]*

[1]*Institute for IT Innovation and Smart Health, USA*

[2]*Institute for Systems Engineering Research, Mississippi State University, USA*

***Corresponding author:** Lidong Wang, Institute for Systems Engineering Research, Mississippi State University, Mississippi, USA

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ABSTRACT

World Health Organization (WHO) has announced the monkeypox (MPX) epidemic as a global public health emergency due to its re-emergence, remarkable increase in the number of MPX cases worldwide, and its potential spread. This paper introduces the symptoms, complications, and features of MPX; its transmission, diagnosis and testing, vaccines, and treatment; MPX and sexually transmitted diseases, especially the human immunodeficiency virus (HIV); possible natural hosts or reservoirs of the monkeypox virus (MPXV). A useful tool for MPX and surgical safety recommendations are presented. The challenges in fighting the MPX epidemic, the One Health strategy, and future research are discussed.

Keywords: Monkeypox; One Health; Big Data Analytics; Deep Learning; Blockchain; Cybersecurity; Vaccine; Sexually Transmitted Diseases; HIV

Abbreviations: WHO: World Health Organization; MPX: Monkeypox; HIV: Human Immunodeficiency Virus; MPXV: Monkeypox Virus; EMS: Emergency Medical Services

Introduction

A global MPX outbreak began in 2022. In May 2022, at least 640 suspected or confirmed MPX cases in 36 countries on various continents were documented [1]. Since the end of June 2022, there has been a remarkable increase in the number of MPX cases globally. WHO has declared the MPX epidemic a worldwide public health emergency due to its re-emergence, re-emerging health threat, and potential spread [2]. By July 21, 2022, WHO declared 15,734 laboratories confirmed MPX infection cases in 75 countries on five continents. However, the number of cases is probably an underestimate of the real infection number because of insufficient clinical verification of MPXV infections and a long virus incubation period (5-21 days) [3]. The first outbreak of MPXV infections was documented in monkeys in Denmark in 1959 [4]. The name monkeypox was therefore derived from the historical fact that the viral disease was reported in research monkeys in a Danish laboratory [5]. MPXV was first recognized as a human pathogen in the Democratic Republic of the Congo in 1970. Two genetic clades of MPXV have been identified: Central African and Western African. The first clade has a larger fatality rate and more human-to-human transmissions compared with the second clade [6]. MPX crossed the boundaries from Africa, and 70 cases of MPX infection related to infected pet prairie dogs were documented in the US in 2003. Then cases of MPX infection were declared in Israel (2018), the United Kingdom (UK) (2018, 2019, 2021, and 2022), Singapore (2019), the USA again (2021), etc.

Between May 7 and 25, 2022, 86 cases of MPX infection were reported in the UK (79 cases being male and 66 cases being bisexual, gay, or other men who had sex with men) [7,8]. MPXV is an orthopoxviral, Chordopoxvirinae, and a close subgroup of variola viruses (smallpox) [9]. Smallpox is highly transmissible, and its mortality rate is approximately 30%. After a great vaccination campaign, it was announced eradicated in 1980; therefore, regular smallpox vaccination stopped [10]. MPX was endemic in Central and West African countries. It can be controlled and eliminated in a semi-endemic equilibrium through vaccination. But in a fully- endemic equilibrium, it cannot be stopped through only vaccination [11,12]. MPXV is an enveloped and double-stranded DNA virus of the genus Orthopoxvirus and family Poxviridae. It can infect and be found in non-human primates,

African squirrels, and rodents [13,14]. In the MPX cases of the USA, 99% happened in men with 94% of the men being infected due to male-to-male sexual or close intimate contact. Clinical signs differed from typical MPX (fewer people with prodrome and more people with genital rashes) [15]. MPXV leads to human monkeypox (human MPX), a neglected tropical zoonotic disease in humans that is like smallpox. There have been many human cases of MPX in five countries in Central and West Africa since 1970. Many cases happened in tropical rainforest areas and the clustering of cases was found in certain areas within countries and within families.

Human MPX was noticed after the smallpox vaccination campaign was ended therefore, immunologically unprotected people were at risk of MPXV infection [16,17]. Human MPX was endemic to central and eastern Africa. A human MPXV outbreak happened in the USA in 2003 due to an import of infected African rodents [18-20]. The efforts in the research of this comprehensive review paper were to introduce and discuss a few important issues regarding MPX. The subsequent sections of the paper are organized as follows: the second section introduces the symptoms, complications, and features of MPX; the third section presents the transmission of MPX; the fourth section introduces the diagnosis and testing of MPX; the fifth section presents the vaccines and treatment of MPX; the sixth section deals with MPX and sexually transmitted diseases; the seventh section discusses possible natural hosts or reservoirs of MPXV; the eighth section introduces a useful tool for MPX and surgical safety recommendations; the ninth section discusses the challenges and One Health strategy; and the tenth section is the conclusion and future research.

Symptoms, Complications, and Features of Monkeypox

MPXV is closely associated with the infamous variola (smallpox) virus, leading to a febrile rash illness in humans that is like smallpox but milder than it [21]. MPXV brings about lymphadenopathy. The beginning of infection with MPXV is headache, backache, muscle aches, chills, fever, and fatigue [22]. After the beginning of the fever, the infected individual has a rash on the face, then diffusion to other parts of the body. Lesions begin within the oropharynx, and then spread throughout the body [23]. Common (nonspecific) symptoms and complications of MPX are shown in Table 1 [24]. A feature rash grows into papules, vesicles, and pustules that ultimately scab over and are healed [25]. Core clinical features of human MPX are rash, fatigue, fever, lesions, respiratory symptoms, and lymphadenopathy [26]. Human MPX can be severe for pregnant women, children, and immune-compromised people. The fatality rate of these people is approximately 3–6% [27]. For pregnant women, MPXV could be transmitted through the placenta and cause fetal death [25]. Atypical manifestations that may be related to the body site of viral entry urge a low threshold for the clinical suspicion of MPX, especially in situations with a large transmission rate or in individuals who are at a high-level risk of contagion [28]. A long-term complication of MPX is vision loss due to the infection of the eye cornea and tissue scarring [29]. Dental care workers ought to be aware that premonitory manifestations of MPX are generally on the oral mucosa as macules and ulcers before typical skin lesions [30].

Table 1: Common symptoms and complications of MPX.

Common Symptoms	Complications
• Headache • Backache • Chills • Fever • Rashes • Exhaustion • Myalgia • Mouth & throat ulcers • Lymphadenopathy	• Respiratory distress • Dehydration • Bacterial superinfection • Cellulitis • Encephalitis • Sepsis & septic shock • Bronchopneumonia • Corneal infection/permanent scarring

The mortality rate of MPX varies with the patient's age, the virus clade, and the outbreak place. The mortality of MPX is generally higher for young adults, children, and immunocompromised individuals. It is like smallpox that MPX is generally more fatal for children than adults [9,25]. In humans, the MPXV infection starts with an incubation period, then a prodrome of fever, disseminated skin lesions (growing from macules to papules, vesicles, and pustules), and scabbing [31]. An MPX outbreak in the USA demonstrated that the incubation interval is various. The incubation period depends on the nature and route of exposure (such as wild animals, infected pets, or infected people). The household attack rate was defined as the rate of persons living with an infected individual and developing the MPX symptoms. An analysis was conducted on the infection dynamics of MPXV, and it showed a 50% household attack rate (on average) which is much higher than the published result [32]. Table 2 summarizes the features of MPX [25,30,33-38].

Table 2: Features of MPX [25,30,33-38].

Aspects of Features	Description
Contagiousness	High
Fatality	From 1 to 10% based on the clade of the infecting MPXV strain and the healthcare availability; 3% to 6% due to a severe disease caused by some strains (WHO reported), less than smallpox (up to 30%).
Spread	Respiratory droplets, close contact, and contact with skin lesions or newly contaminated items.
Incubation period	5-21 days (on average 7-14 days).
Agent	Monkeypox virus
Sickness	Mild sickness with swollen lymph nodes (lymphadenopathy); chills, fever, exhaustion, headache, backache, and muscle aches are initial symptoms.
Oral lesions	The oral mucosa among 70% of cases are affected as macules and vesicles; lips can be affected too
Rash	Begins on the face usually, then reaches to other parts of the body; forms a scab eventually that falls off.
Beginning of a fever	1 to 5 days (before rash)
Period of symptoms	2-4 weeks
Isolation	21 days, avoiding contact with immunosuppressed individuals, pregnant individuals, and children under 12 years old.
Diagnosis	Electron microscopy, virus isolation, and the PCR (polymerase chain reaction) test are the gold standard methods to confirm the MPXV infection, but most of cases in remote settings can be clinically diagnosed.
Recommendation of vaccines for health care workers (HCWs)	Desirable for HCWs in monkeypox-endemic areas or during an outbreak
Prevention	Traditional smallpox vaccines are useful for monkeypox; a vaccine approved for preventing monkeypox is available based on the strain of the vaccinia virus.

Transmission of monkeypox

Modes of transmission of MPXV include fomites, respiratory, direct contact with infected animals or humans, and eating infected meats [26]. There are two types of MPXV transmission: animal–human transmission (also called zoonotic transmission) and human–human transmission [39,40]. MPX transmits somewhat inefficiently from person to person. MPXV can be transmitted from pregnant ladies to fetuses by the placenta, or from infected parents to their children by skin contact after or during the birth of children [41]. Both smallpox and MPX are thought to be transmitted among humans mainly through respiratory secretions [42]. Clinical samples were collected by real-time PCR; MPX DNA was found in saliva and skin lesions in all cases; and there were great viral loads in some of the cases, especially in the skin pustules. Most samples in the following sample types are positive: nasopharyngeal swab, rectal swab, urine, semen, and feces. This is valuable information regarding virus shedding and the possible role of body fluids in MPX transmissions [43]. Table 3 [24] shows the suspected transmission modes of MPX to humans. The reproductive number (denoted as R_0) of MPXV for the Central African clade has been assessed and it ranges from 0.6-1.0. The R_0 for the West African clade of MPXV has not been assessed; however, it is thought to be less than that of the Central African clade [44,45].

Table 3: Suspected transmission modes of MPX to humans.

Suspected Transmission Modes	Transmission Approaches
Animal-to-human Transmission	• Hunting, cooking, and consuming infected animals • Blood or body fluids • Scratches/bites from infected animals • Contact with cutaneous/mucosal lesions
Human-to-human Transmission	• Respiratory droplets • Close contact • Direct contact with cutaneous lesions • Recently contaminated surfaces or objects

Diagnosis and Testing

Whole genome sequencing is a gold standard used to distinguish MPXV from other orthopoxviral, but it is limited in some areas because it is very costly. Loop-mediated isothermal amplification technology, restriction length fragment polymorphism, and recombinase polymerase amplification have been developed for MPXV DNA detec-

tion [46]. Diagnosis is primarily clinical; however, laboratory testing is required for a conclusive diagnosis [47]. PCR is a preferred laboratory testing method in clinical diagnosis owing to its high sensitivity and accuracy. The serology and antigen detection approaches are not suggested due to their cross-reactivity. The ideal samples for MPX testing are skin lesions, dry crusts, and fluid from vesicles and pustules [48]. Table 4 [49] shows diagnostic tests for MPXV or orthopoxviral (OPXV). Real-time PCR (RT-PCR) is the desired testing method for detecting MPXV during acute infections [50]. Diagnostic methods of identifying human MPX and their pros/cons are shown in Table 5 [51]. They work better if they are integrated with medical and epidemiological information such as patient immunization history.

Table 4: Diagnosis and tests for MPXV or OPXV.

Tests	Description
PCR (including RT-PCR)	Test for the specific DNA signatures of MPXV
Electron microscopy	Imaging of a brick-shaped particle for the poxvirus classification
Immunohistochemistry	Test for the specific antigens of OPXV
Viral culture/isolation	Live virus grows and is featured from a patient specimen
Anti-OPXV IgG	Test for the antibodies of OPXV
Anti-OPXV IgM	Test for the antibodies of OPXV
Tetracore OrthopoxBio-Threat	Alert testing for the antigens of OPXV

Table 5: Diagnostic methods of identifying human MPX.

	Based on	Pros	Cons
Phenotypic methods	Clinical diagnose	Possible diagnosing according to clinical signs is necessary to uncover suspected cases during examination	Research on 645 individuals with clinical diagnosis of MPX (not accompanied by a lab verification) indicates a high sensitivity (93–98%) and low specificity (9%–26%).
Genetic methods	PCR or qPCR	• PCR is a standard method of finding MPX-specific DNA sequences owing to its high sensitivity and accuracy. • Suggested testing samples are from cutaneous lesions or a biopsy when possible.	• High-cost tools, reagents, and skilled techniques are needed. • Highly sensitive examinations due to a concern about sample contamination.
Electron microscopy	Electron microscopy	• Provides testimony that MPX is of the Poxviridae family. • Differentiate orthopoxvirus from herpes simplex virus.	Orthopoxviruses cannot be distinguished from each other, requiring additional diagnosis.
Immunological methods	• Delicate discovery of IgG or IgM antibodies fighting MPX through the Elisa test. • Immunohistochemical (IHC) to detect virus antigens	• Increase of anti-viral antibodies and T-cell activation fighting MPX are reported with the illness beginning. • At the time of the development of a rash, IgG and IgM are detectable in serum around 5 days and more than 8 days in a row. • An indirect diagnosis can be found if both IgG and IgM exist in unvaccinated people who have a rash history and symptoms of severe disease.	The above approaches are not regard as qualitative ones for human MPX.

Vaccines and Treatment

There is no specific vaccine for MPXV. Vaccines for the prevention of MPX in high-risk groups or post-exposure prophylaxis are still smallpox-specific vaccines. The use of smallpox vaccine for MPX prevention is still mainly restricted to high-risk groups or health personnel who treat MPX, but mass vaccination against MPX has not been required or recommended [2]. Many patients infected with MPX have mild symptoms and can recover without any medical treatment [52]. The vaccination of humans with LC16m8 has long-term protection against MPX. LC16m8 is a highly attenuated smallpox vaccine that was developed in Japan. Although smallpox has been eradicated, it is possible for it to re-emerge in the future. Therefore, the smallpox vaccine such as LC16m8 is still necessary not only for the protection of people in the human MPX-endemic regions from human MPX but also for stockpiling in preparation for a possible future outbreak of smallpox [18]. In the USA and Canada, the modified vaccinia Ankara vaccine (MVA-BN; Bavarian Nordic, Denmark) has been licensed for adults infected with smallpox or MPX [3]. IMVAMUNE is the third-generation smallpox vaccine. It has been used in people infected with HIV as well as individuals with atopic dermatitis. It has been purchased for the U.S. Strategic National Stockpile (SNS) for use under an Emergency Use Authorization. Table 6 shows its features [53]. Third-generation

vaccines are now feasible in preventing MPX. There is no licensed antiviral drug for MPX, but it has been proven that antiviral drugs used for smallpox are also useful for patients infected with MPX. As of January 2022, Tecovirimat (also known as TPOXX) has been authorized to treat MPX [47,48].

Table 6: Features of IMVAMUNE.

Characteristics	Potential adverse events
• Developed for people with increased risk factors for adverse events. • No lesion is produced at the site of vaccination; a risk of autoinoculation, inadvertent transmission, or systemic spread is no longer presented. • Derived from Modified Vaccinia Ankara which is a vaccinia virus with a loss of the ability to replicate in mammalian cells.	• Local symptoms and signs, for example, pain, swelling, induration, erythema, and pruritus at the administration site. • Systemic symptoms and signs have been documented, for example, nausea, fatigue, headache, chills, pyrexia, and myalgia.

Monkeypox and Sexually Transmitted Diseases

MPX lesions are susceptible to bacterial superinfection. In the recent MPX outbreak, most cases were recognized in men who had sex with men (MSM), leading to a vesicular–pustular rash or genital lesions. The rash usually appears on the perineal area and genitals, indicating that the transmission due to sexual intercourse can easily be confused with other sexually transmitted diseases [54]. Examinations revealed proctitis, as well as anal and rectal ulcers with the detection of MPXV, indicating that sexual transmission plays a role in the MPX outbreak [55]. Sexual contact has been regarded as a probable route of human spread, particularly male-to-male contact [41]. Notable MPX incidents were recognized among gays, bisexuals, and MSM [56]. Sexual activities, mostly among gays or bisexual men, were the most often suspected route of human MPX transmission. Documents of clusters related to sex parties or saunas highlight the prospective role of sexual contacts as a transmission supporter. International travels and participation in big gatherings linked to sex-onsite activities might justify the worldwide spread of MPX through the sexual network [57]. MPX spread among MSM has been a major concern; however, heterosexual intercourse could not be ignored [44]. The overlapping of MPX with other endemic transmissible diseases in the globe such as HIV infection, measles, malaria, ortho-hantavirus, arboviral diseases, etc. has led to a worse complex scenario, especially for unvaccinated children [27]. Immunodeficiency may lead to worse clinical outcomes of an MPX infection.

Table 7: Management of people with MPX and HIV infection.

Patient groups & treatments	Precautions/ recommendations	Availability/effectiveness in the treatment of MPX
MPX management for people with HIV		
Cidofovir (Vistide)	Contraindicated if serum creatinine >1.5 mg/dL.	Available from SNS Effectiveness in the treatment of MPX unknown
Tecovirimat (TPOXX, ST-246)	Review potential interactions with antiretroviral therapy (ART).	Available from SNS Oral and intravenous formulations available
Vaccinia immune globulin intravenous	May be thought in severe cases.	Available from SNS Effectiveness in the treatment of MPX unknown
Brincidofovir (CMX001, Tembexa)	May increase serum transaminases and bilirubin.	Not available from SNS Effectiveness in the treatment of MPX unknown

HIV management for people with MPX		
Newly diagnosed HIV	Begin ART as soon as possible.	Not applicable
Known HIV infection	Keep on ART and opportunistic infection prophylaxis, as designated.	Not applicable
HIV postexposure prophylaxis	Keep on treatment or begin as designated.	Not applicable
HIV pre-exposure prophylaxis	Keep on treatment or start as designated.	Not applicable
MPX postexposure prophylaxis		
JYNNEOS vaccine	Safety and immunogenicity similar in people with or without the HIV infection.	Available data are limited, may prevent infection if administered ≤ 4 days after exposure; may reduce disease severity if administration ≥5 days after exposure and infection happens.
MPX pre-exposure prophylaxis		
JYNNEOS vaccine	Safety and immunogenicity similar in people with or without the HIV infection.	Licensed for preventing orthopoxvirus infections, such as MPX

An advanced or poorly virally controlled HIV infection may lead to more severe outcomes after MPX infection [2]. HIV-1 infected persons have elongated MPX sickness, bigger lesions, and greater rates of secondary bacterial skin infections as well as genital ulcers [58]. HIV-positive people can be infected with MPX independent of CD4+ count; the clinical sign is usually a large skin lesion in the genital area. Syphilis coinfection is conceivable. If a patient's CD4+ count is exceptionally low, death may happen [59]. Recommendations (United States, August 2022) for the management of people with monkeypox and HIV infection are shown in Table 7 [60].

Possible Natural Hosts and Reservoirs of MPXV

There is no definitive natural host or reservoir for MPXV, but rodents and non-human primates are considered potential natural hosts and reservoirs of MPXV [39,61]. A few rodent species such as African pouched rats (Cervicectomies spp.) have been regarded as potential reservoirs [62]. The rope squirrel and the Gambian pouched rat are the most possible natural hosts of MPXV. In addition, the sooty mangabey monkey has been regarded as a suspected host of MPXV [26]. Acute MPXV infection and positive serology have been found in several animal species including non-human primates as well as small mammals. Despite the growing evidence of acute or prior infection, MPXV has been isolated from wild animals in only two situations, one from a rope squirrel and the other from a sooty mangabey [63]. Some aspects of the MPXV transmission cycle, such as the natural host of MPXV, are still unidentified. MPXV caused noteworthy pathology in African rope squirrels and infected rope squirrels shed substantial quantities of the virus, indicating their effect on the MPXV epidemiology in Central Africa as a prospective source of the MPXV transmission to humans and animals in endemic MPX zones [64].

A Useful Tool for Monkeypox and Surgical Safety Recommendations

Table 8 shows a prehospital adaptation of the MPX Identify-Isolate-Inform (3I) Tool with specific considerations for Emergency Medical Services (EMS) professionals [65,66]. Significant suggestions from admission to the emergency room, during surgery, hospitalization, and hospital discharge are listed in Table 9 [67].

Table 8: A 3I tool of MPX 2022 for EMS professionals.

3I	Description
Identify	• Signs and symptom such as chill, fever, backache, etc. • Exposure ➢ Contact individual(s) with suspected or confirmed MPX. ➢ Contact individual(s) with rash consistent MPX. ➢ Attended a large party that included sex with multiple partners. ➢ Multiple or anonymous sexual partners. ➢ Contact animals with suspected MPX. ➢ Travel within 21 days to a region with endemic MPX.
Isolate	• Don personal protective equipment (PPE): N95 respirator/equivalent (or higher), gown, gloves, eye protection, and shoe covers (if available). • Cover patient lesions and rashes. • Put a surgical mask on the patient. • Avoid aerosol-generating procedures. • Carefully discard stretcher covers. • Disinfect contaminated surfaces.
Inform	• Agency's infection-control officer. • Receiving facility's healthcare staff. • Local health department (if the patient was not transport).

Table 9: MPX surgical safety recommendations.

Outpatient care or in emergency services/preoperative	Operating theaters	After surgery and hospitalization
• Appropriate use of personal protection elements • Diagnosis in time for suspicious patients • Completed medical history, looking for the signs of skin lesions or flu • If a person is a confirmed infection case, it ought to be assessed with the surgeon to take into account the relevance of the procedure • Exclusive office for the care of people confirmed with Monkeypox. • The procedure needs to be monitored in person or virtually in case a patient's situation is not an emergency.	• Only necessary personnel • Minimally invasive procedures • Decrease in surgical times • Sufficient disinfection for the surgical environment before & after the procedure • Sufficient use of personal protection elements	• The entry of visitors will be considered according to institutional & national health regulations • Appropriate use of personal protection elements • Reduction in the hospital stay • Hospitalization in single-person rooms or sufficient patients' classification with/without a diagnosis of MPX • Recommendation and direction for departure

Challenges and One Health Strategy

MPX can be re-emerging from time to time. The core reason for the current outbreaks should be further studied. The key issue should be disclosing the zoonotic reservoir, zoonosis, spillover of the virus from the host, etc. [68]. One of the major challenges lies in that the main source of infection has not been confirmed, and the main source is a major determinant in breaking the disease transmission chain in a population [4]. Human MPX is the most noteworthy orthopoxviral infection disease since the smallpox extermination [69]. There are challenges in handling human MPX with potential human-to-human transmission through sexual contact. Contact tracing is difficult because some patients had sex with multiple anonymous partners. Attention among healthcare providers in nonendemic countries must be paid [70]. In addition, the vaccine acceptance of MPX remains a challenge, which is like during the COVID-19 pandemic. Humans, animals, and the environment are interconnected closely. One Health strategy is needed in fighting epidemics or pandemics of infectious diseases

(such as MPX, COVID-19, and Ebola). One Health is a cross-sectoral, collaborative, and multidisciplinary approach that works at the local, regional, national, and global levels [71]. It is a system engineering method. It facilitates data and knowledge sharing and unified decision-making [71], promotes resolving complicated health threats, reduces duplications among sectors [72], and improves medical supply chain management and operations. One Health strategy should be fulfilled based on cutting-edge technologies, including Big Data analytics, blockchain, artificial intelligence (e.g., machine learning, especially deep learning), etc.

During epidemics, Big Data analytics helps fix problems such as data heterogeneity, incomplete data, and geographical data merging and sharing; deep learning is powerful in the prediction of trends and infection cases of diseases. Patient information sharing can bring up privacy problems. Blockchain helps protect privacy, improve the management of electronic medical records (EMR), facilitate pharmaceutical supply chain management, and finally enhance the cybersecurity of One Health programs. During the spread of MPX and COVID-19, One Health's strategy and programs were not developed well due to complicated reasons such as politics. Some politicians in some countries were very active in distorting facts based on their political opinions during speeches via social media, which led to high infection cases, hospitalizations, and deaths because science-based decision-making was weak. This situation brought negative effects on global cooperation and One Health.

Conclusion and Future Research

MPX is a zoonotic disease milder than smallpox and has a mortality rate higher in young adults, children, and immunocompromised patients compared with other people. RT-PCR is the preferred test of MPXV during acute infection. Smallpox-specific vaccines are still used for the prevention of MPX in high-risk groups or post-exposure prophylaxis. Sexual contact, especially MSM, is a potential route of human spread; heterosexual intercourse should not be ignored. HIV infection can lead to more severe outcomes after MPX infection. The natural host or reservoir for MPXV has not been confirmed, but rodents and non-human primates are potential natural hosts or reservoirs. There are challenges in vaccine acceptance and handling human MPX with potential human-to-human transmission through sexual contacts due to difficult contact tracing. One Health strategy is required in fighting MPX, COVID-19, Ebola, etc. Big Data analytics, deep learning, blockchain, etc. help fulfill One Health strategy and enhance the cybersecurity of One Health programs. All the challenges listed in this paper can be future research topics. We will focus on the predictive modelling of MPX using Big Data analytics, deep learning, and blockchain-based cybersecurity for One Health.

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Conflicts of Interest Statement

The authors declare no conflict of interest.

Author Contributions

Cheryl Ann Alexander: Conceptualization, writing. Lidong Wang: resources, writing - tables.

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